Cellulose Nanocrystals: A Versatile Nanoplatform

Lekha Dhurjad*1, Dhanshri Sagle 2, Amol Deshmukh 3, Minal Narkhede 4
SMBT College of Pharmacy, Nandi-Hills, Dhamangaon, Nashik, Maharashtra, India

A B S T R A C T

The developing natural and ecological awareness has driven endeavors for advancement of new inventive products for different end-use applications. Nanotechnology executes a significant contribution in the improvement of such product. Cellulose nanocrystals are one of a kind nanomaterial obtained from the most copious and practically boundless natural polymer, cellulose. These nanomaterials have obtained remarkable interest due to their mechanical, optical, chemical, and rheological properties. Cellulose nanocrystals basically derived from naturally existing cellulose fibres, are biodegradable and inexhaustible in nature and consequently they fill in as an eco-friendly material for most applications. Considering the ever-expanding interdisciplinary research being done on cellulose nanocrystals, this review means to collate the information accessible about the preparation technique, modification and application of cellulose nanocrystals. Cellulose nanocrystals can be sourced from biomass, plants, or microbes, depending on genuinely basic, versatile, and productive isolation methodology. Mechanical, synthetic, and enzymatic treatments, or a blend of these, can be utilized to separate nanocellulose from natural sources. Nanocellulose cellulose surface modification strategies are commonly used to introduce either charged or hydrophobic moieties, and comprises amidation, esterification, etherification, silylation, polymerization, urethanization, and phosphorylation. This nanomaterial is a promising contender for applications in fields, for example, biomedical, pharmaceuticals, electronics, barrier films and so forth.

Keywords: Cellulose nanocrystal, Cellulose, Nanotechnology

INTRODUCTION

Cellulose represents the most prevalent amphiphilic inexhaustible polymer asset in the biosphere. Cellulose is one of the fundamental auxiliary units of green growth, tunicates, and certain microscopic organisms. 1,12 The worldwide yearly yield of cellulose is around 75 to 100 billion tons. 13 Cellulose is inexhaustible, biodegradable, and nontoxic, and is the most eminent nanostructured segment existing in (i) agrarian residues (sugarcane bagasse, straw, corn stover, coconut husks, corncobs, wheat and rice husks, palm oil builds, maize straw, and organic product skins); (ii) tree trunks and dead woodland matter (hardwood and softwood); (iii) energy crops; (iv) food waste; (v) city and modern biowaste, for example, utilized paper, container, and wood from destruction locales. 1,7, 8,12 Apart from plants, cellulose is additionally present in a wide assortment of living species, for example, algae, fungi, bacteria, and even in some sea animals, for example, tunicates. 4

Cellulose is being utilized for considerably more complex applications in present day times dependent on the way that when cellulose strands are exposed to mechanical shear or controlled acid hydrolysis, stretched fibrillar rod like crystalline particles are delivered, including nanosized width and lengths ranging from 50 nm to micrometres. Cellulose fibrils are basic elements framed through a cellular fabricating process, cellulose biogenesis, stabilized out by hydrogen bonds and van der Waals forces. The fibrils contain crystalline and amorphous areas, which deteriorate to liberate nanoscale parts from the cellulose source by mechanical, substance, or a blend of mechanical, chemical, and enzymatic procedures. 1

Nanocellulose is a product secluded from the cellulose which is available in the plants, creatures and microscopic organisms. Nanocellulose is classified as follows:

1. Cellulose nanocrystals (CNC) – nanocrystalline cellulose, nanowhiskers and nanorod
2. Cellulose nanofibrils - nanofibrillated cellulose, microfibrillated cellulose (MFC), and cellulose nanofibers

3. Bacterial cellulose [BNC] 8

Nanocellulose holds a large number of the alluring properties for which cellulose is known, including low density, nontoxicity, and high biodegradability. However, it additionally holds exceptional properties, for example, high mechanical quality, reinforcing capacities, and tunable self-assembly in aqueous media, emerging from its interesting shape, size, surface chemistry, and high level of crystallinity. 1,3 Chemical, biochemical, and mechanical strategies give approaches to modify nanocellulose, yielding improved properties, for example, fire retardancy, transparency, and high flexibility, in this way significantly growing customary utilisations of wood. 1

CNCs, show prolonged crystalline rod like shapes, and have high rigidity nature contrasted with NFC on the grounds that a higher extent of the amorphous areas is expelled. CNCs range in width from 5 to 35 nm and have a length of few hundred nanometres. Level of crystallinity in CNCs ranges from 54 to 88%. 1,11,12 It was accounted for that NCC which is delivered from tunicate and bacterial cellulose is typically bigger in size contrasting and the ones created from wood and cotton. 2 Nickerson and Hablre reviewed first successful production of CNC in 1947 through hydrolysing cellulose with hydrochloric acid and sulfuric acid 5,13

Strong acid hydrolysis, especially sulfuric acid hydrolysis, is the most well-known procedure for isolation of CNC. A prototype for the manufacturing of CNC starts with alkali and bleaching pre-treatment followed by acid hydrolysis, washing, centrifugation, dialysis, and ultrasonication to form a suspension which might be additionally exposed to lyophilization (freeze-drying or spray drying) as required. 4 The reaction conditions, origin of cellulose, extraction condition sway a few of the acquired properties of CNCs, for example, the level of crystallinity, the aspect ratio, dimensional dispersity, and the morphology. 1,2,5,12

CNCs join high axial stiffness (105–168 GPa), high Young’s modulus (20–50 GPa), high tensile quality (~9 GPa), low coefficient of thermal expansion (~0.1 ppm/K), high thermal stability (~260°C), high aspect ratio (~10–70), low density (1.5–1.6 g/cm3), lyotropic liquid crystalline conduct, and shear thinning rheology. 1

Under appropriate conditions and at critical concentration, all asymmetric rod like or plate-like particles suddenly form ordered structures, prompting the development of a nematic stage. Rod like CNCs, when scattered in water, self-orient to form chiral nematic stages with fluid crystalline properties. Their stiffness, aspect ratio and the capability to align under specific conditions make them perfect for showing fluid crystalline conduct. Nonetheless, cellulose crystallites are known to have a helical bend down the long pivot, like a screw which can either prompt a chiral nematic or a cholesteric phase of stacked planes adjusted along perpendicular axis relying upon the concentration. CNC prepared by sulfuric acid hydrolysis ordinarily possesses a negatively charged surface, which aid uniform dispersion in water because of electrostatic repulsions. Even however the interaction between nanocrystals are strong, exceptionally sulfonated CNC is promptly dispersible and this elicits the improvement of lyotropic behaviour. Sulfuric acid and phosphoric acid-derived CNCs regularly give chiral nematic structure, while hydrochloric acid derived CNCs with postreaction sulfonation offer ascent to a birefringent glassy stage. Rheological parameters of CNC are affected by various properties, for example, liquid crystallinity, ordering, and gelation properties. Dilute CNC suspensions show shear diminishing conduct, which shows concentration dependence at low rates. At higher concentration, in which the suspensions are lyotropic, they show bizarre behavior. The fundamental purpose behind such conduct is that the rod-shaped nanocrystals will in general adjust at a critical shear rate. As the shear rate arrives at a critical point, the chirality of the CNC suspension separates for a straightforward nematic structure. The sort of acid utilized for hydrolysis can likewise impact the rheological properties of CNC suspensions. Sulfuric acid treated crystal give some shear diminishing that is independent of time, while HCl-derived crystals show a lot higher shear thinning conduct, anti-thixotropy at lower concentrations and thixotropy at higher concentrations. 4 Surface modification methods are found to change the self-congregation behaviour of CNCs in suspensions and control the interfacial properties inside composites. CNCs offer composite materials with upgraded mechanical properties, low density and high surface zone. 1

These nanocrystals grant alluring blends of biophysiochemical qualities, for example, biocompatibility, biodegradability, light weight, nontoxicity, stiffness, inexhaustibility, viability, optical transparency, low thermal expansion, gas impermeability, versatile surface chemistry, and improved mechanical properties. 11,12 CNCs have been generally utilized as feasible inexpensive ecologically favourable materials in diverse fields including composites, separation membranes, barrier films, specific enzyme immobilization, super capacitors, antimicrobial films, clinical inserts, green catalyst, emulsion stabilizers, biosensors, drug delivery, batteries, and templates for electronic devices. 12

**Advantages**

- Administered by all routes in any dosage form.
- Increased rate of absorption, bioavailability.
- Rapid, simple and cost-effective formulation development.
- Reduction in required dose and fed/fasted variability.
- Increased reliability.
- Improved biological performance of drugs.
- High stability and adhesiveness.
- Rapid effect.

**Disadvantage**

- Production of drug nanocrystal requires high cost instrument, that increase the cost of dosage form.
- The development of nanocrystals and their stability is relied upon the atomic structure of the drug, so just certain classes of compound will qualify. 3

**STRATEGY OF PREPARATION**

The way wherein nanocellulose is secluded from plant matter largely affects the morphology and properties of the acquired material. The primary separation strategies are mechanical treatment, chemo-mechanical treatment (kraft pulping), and enzymatic treatment. 1
Mechanical treatment

Cellulosic filaments deteriorate into their sub basic fibrils, having a length on the micrometres scale and a width extending from 10 nm to a couple hundred nanometres, contingent upon the sort of cell walls common to the plant source. High pressure homogenization, cryocrushing, high speed blending, micro fluidization, grinding, high intensity ultrasonication, hammer milling, and electrospinning are different mechanical approaches revealed in the writings. These various approaches have been utilized freely and in blend to acquire cellulosic nanomaterials. Energy utilization and production costs are high when mechanical treatment alone is utilized to delaminate the strands. A lot of energy is required to free nanosized cellulose from the normal filaments, because of the exceptionally organized hydrogen bond system of cellulose. The product, obtained from the mechanical treatment, presents generally comparable structure to that of the original feeding. Various mechanical procedures have been as often as possible utilized for the extraction cellulose fibrils from a wide scope of cellulose sources. The absolute most mechanical strategies incorporate comminution, high pressure homogenization, micro fluidization, cryocrushing, high intensity ultrasonication. 

Chemical pre-treatment (kraft pulping)

The kraft extraction is done to solubilize the majority of the lignin and hemicelluloses and the bleaching preparation made to disintegrate phenolic mixes/particles with chromophoric gatherings (in lignin) and to remove the by-product of such breakdown, to brighten the material. A pre-treatment can diminish the energy devoted by mechanical procedure from between 20 000 and 30 000 kWh/ton to 1000 kWh/ton. Alkaline treatment focuses on the elimination of the lignin content and the deterioration of hemicelluloses; however, hemicellulose is rarely totally expelled. Response conditions ought to be controlled, to forestall cellulose deterioration. Alkali treatment ordinarily utilizes 5 wt. % NaOH at 90 °C for right around 1 h. The acquired pulp is then washed with deionized water until neutralized. The cycle might be reheated a few times relying upon the lignin substance of the source material. The hemicellulosic content that triumphs are generally expelled by means of hydrolysis. In acid hydrolysis, the hydronium particles pierce the amorphous region of cellulose chains and hydrolytically cleave glycosidic bonds, to discharge individual crystalline cellulose nanoparticles upon homogenization/ultrasonication. Sulfuric acid is the most widely recognized reagent reported for acid hydrolysis to date, and is utilized highly concentrated (~64%). Most mineral acids, including hydrochloric acid, phosphoric acid, hydrobromic acid, and nitric acid, have the potential for yielding crystalline cellulose nanoparticles, in spite of the fact that with lesser properties regarding CNC suspendibility, since they bring about less or no charge joining to the surface.

Truth be told, the sulfuric acid treated suspension has demonstrated no time-subordinate viscosity, though the hydrochloric acid treated suspension indicated a thixotropic conduct at concentration above 0.5% (w/v) and antithixotropic conduct at concentration underneath 0.3%. With regard to the morphology of the particles, a blend of both sulfuric and hydrochloric acids during hydrolysis steps seems to create spherical CNCs rather than rod like nanocrystals when completed under ultrasonic treatment. These circular CNCs exhibited better thermal stability owing to the fact that they have less sulphate groups on their surfaces. On the off chance that the CNCs are set up by hydrolysis in hydrochloric acid, their capacity to disperse is restricted and their aqueous suspensions will in general flocculate. Then again, when sulfuric acid is utilized as a hydrolyzing agent, it reacts with the surface hydroxyl group of cellulose to yield charged surface sulphate esters that advance dispersion of the CNCs in water. 

Various scientists had examined the impact of preparing conditions, for example, temperature and time of hydrolysis system, nature and concentration of acid just as the fibre-to-acid proportion on the physicochemical, warm and mechanical properties. Augmentation in the hydrolysis time has been accounted for to lessen the length of the nanocrystals just as increment the acid/fibre proportion and decrease the nanocrystal size. The actual phenomenon of the acid cleavage event is associated with variance in the kinetics of hydrolysis among amorphous and crystalline areas. In most cases, acid hydrolysis of indigenous cellulose instigates a quick decline in its level of polymerization (DP), to the alleged level-off DP (LODP). The DP hence decrease substantially more gradually, in any event, during prolonged hydrolysis times. The estimation of LODP differs relying upon the cellulose source, where cotton-derived cellulose has a LODP of 250, 300 for ramie filaments, 140–200 for bleached wood pulp fibres, and up to 6,000 for cellulose got from Valonia. 32 CNCs acquired by the acid hydrolysis of cellulose from microbes, tunicates, or Valonia show a high polydispersity in the sub-atomic weight, with no proof of the LODP, presumably because of the nonappearance of the regular arrangement of amorphous areas. Prolonged hydrolysis can prompt further decrease in the molecular weight, and subsequently, to get CNCs, acid hydrolysis must be halted in the wake of accomplishing LODP. The purpose behind the underlying decrease of DP is proposed to be because of rapid hydrolysis of amorphous regions owing to the fact that a bordered micelle-like structure of microfibrils where amorphous and crystalline regions are found. The present constraint with acid hydrolysis comprises the harsh nature of the acids and the creation of a lot of chemical waste, despite the fact that recycling techniques have been contrived at the industrial scale.

In any case, one drawback of this technique is that sulphate groups catalyse and start the degradation of cellulose, especially at high temperatures. Henceforth the CNCs have been found to have constrained thermal stability, which surely limits the preparation of CNCs based composites at high temperature. A few different methodologies have been proposed to address thermal stability issue. For example, the utilization of blends of hydrochloric acid and sulfuric acid created CNCs with high thermal stability, unfortunately at the expense of lower dispersibility. As of late, profoundly thermally stable CNCs have been prepared through mild acid hydrolysis (phosphoric acid) and hydrothermal treatment (hydrochloric acid). Nevertheless, these techniques are seriously limited by low yields and poor versatility on account of the high utilization of solvents and time,
Enzymatic hydrolysis

Enzymatic treatment permits milder hydrolysis conditions than acid hydrolysis. Enzymatic hydrolysis is viewed as naturally benevolent. For instance, of enzymatic hydrolysis, xylanases are hydrolytic enzyme that change the hemicelluloses present in plant fibre. They can likewise start arbitrary hydrolysis of the β-1,4 nonreducing terminal areas situated between the glycosidic linkages of the glucose units. Enzymes modify or degrade the lignin and hemicellulose, limiting the level of hydrolysis or specifically hydrolyzing particularized constituent in the cellulosic filaments. The surface charge of nanocellulose is likewise influenced by the nature of the treatment. Enzymatic treatment, utilizing xylanase so as to eliminate lignin and hemicellulose, provides nanocellulose strands with a higher zeta potential contrasted with an exemplary sulfuric acid treatment. These hence formed increasingly more stable suspensions.1,8,12

Cellulases (blends of endoglucanases, exoglucanases, and cellobiohydrolases) are one such fascinating class of enzymes having capacity to go about as a catalyst for the hydrolysis of the cellulose. These enzymes function synergistically in the hydrolysis of cellulose. Endoglucanase arbitrarily attack and hydrolyses the amorphous domain while exoglucanases react with the cellulosic chain from either the reducing or nonreducing ends. Cellobiohydrolases hydrolyse cellulose from either the C1 or the C4 ends utilizing a protein for each situation, into cellobiose sub-units.1,2,12,13

Combinatorial methods

Pre-treatment techniques are generally more compelling in expanding the biomass digestibility and improving the cellulose separation, and regularly utilized in designing noteworthy pre-treatment technologies.12 The prominent physicochemical procedure includes the blend of a mechanical technique and chemical pre-treatment, for example, acid hydrolysis, enzymatic exposure, ionic liquid treatment, and carboxymethylation, and 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO)-mediated oxidation so as to reduce the reaction times by improving chemical availability just as to decrease the energy requirement of the mechanical isolation process.1,8,12

The tight entwined fibre design is slackened by mechanical interaction, and the areas subjected to the chemical action is expanded. In every one of these cases charged functionalities are acquainted with the cellulose backbone, internal repulsion emerges, and defect to the hydrogen bond network are generated. By consolidating chemical and mechanical procedure (chemomechanical treatment), individual fibrils (3–5 nm wide) or fibril aggregates (10–20 nm wide) a few micrometres long can be derived economically when contrasted with the utilization of mechanical treatment alone.1,8

In these regards, the improvement of extraction technologies and advancement of combined procedures utilizing a blend of two or a few of the techniques could be one of the best approaches to upgrade CNCs properties and address the yield limitation issue. Ultrasonication and microwave methods have likewise been utilized as supporting technologies in physicochemical treatment of plant fibre materials to achieve high productivity. Besides, various constraints should be thought of, for example, the contamination of the environment, the erosion of hardware's and the trouble in controlling the hydrolysis level of cellulose.12

MODIFICATION

The surface chemistry of cellulose can betuned with ease. Surface modified cellulosic nanomaterials are an outstanding platform, intended for targeted applications. The wide relevance of nanocellulose is undermined by its poor dispersibility in nonpolar solvents, and its incompatibility and poor interfacial adhesion with hydrophobic matrices. To solve this issue, researchers have attempted various modification both to the surface and to the nanocellulosic structure. Different chemical modification techniques were performed on nanocellulosic materials with the goal to

- Upgrade the effectiveness of the isolation procedure and
- To alter the surface hydrophobicity, which thus improves the compatibility and the dispersibility of nanocelluloses in specific solvents.1,5

As a result of a characteristic preferred position of a plenitude of hydroxyl groups at the surface of CNCs, diverse chemical modification has been endeavoured, including esterification, etherification, oxidation, silylation, polymer grafting, and so on. The main challenge for the chemical fictionalization of CNCs is to lead the procedure so that it just changes the surface of CNCs, while safeguarding the original morphology to stay away from any polymorphic transformation and to keep up the integrity of the crystal.3 Either negative or positive electrostatic charges can be introduced over the surface of the NCC while utilizing chemical functionalization, which at last gives better dispersibility in any solvent/polymer. It likewise assists with tuning the surface energy qualities to improve compatibility, particularly when utilized alongside nonpolar or hydrophobic polymer matrices.2,4

Non-covalent surface modification

Fundamentally these strategies take benefit of electrostatic adsorption of surfactants on the CNC surface to modulate the surface attributes. Many ionic and non-ionic surfactants, for example, mono and di-esters of phosphoric acid bearing alkylyphenol tails Beycostat A B09 and acid phosphate ester of ethoxylated nonylphenol; sorbitan monooctearte; xyloglucan oligosaccharide-poly (ethylene glyco)-polystyrene triblock copolymer; cetyl tetramethyl ammonium bromide (CTAB) epoxy propyl trimethylammonium chloride have been regularly utilized.5,11

Covalent surface modification

This strategy incorporates TEMPO-mediated oxidation which take advantage of particular oxidation of hydroxymethyl groups of polysaccharides into carboxylic group by 2, 2, 6, 6 Tetramethylpiperidine-1-oxyl (TEMPO).Additionally, a portion of the ordinarily utilized modification incorporates Esterification, silylation, phosphorylation, carboxylation, etherification.1,5,11
Polymer grafting

Polymers onto cellulose is an astounding method to alter the compound and physical properties of the material. Polymer–cellulose composites have been prepared to stabilized nanocellulose, for abrasion and wear resistance, for shape-retaining materials, to change the hydrophilicity/hydrophobicity of the surface and the sorbancy, and to acquire flexibility, stimuli responsive materials, ion exchangers, electrolytes, thermal resistance, and self-cleaning surfaces. Polymer-grafted cellulose joins great mechanical properties with great biocompatibility and low degradability; along these lines such materials have been utilized in surgical repair. Polymer grafting has been performed utilizing various techniques that can be partitioned into three classes: grafting to, grafting from, and grafting through. 1, 3

APPLICATIONS

The distinctive biophysicochemical properties of CNCs have influenced numerous scientists to utilize them in different blends to design materials with desired properties. 11

CNC is a competent nanomaterial for a wide scope of applications, for example, enzyme immobilization, synthesis of antimicrobial and medical materials, green catalysis, synthesis of drug carrier in therapeutic and diagnostic medicine, and so on. Because of their enormous surface area and probability of acquiring negative charge during hydrolysis, huge amounts of medications can be bound to the surface of these materials with the potential for optimal control of dosing. 4

K Jackson et al investigated the utilization of nanocrystalline cellulose (NCC) as a drug delivery excipient for delivery of water soluble, ionizable medications tetracycline and doxorubicin, which were released quickly over a 1-day time frame. Likewise, NCC crystallites with CTAB-modified surfaces bound significant amounts of the hydrophobic anticancer medication’s docetaxel, paclitaxel, and etoposide. These medications were released in a controlled way over a 2-day time frame. 5

Profoundly permeable nanocellulose aerogel scaffolds were accounted for to accomplish sustained drug release, which likewise uncovered additional opportunities as carrier for controlled drug delivery. Because of their distinctive properties, as-integrated CNCs have the potential for being utilized in different and various applications, for example, nanopaper, barrier films, and pH sensors, to stabilization of oil/water interfaces, to production of Pickering emulsions and so on, yet CNC-containing polymer nanocomposites has a lot more applications. These kinds of nanocomposites are utilized for making biomimetic foams toughened paper, flexible panels for flat panel display, water repellents, and high-security papers. They are likewise valuable for different biomedical applications, for example, wound healing patches, tissue engineering scaffolds, and hydrogels for clinical and pharmacological applications, and so forth. Considering the biocompatibility of CNC and the probability of chemical modification, for example, fluorescent labelling, CNCs are possibly valuable in the field of biomedical applications, for example, biosensors, bioprobes, fluorescence bioassays, bioimaging applications, etc. The fuse of CNC can fundamentally improve the mechanical performance 10, thermal stability, and barrier and optical properties because of its improved crystallinity and better interfacial interaction. Biodegradable nanocomposite films with prevalent properties can likewise find their applications in nourishment and biomedical packaging areas, wherein lower permeability to dampness, gases, aroma, and oil are especially required. 4

By the steady advancements in the researches, the applications in various fields have been recommended ranging from iridescent pigments to biomolecular NMR contrast agents. The solidification of the liquid crystal makes the NCC valuable in the use of security paper. The NCC is additionally under research for the utilization in lithium battery products. The different researches with respect to the NCC has had the option to deliver the applications like the creation of foam, aerogels, building block for permselective membranes, enhancements in the materials of the glues utilizes in the lithium battery has likewise been acquainted with improve the physical properties and furthermore it have been used in biomolecular NMR. 2

By controlling the concentration of CNCs, it is feasible to modify the rheological conduct of liquids, polymer melts, and particle suspensions. Rheological control is an essential for CNC applications in paints, glues, polishes, nourishment, cosmetics, pharmaceutical, and other modern items. CNC-based packaging materials could be used for increasing the shelf-life of pharmaceutical, food and drink items, ensuring against physical, biochemical, and microbiological degradation and deterioration. 11

CONCLUSION

Cellulose nanocrystal, an eco-friendly bio-inexhaustible material is derived from various natural sources. Due to their crystalline nature and the properties it has being investigated for various advanced application in the distinctive field. These remarkable nanosized material lend themselves to a plenty of synthetic changes and have in this manner been controlled to give a rich set-up of new materials and stages for additional application, for example, drug delivery system, biomedical applications, tissue engineering, bioimaging, energy storage, biphotonic, and smart polymers. The ceaselessly increasing new applications in different fields are anticipating CNCs’ potential to become sustainable source for commercial production of many propelled “green” materials and devices.

REFERENCES

