



Modification of Nanocellulose

Marta Fernandes, Cátia Alves, Liliana Melro, Rui D. V. Fernandes, Jorge Padrão, António J. Salgado, and Andrea Zille

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Abstract

Nanocellulose (NC) represents a pivotal material for the sustainable strategies of the future. NC comprises cellulose nanofibrils (CNFs), cellulose nanocrystals (CNCs), and bacterial nanocellulose (BNC), each exhibiting unique and exceptional physicochemical properties. These properties encompass high specific surface area, high tensile strength, lightweight, biodegradability, good barrier properties, and high processing versatility. However, the range of properties and applications can be significantly expanded through the modification of NC, involving both chemical and physical methodologies, which introduce a plethora

M. Fernandes (✉) · C. Alves · L. Melro · R. D. V. Fernandes · J. Padrão · A. Zille (✉)
Centre for Textile Science and Technology (2C2T), Campus de Azurém, University of Minho,
Guimarães, Portugal
e-mail: marta.fernandes@det.uminho.pt; azille@2c2t.uminho.pt

A. J. Salgado
Life and Health Sciences Research Institute (ICVS), Campus de Gualtar, University of Minho,
Braga, Portugal

of functional groups to the densely populated hydroxyl groups present in pristine NC. The modification processes discussed in this chapter encompass chemical and physical modifications that were reported mostly within the last 5 years. The described methodologies emphasize the potential of NC as a substrate for advanced functional and sustainable materials.

Keywords

Nanocellulose modification · Esterification · Oxidation · Silylation · Graft copolymerization · Gamma radiation · Plasma treatment

Introduction

Cellulose is one of the most abundant materials on Earth and can be obtained from different sources, such as plants, microorganisms (bacteria and fungi), and tunicates (Bangar et al. 2022). As a renewable, sustainable, ecological, and biocompatible material, cellulose has gained increasing interest in the development of various emerging technological applications (Aditya et al. 2022). Chemically, cellulose is composed of a linear chain of monomeric units of D-glucose linked by β -1,4-glycosidic bonds. The glucose units are linked together through hydroxyl (OH) groups that form intra- or intermolecular hydrogen bonds, resulting in a strong network of insoluble cellulose with rigid and stable molecules, and a degree of polymerization ranging from several hundred to over ten thousand (Patil et al. 2022; Thomas et al. 2020; Noremlyia et al. 2022).

Nanocellulose (NC) occurs in the form of nano-scaled cellulose, presenting superior physicochemical properties such as high crystallinity (Lunardi et al. 2021), large specific surface area (Reshmy et al. 2021), and abundant OH groups on its surface, which represent easy targets for modification (Ning et al. 2022). Different techniques can be used to extract NC from vegetable sources, which includes mechanical, chemical, and biological processing, or any combination thereof. In the mechanical method, a critical tension is created in the core of the cellulose fibers by applying mechanical forces, resulting in the defibrillation of the cellulose (Salimi et al. 2019). Examples of mechanical processes are high-pressure homogenization, microfluidization, grinding, refining, and cryocrushing. These methods are simple and use relatively inexpensive equipment, producing NC in large quantities at standard temperature and pressure from broad types of biomass (Noremlyia et al. 2022). However, they still require high energy to break down cellulose to nanoscale (Sanchez-Salvador et al. 2022). In chemical methods, a wide variety of chemical agents can be used to degrade cellulose by breaking down the amorphous sections of cellulose. Acid hydrolysis (using sulfuric acid (H_2SO_4), hydrochloric acid (HCl), phosphoric acid (H_3PO_4), or hydrobromic acid (HBr)), 2,2,6,6-tetramethylpiperidine-1-oxyl radical (TEMPO)-mediated oxidation, and ionic liquids are some of the treatments used (Salimi et al. 2019). In biological methods, cellulose is exposed to cellulolytic enzymes that cleave the fiber structures.

Table 1 Main characteristics of different types of NC

	CNFs	CNCs	BNC	References
Source, production	Plants, mechanical fibrillation	Plants, acid hydrolysis	Microorganisms, polymerization and crystallization	Norrahim et al. (2021)
Morphology structure	Smooth, and flexible long-chain	Needles-like shape, elongated rod-like shape, and spindle shape	Twisted ribbons-like shape	Lunardi et al. (2021)
Diameter	20–60 nm	3–70 nm	10–100 nm	Padrão et al. (2022)
Length	500 nm–over 1 μ m	25–150 nm	50 nm–100 μ m	Padrão et al. (2022)
Degree of polymerization	≥ 500	500–15,000	4000–10,000	Salimi et al. (2019) Das et al. (2022a)
Crystallinity	–	54–88%	84–89%	Lunardi et al. (2021)
Specific surface area	51 m ² /g	533 m ² /g	125 m ² /g	Reshmy et al. (2021)
Density	1.42 g/cm ³	1.6 g/cm ³	1.1 g/cm ³	Salimi et al. (2019)

As these processes are time-consuming, they are normally carried out in combination with mechanical and chemical methods to optimize the process of obtaining NC (Noremylia et al. 2022). The type of lignocellulosic source and processes of purification and hydrolysis used in the NC extraction will govern the crystallinity index of the fibers (Bangar et al. 2022).

Based on the sources and morphology, NC is categorized into three main groups: cellulose nanofibrils (CNFs), cellulose nanocrystals (CNCs), and bacterial nanocellulose (BNC). Table 1 presents the main characteristics of different types of NC.

CNFs are usually obtained using mechanical techniques (fibrillation) or by combining mechanical with a chemical (TEMPO-mediated oxidation) or enzymatic pretreatment (Das et al. 2022b). This form of NC consists of an entangled network structure of smooth and flexible long-chain nanofibers with both amorphous and crystalline parts (Lunardi et al. 2021; Noremylia et al. 2022). Individual CNFs possess diameters from 20 to 60 nm and lengths ranging from 500 nm to over one micrometer (Padrão et al. 2022). Regarding CNCs, they are obtained by the traditional and controlled acid hydrolysis treatment by exposing cellulose to acids, such as H₂SO₄, HCl, H₃PO₄, and HBr. In this process, the relatively disordered

amorphous domain of the cellulose is destroyed, resulting in highly crystalline CNCs charged with negative acidic sulfate groups on its surface, creating an electrostatically stable colloidal suspension (Noremylia et al. 2022; Bangar et al. 2022; Das et al. 2022b). CNCs have a needle-like or rod-like structure with typical dimensions of 3–70 nm width, which is similar to CNFs, but with the acid hydrolysis, there is a substantial reduction in microfibril length to around 25–150 nm (Lunardi et al. 2021; Padrão et al. 2022). In the case of BNC, unlike CNFs and CNCs, it is produced in a bottom-up process by the fermentation of certain aerobic Gram-negative bacterial genera, including *Gluconobacter*, *Aerobacter*, *Agrobacterium*, *Alcaligenes*, *Achromobacter*, *Rhizobium*, *Azotobacter*, *Salmonella*, *Sarcina*, and *Escherichia* (Das et al. 2022b). BNC is the purest form of NC as it has no lignin, pectin, hemicellulose, or extractives, and the controlled formation by bottom-up synthesis allows producing NC with better mechanical properties than lignocellulosic nanofibers (Samyn et al. 2023).

Besides being a relatively low-cost material highly available, renewable, and biodegradable, NC possesses a wide spectrum of advantageous physical, chemical, and biological properties. Many interesting features, such as high specific surface area, high mechanical strength, chemical inertness, tailorable morphological, physical, chemical, electrical, thermal, optical, and barrier properties, biocompatibility, nontoxicity, and low immunogenicity, render NC a versatile material for a broad spectrum of applications in almost all the material science fields (Bacakova et al. 2019; Tortorella et al. 2020). However, despite the many advantages of NC, the abundant number of OH groups on its surface implies some disadvantages, including high hydrophilicity/moisture absorption, low dispersibility/incompatibility with hydrophobic polymers, and poor thermal stability (Noremylia et al. 2022). This restricts a wider range of applications; thus NC may undergo surface modifications through chemical and physical methodologies to generate novel functional groups or moieties on the NC's surface, greatly broadening its functionality and industrial applications (Tortorella et al. 2020).

Chemical Modification of NC

Chemical modification of NC is a straightforward strategy to introduce desired functionality by adding new functional groups in its structure. These characteristics enhance the potential of NC as a promising material for diverse industrial applications. Common chemical modifications methods of NC include esterification, oxidation, silylation, sulfonation, amination, amidation, and carbamation, among others (Fig. 1).

Esterification

Esterification is the most well-known and simplest method to reduce the OH density of NC to render it hydrophobic. It consists in the introduction of ester groups onto

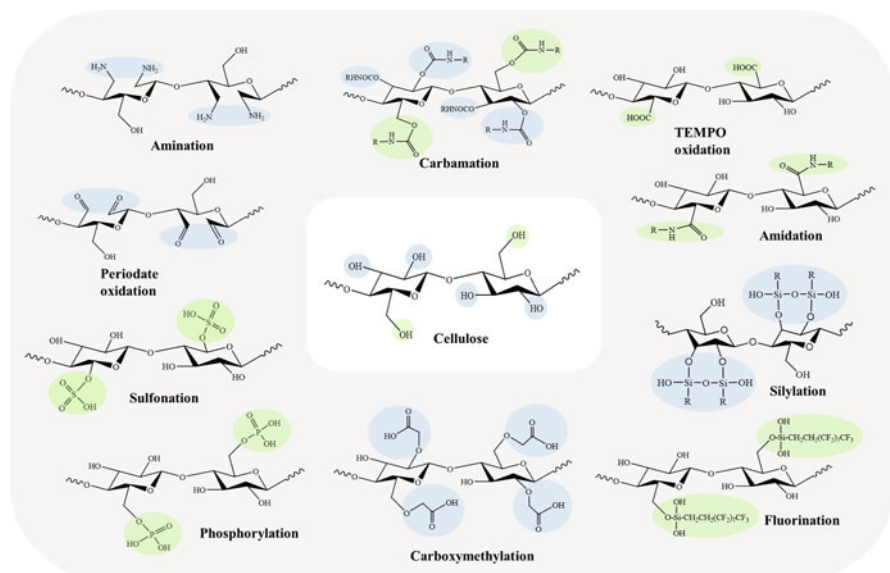


Fig. 1 Main surface chemical modifications of NC

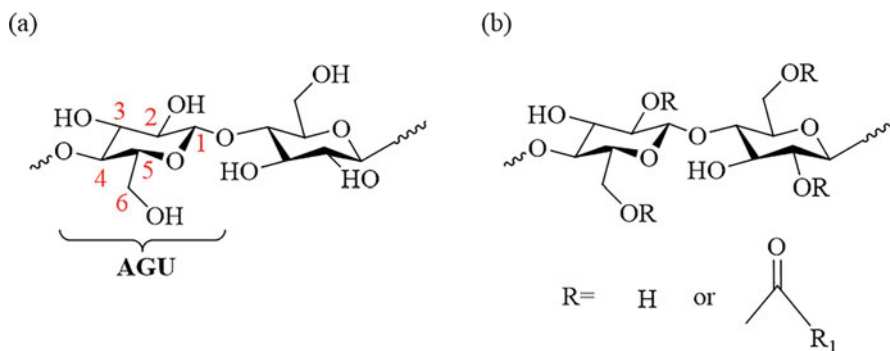


Fig. 2 Schematic representation of (a) the molecular structure of NC with the numbering for carbon atoms within a single AGU and (b) the molecular structure of cellulose ester

NC through the reaction between the OH groups present in its structure and different acids. The three OH groups present in the anhydroglucose unit (AGU) of cellulose, primary OH group at C6 and secondary OH groups at C2 and C3, can participate in esterification reactions (Fig. 2) (Wang et al. 2018).

Esterification reactions occur either at the surface of the cellulose fibers or on the whole cellulose polymer chains, named as heterogeneous esterification and homogeneous esterification, respectively (Wang et al. 2018). The use of organic acids such as carboxylate anhydrides, adds an acyl functional group onto the cellulose surface, a process designated as acylation, which results in cellulose acetate. Acetylation of NC

is the most common esterification reaction. It reduces degradation by hydrolytic cleavage and increases thermal stability due to OH density on the NC. This is generally performed by introducing ester groups through condensation of carboxylic acid and alcohol groups. Esterification of cellulose can also be done using fatty acids and different chemicals: acetyl chloride, acetic anhydride, and vinyl acetate. Acid anhydrides or acyl chlorides act as an acyl donor in the presence of reduced amounts of catalysts sulfuric or perchloric acid (Zhang et al. 2022). Furthermore, these solvents have good cellulose solubilization properties, acting as organocatalysts, if needed (Aziz et al. 2022). Inorganic acids originate cellulose nitrate, cellulose xanthate, cellulose sulfate, and cellulose phosphate. NC esters can contain nonionic, anionic, or cationic groups, interesting for different technological applications (Wang et al. 2018; Muqet et al. 2020). For example, the linking of anionic groups (sulfate, carboxylic acid, and phosphate) to the surface of CNCs or CNFs leads to the formation of stable aqueous suspensions. Due to the enhancement of charge repulsions on their surface, the fibrils become increasingly individualized, hence the aggregates decrease (Zhang et al. 2022). Esterification can also be used to conjugate proteins onto NC for drug delivery. Via Fischer esterification, a peptide (chlorotoxin) was linked to the OH groups of CNCs, through its carboxylic acid groups, derived from the three aspartic acids present on the protein backbone, using a Brønsted acid ionic liquid that acted both as a solvent and a catalyst. Functionalized CNCs showed excellent biocompatibility and internalization of chlorotoxin in U87MG glioblastoma cells (Cellante et al. 2018). Production of cellulose nitrate is generally based on the fast heterogeneous equilibrium reaction between cellulose and nitric acid or its derivatives (Wang et al. 2018). With a broad variety of applications, it can be used as a film base for photography and as a mild explosive. The nitration of freeze-dried BNC was performed with sulfuric-nitric mixed acid containing 14% water at room temperature for 40 min. This synthesis resulted in a nitrogen content of 10.96%, 47% solubility in the alcohol-ester mixture, and 100% in acetone (Budaeva et al. 2019). Cellulose sulfate is synthesized by the direct esterification of cellulose using H_2SO_4 (see section “Sulfonation”). Other solvents such as sulfur trioxide, chlorosulfonic acid, sulfonyl chloride, fluorosulfuric acid, ethyl chlorosulfonate, and sulfoacetic acid can also be used (Wang et al. 2018).

Pentavalent phosphorus reagents, phosphoryl chloride, phosphorus pentoxide, and H_3PO_4 , introduce H_3PO_4 ester moieties onto cellulose. Notwithstanding, these present lower reactivity compared to sulfating agents. Phosphorylation usually occurs in a heterogeneous system or uses a non-derivatizing solvent system such as N-methylmorpholine N-oxide, lithium chloride/dimethylacetamide, and dinitrogen tetroxide/dimethylformamide (Wang et al. 2018). The surface of CNCs was successfully modified with methacryloyl chloride to create esterified CNCs via the dispersion of the NC in pyridine via sonication for 30 min (see Fig. 3). The solution was then purged with nitrogen gas for another 30 min followed by the addition of methacryloyl chloride and stirring for 6 h at 50°C. The modified CNCs exhibited increased surface hydrophobicity and better dispersion, thus higher compatibility with the filler epoxy resin (Thompson et al. 2022).

Fig. 5 Schematic representation of the reaction between lactic acid and a single OH group on the CNFs surface

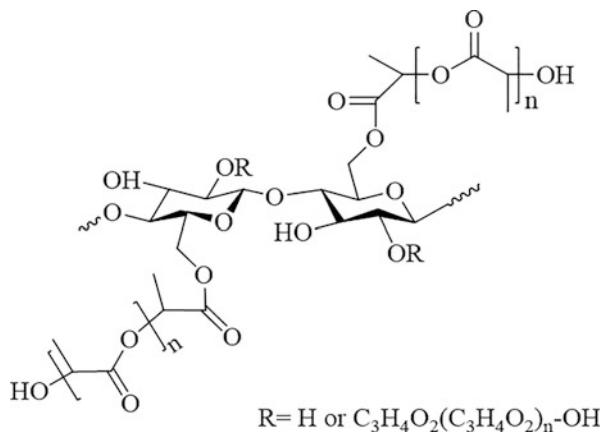
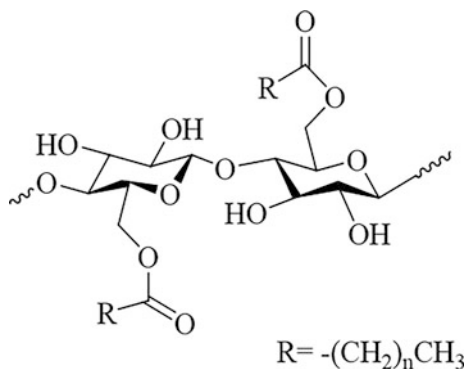


Fig. 6 Schematic representation of the reaction between vinyl esters and OH groups of cellulose



and the precipitates were washed with methanol and dried after filtration. Results show that esterification offers a controlled degree of hydrophobicity to CNFs, enabling them to be dispersed in nonpolar organic media (Her et al. 2020). The reaction between vinyl esters and hydroxyl groups is represented in Fig. 6.

Another method for hydrophobization of CNFs films was accomplished using vinyl esters of variable alkyl chain lengths using a deep eutectic solvent of imidazole and triethylmethylammonium chloride as a reaction medium. The reaction occurred at 80 °C for 15 min. After rinsing and drying, the resulting modified films showed improved water vapor barrier properties and improved mechanical properties in a wet state, especially with films treated with ultraviolet (UV) and ozone before modification (Lakovaara et al. 2022). A summary of the different esterification reactions for NC surface modification is displayed in Table 2.

Table 2 Surface modification of NC through esterification reaction

NC type	Other components	Modification method	Properties	Application	References
CNC	Chlorotoxin	Fisher esterification with <i>N</i> -Methylpyrrolidinium hydrogen sulfate (ionic liquid)	Noncytotoxic (U87MG and MCF7 cells) Cellular uptake of CNCs can be modulated in relation to their linkage with the peptide	Drug delivery carrier	Cellante et al. (2018)
BNC	–	Nitration with sulfuric-nitric mixed acid	High nitrogen content (10.96%) High viscosity (916 cP)	n.d.	Budaeva et al. (2019)
CNC	Epoxy resin	Dispersion of CNCs in pyridine via sonication Addition of methacryloyl chloride	Improved storage modulus (2850 MPa)	n.d.	Thompson et al. (2022)
CNC	PNIPAm	Succinylation with succinic anhydride + free radical polymerization	Decreased hydrophilicity pH and thermo-responsive Enhanced release of famotidine by altering the pH from 10 to 2	Drug release	Enam and Shaheen (2022)
Lactic acid-CNF	PLA	Grafting of lactic acid onto CNFs with catalyst SnCl ₂ + injection molding	Improved water vapor permeability (decreased)	Packaging	Lafia-Araga et al. (2021)
CNF	VA or HA	VA or HA in trifluoroacetic anhydride	Improved porosity Reduced hydrophilicity (79.2°, VA-CNFs and 85.0°, HA-CNFs) Better thermal stability	Porous membranes, packaging, coatings, and films	Her et al. (2020)
CNF	Vinyl butyrate, vinyl octanoate, vinyl laurate, or vinyl palmitate	Immersion in a deep eutectic solvent containing vinyl esters	Improved contact angle Improved water vapor barrier properties Improved mechanical properties (wet state)	Packaging	Lakovaara et al. (2022)

n.d. – not defined

Oxidation

Oxidation is a versatile and effective process commonly used to impart specific properties on different cellulosic sorts by introducing new functional groups (e.g., carboxyl, aldehyde, and carbonyl functional groups) (Zhang et al. 2023; Dalei et al. 2022). Cellulose is highly responsive to reaction conditions, including the type of oxidizing agent, pH of the reaction medium, temperature, solvent, and more. These variables not only influence the nature of the functional groups that are introduced but also impact their position within the cellulose structure. By carefully controlling these factors, unique and tailored NC derivatives can be obtained (Duceac et al. 2022).

TEMPO-Mediated Oxidation

TEMPO-mediated oxidation is one of the most popular processes for the modification of NC surface, by converting the OH groups into their carboxylic forms. With this oxidation, the breakdown of glycosidic bonds does not occur due to the mildness of the process (Bangar et al. 2022). The nitroxyl-based oxidation process uses a stable nitroxyl radical TEMPO in the presence of sodium bromide and sodium hypochlorite to catalytically and selectively oxidize the primary OH group in the AGU C6 position of the cellulose molecule, at pH 10–11, introducing a negatively charged surface. The remaining OH groups are not affected by the oxidation process, including the secondary OH groups at the C2 and C3 positions (Ning et al. 2022). Figure 7 shows the mechanism of TEMPO-mediated oxidation.

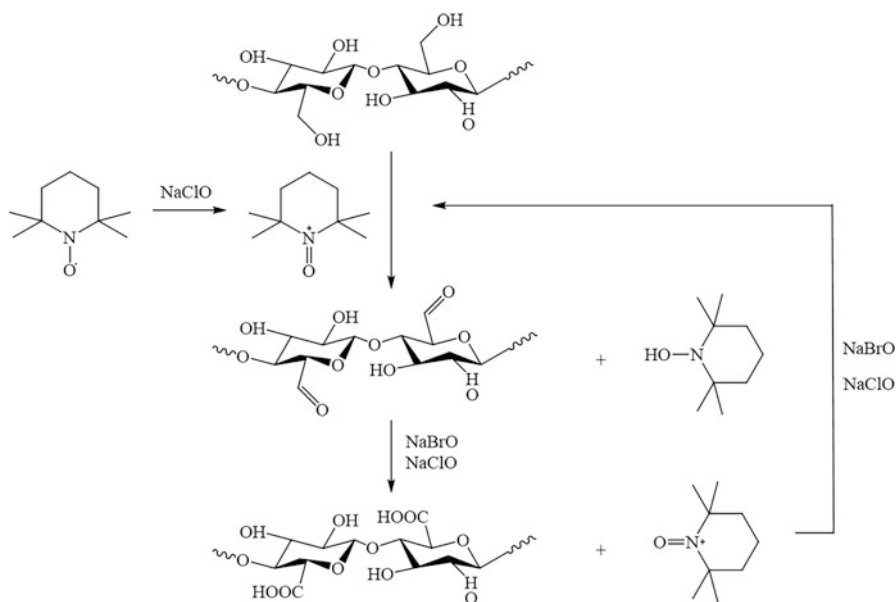


Fig. 7 Mechanism of TEMPO-mediated oxidation of NC

In the work carried out by Mendoza et al., NC superabsorbent foams were developed by TEMPO-mediated oxidation/high-pressure homogenization, followed by freeze-drying. The authors found that the oxidized NC produced foams of high absorption capacity and tunable absorption kinetics by manipulating the processing conditions, such as the fiber content and the oxidation degree. Water molecules are strongly attracted to negatively charged carboxyl groups, consequently, the fiber surface charge, indicative of the amount of COO^- groups, influences the absorption capacity of the foams. So, the obtained NC foams with a carboxylate concentration of 1.2 mmol/g, a near-complete oxidation of the C6 OH group, were capable of absorbing 120 g/g H_2O and 60 g/g of saline solution (Mendoza et al. 2019b). Suárez-Avendaño et al. performed a comparative study on the efficiency of mercury removal from wastewater using BNC and oxidized BNC membranes. The modification of the BNC membranes by oxidation considerably improved the ability to remove mercury due to the presence of a greater number of carboxylic groups that promote greater interaction between the NC and the ions, reaching a maximum removal close to 93%. However, it was observed that the modification must be carried out in such a way to achieve the highest possible number of carboxyl groups incorporated without affecting the membrane morphology. Their study showed that with the excessive increase in the concentrations of the oxidizing agent, an undesirable loss of surface area occurred, which reduced the number of carboxylic groups available for the removal process (Suárez-Avendaño et al. 2022). In the study by Yang et al., carboxylated NC was used in the development of ultrafiltration membranes for wastewater purification with antifouling properties. Negatively charged TEMPO-oxidized CNFs were coated on porous electrospun polyacrylonitrile (PAN), which results in strong electrostatic repulsion between the membranes and similarly charged suspended particles present in wastewater and hinder the adhesion of biomolecules on the membrane surface. The PAN membrane coated with TEMPO-CNFs with a degree of oxidation of 1.80 displayed excellent permeation flux (25.3 $\text{L}/\text{m}^2/\text{h}$), high flux recovery (>98%), and good antifouling properties against the model pollutant bovine serum albumin. The permeation flux and water flux recovery ratio were about two times and three times higher, respectively, than that of the commercial poly(vinylidene fluoride) membrane (Yang et al. 2021).

For a different application, TEMPO-oxidized CNFs with an oxidation degree of 1.51 mmol COOH/g cellulose were used for the development of injectable hydrogel matrices with the potential for the fabrication of materials with embedded cells, such as bioprinted structures. The hydrogel produced by ultrasonication of an aqueous dispersion of CNFs and calcium chloride showed tunable rheological features due to the presence of Ca^{2+} ions. The TEMPO-oxidized CNFs were able to interact with the polyvalent electrolytes due to the COO^- groups on the fibers' surface, leading to cross-linking and consequently inducing nonreversible gelation. Moreover, the proposed hydrogel proved to be suitable for control drug delivery of ibuprofen and no cytotoxic effects were observed, indicating its suitability to be used as an injectable drug-delivery system (Fiorati et al. 2020).

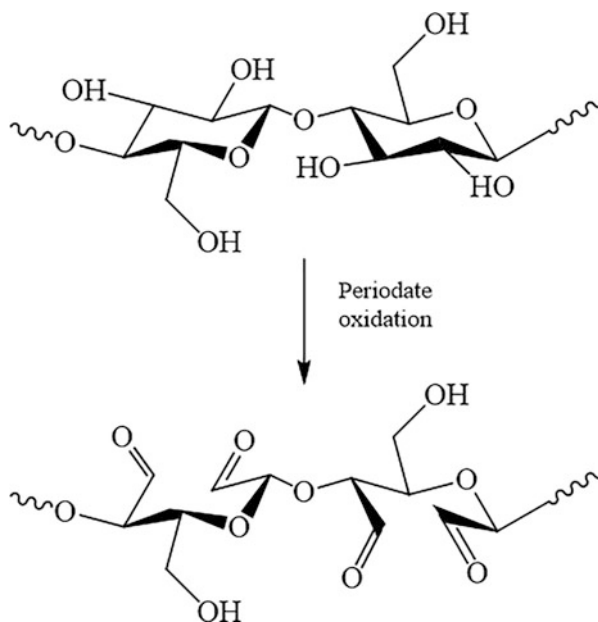
Despite the simplicity of the TEMPO-mediated process, it has some disadvantages, such as being time-consuming, using chemicals that are very polluting for the environment, and consuming large quantities of water (Zhang et al. 2023).

Periodate Oxidation

In periodate oxidation, instead of reacting with the C6–OH groups of cellulose as occurs in TEMPO, sodium periodate (NaIO_4) selectively oxidizes secondary OH groups at the C2 and C3 positions of the AGU unit, cleaving breaking bonds between vicinal carbons through a ring-opening reaction and forming two aldehyde groups (Copenhaver et al. 2022; Mendoza et al. 2019a), as represented in Fig. 8. This method has the advantage of enabling further oxidation of the dialdehyde groups to carboxylic groups (Duceac et al. 2022).

Kriechbaum et al. designed wet-stable multifunctional films highly suitable for food packaging by covalently grafting gelatin to periodate-oxidized CNFs (aldehyde content of 0.74 mmol/g). To avoid depolymerization of the modified NC, the grafting was performed via a Maillard-type reaction at pH 6.5. Then, the hybrid films were physically cross-linked by adding tannic acid, which forms insoluble complexes. The obtained films showed antioxidant activity (>90%), UV-blocking by absorbing 100% light in the UV-B/UV-C range, and high wet mechanical properties (tensile strength of 33 MPa, strain at failure of 22%, and Young's modulus of 310 MPa) due to the tannin-induced precipitation of gelatin grafted on surface-modified CNFs (Kriechbaum and Bergström 2020). In another work, Kwak et al. prepared gelatin films cross-linked and reinforced with dialdehyde CNCs. They

Fig. 8 Periodate oxidation of NC



noted that the modified-CNCs could react and covalently cross-link with the amine (NH) group of the gelatin molecules via a Schiff base reaction and the degree of cross-linking increased with the increased amount of the dialdehyde CNCs in the gelatin films. Furthermore, the reinforced biocomposite showed high potential for the food packaging and biomedical fields by exhibiting excellent mechanical properties and water resistance, which are tailorable by adjusting the CNCs content (Kwak et al. 2020). Lee et al. studied the reinforcement of poly(vinyl alcohol) (PVA) films with dialdehyde NC (CNFs and CNCs) by using a chemical cross-linking strategy to enhance its hydrophobicity and water resistance. Dialdehyde CNFs-based nanocomposite films showed the most improved results where the water contact angle (WCA) increased from ~ 40 to 75° . This increase was a result of the cross-linking reaction and the unreacted aldehyde groups on its surface, and due to the chemical network structure generated with PVA, which effectively prevents the penetration of water molecules (Lee et al. 2020).

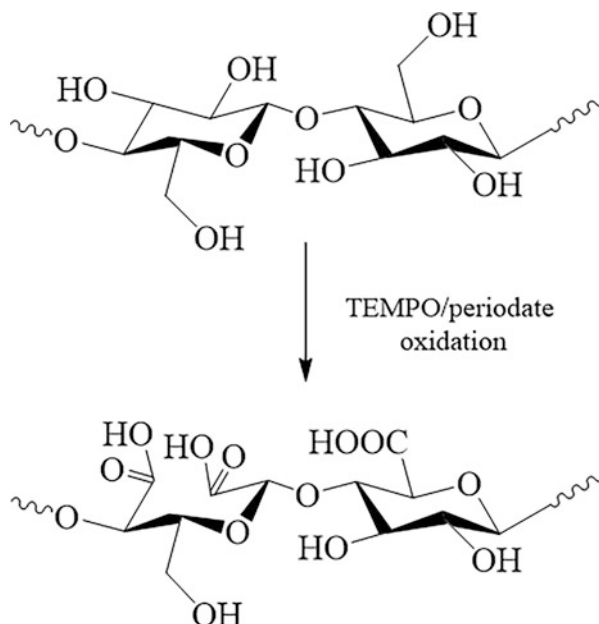
Recently, Huang et al. carried out a study where anionic and cationic dialdehyde NC adsorbents were prepared via a two-step reaction, using NaIO_4 and Girard's reagent T (containing both amino and quaternary ammonium groups) as oxidizing and cationizing agents, respectively, and examined for adsorption and selective separation of organic dyes. Both anionic and cationic dialdehyde NC adsorbents possessed the capability to remove the dyes with a stable adsorption efficiency in the pH range of 4–10. However, the anionic adsorbent exhibited high and selective uptake capability toward cationic dyes, whereas the cationic one showed superior adsorption capability toward anionic dyes. Furthermore, both adsorbents could adsorb Congo red under strong alkalinity and an increase in the dye adsorption capability with increasing salt concentration was observed. The good adsorption capability of the adsorbents toward different dyes was attributed to the covalent bond and the electrostatic interaction between the aldehyde groups on NC and the amino groups on dyes (Huang et al. 2023).

CNCs have the potential as antibiotic substitutes to fight against multidrug-resistant bacteria by introducing aldehyde groups on their surface. As reported by Luo et al., the increasing content of aldehyde groups in the CNCs (1.28, 2.44, and 3.72 mmol/g) increased the antibacterial activity against Gram-positive pathogens in vitro by lowering the pH in the microenvironment of bacteria. With low pH, the protein activity is decreased and the difference between the extracellular and intracellular environment of bacteria is widened due to the aldehyde groups. These cause the increase in bacteria volume, destruction of the cell membrane, outflow of intracellular contents, and the inactivation of pathogens. Moreover, CNCs with the higher number of aldehyde groups also showed in vivo antibacterial effect against *Staphylococcus aureus* on the skin of infected mice models, with low cytotoxicity, excellent skin compatibility, and no acute oral toxicity (Luo et al. 2021).

Combined Oxidation Methods

To increase the number of functional groups in NC, selective oxidation methods can be combined with each other or with other methods to produce carboxylated NC with a wide range of degree of substitution (DS). Thus, by oxidizing the primary and

Fig. 9 TEMPO/periodate oxidation of NC



secondary alcohols to carboxylate groups, the modified NC may have three carboxylic acid groups at C2, C3, and C6 positions (Duceac et al. 2022).

Mendoza et al. introduced a one-shot TEMPO-periodate method to oxidize cellulose by targeting the C2, C3, and C6 OH groups in the cellulose molecule. NC was produced with a wide range of DS (0.39–1.1) by varying the periodate concentration. Furthermore, depending on DS, different crystalline/amorphous fractions are obtained (Mendoza et al. 2019a). Later, the authors used this oxidation method to produce gels with excellent optical properties. The highly carboxylated NC obtained had a diameter of 2–4 nm and a high charge of -80 mV, resulting in nanofibers well-separated due to the strong electrical repulsion between them. Moreover, gels obtained after freeze-drying were highly transparent, as a result of the smaller aspect ratio and high surface charge, and displayed remarkable water-holding capacity due to enhanced capacity to immobilize water molecules (Mendoza et al. 2020). Figure 9 shows the TEMPO/periodate oxidation reaction.

In the study by Plappert et al., periodate–chlorite oxidation as a pretreatment to tailor the surface charge density of CNFs was employed in open-porous anisotropic hydrogel membranes for transdermal drug delivery systems. With this method, periodate converts selectively and simultaneously the two vicinal secondary OH groups of the cellulose into aldehydes and chlorite ions further oxidize the latter to carboxyl moieties. The NC exhibited completely individualized nanofibers with diameters of about 2.5 nm and a carboxylate group content within the range of 0.74–2.00 mmol/g. The anisotropic layered gel membranes obtained by vacuum filtration featured high specific surface (≤ 500 m²/g), providing sufficient adsorption sites for drug molecules,

Table 3 Surface modification of NC through oxidation reaction

NC type	Other components	Modification method	Properties	Application	References
CNF	–	TEMPO oxidation	Superabsorption capacity (120 g H ₂ O/g fiber; 60 g saline H ₂ O/g fiber)	Superabsorbents	Mendoza et al. (2019b)
BNC	–	TEMPO oxidation	Good mercury removal capacity (92.97%)	Mercury removal in wastewater	Suárez-Avendaño et al. (2022)
CNF	PAN	TEMPO oxidation	Excellent permeation flux (61 L m ² /h at 0.5 psi) High rejection ratio (>98%) Good antifouling tendency (bovine serum albumin (BSA))	Antifouling ultrafiltration membranes for wastewater treatment	Yang et al. (2021)
CNF	–	TEMPO (containing Ca ²⁺ ions) oxidation	Release of ibuprofen (9.0×10^{-10} m ² /s) Noncytotoxic (L929 cells)	Hydrogels for controlled release systems	Fiorati et al. (2020)
CNF	Gelatin and tannic acid	Periodate oxidation	Excellent mechanical properties in wet state (tensile strength (33 MPa); Young's modulus (310 MPa); strain at failure (22%)) Excellent antioxidant (>90% free radicals scavenging) Excellent UV-blocking (100% of light absorbing in the UV-B/UV-C range)	Food packaging	Kriechbaum and Bergström (2020)
CNC	Gelatin	Periodate oxidation	Excellent mechanical properties (15 wt% CNCs; Young's modulus 330.4 MPa; tensile strength 31.7 MPa) Excellent water resistance	Food, pharmaceutical, and biomedical	Kwak et al. (2020)
CNF or CNC	PVA	Periodate oxidation	Increased thermal stability, water resistance, and mechanical properties	Food packaging	Lee et al. (2020)
CNF	Girard's reagent T (cationizing agent)	Periodate oxidation		Dyes absorbents for wastewater treatment	Huang et al. (2023)

(continued)

Table 3 (continued)

NC type	Other components	Modification method	Properties	Application	References
			High adsorption efficiency against cationic dyes (anionic CNFs: Bismarck brown Y 552.1 mg/g; cationic CNFs: Congo red 540.3 mg/g)		
CNC	–	Periodate oxidation	In vitro antibacterial activity against gram-positive pathogens In vivo antibacterial activity against <i>S. aureus</i> on the skin of infected mice models Low cytotoxicity Excellent skin compatibility No acute oral toxicity	Antibiotic substitutes to fight against multidrug-resistant bacteria	Luo et al. (2021)
n.d.	–	TEMPO-periodate oxidation	NC containing partially oxidized water-insoluble (crystalline-rich) and fully oxidized water-soluble fractions (polyglucuronans from the amorphous regions)	n.d.	Mendoza et al. (2019a)
n.d.	–	TEMPO-periodate oxidation	Highly transparent gel High water holding capacity (150 g/g)	Red blood cells analysis and diagnostic applications	Mendoza et al. (2020)
CNF	–	Periodate–chlorite oxidation	High specific surface ($\leq 500 \text{ m}^2/\text{g}$) Small pore size (40 nm) Prolonged drug release of piroxicam (PRX) upon exposure to simulated human skin fluid conditions	Hydrogel membranes for transdermal drug delivery	Plappert et al. (2019)

n.d. – not defined

small average pore size (40 nm), and tunable surface charge (−128 to −66 mV). In addition, loading and release experiments of the hydrophobic nonsteroidal anti-inflammatory drug piroxicam were investigated. The results showed that the surface charge density and carboxylate group content of the CNFs membrane significantly affect the drug loading and release capacity. The main driving factor behind this behavior is the electrostatic interaction between the cationic drug and the anionic surface of CNFs membranes. Moreover, the *in vitro* drug release upon exposure of the loaded membranes to simulated human skin fluid conditions was prolonged over several hours, confirming that these membranes have the potential to be used as patches for transdermal drug delivery (Plappert et al. 2019). Table 3 summarizes recent works on the surface modification of NC through oxidation.

Silylation

Silylation is a process that allows to superficially modify cellulose biopolymer through the incorporation of hydrophobic alkyl moieties (silanes) in its structure to enhance its properties or enable specific functionalities, expanding its potential applications. Furthermore, it is distinguished from other chemical modification processes since its coupling agents (silanol) can establish covalent bonds with the OH groups of the cellulose and the reinforcement, promoting their interaction (Liu et al. 2019). Notwithstanding, the silanes must present functional groups that exhibit high affinity between the reinforcement and the cellulosic matrix. These functional groups can serve as anchor points for the attachment of biomolecules (amino acids), drugs (metal nanoparticles (NPs)), biopolymers (chitosan), or different composite matrixes (Fig. 10).

Moreover, silane encompasses different groups, such as alkyl, amino, epoxy, or metacryloxy. Thus, the type of silane selected influences the achievement of the

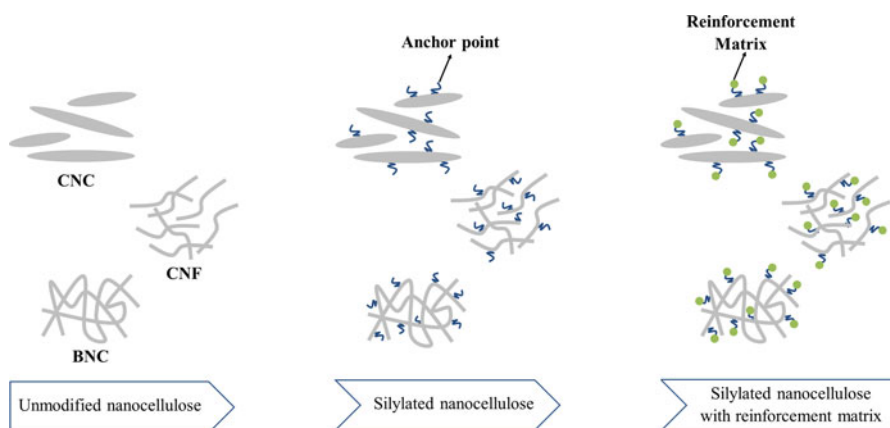
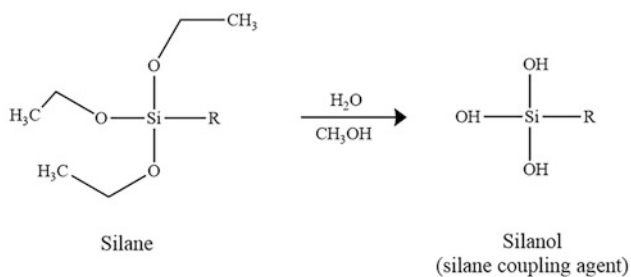
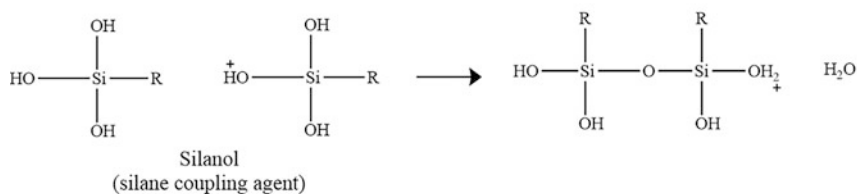
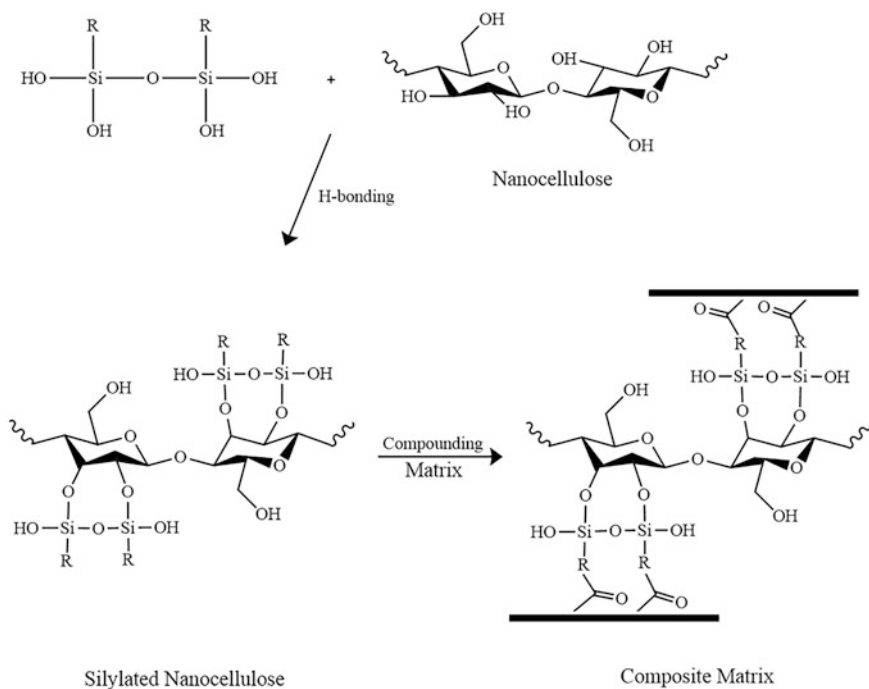


Fig. 10 Modification of NC by silylation

desired properties, including hydrophobicity/hydrophilicity, adhesion, or chemical reactivity (Neves et al. 2021).

The silylation process comprises three chemical stages: (i) production of silanol (SiH_3OH) through acid hydrolysis ($\text{pH} \approx 4$) of the silane alkoxy groups in an aqueous medium; (ii) adsorption of the SiH_3OH groups by the cellulose through the establishment of hydrogen bonds between these groups and the OH of the cellulose, as well as the production of silane bonds (Si-O-Si) through chemical condensation; (iii) grafting of the cellulose surface (Si-OC bonding), reducing the number of OH groups on the surface of the cellulose matrix and assembling stable covalent bonds (Liu et al. 2019) (Fig. 11). Regardless of the applied silane type, the mechanism is based on acid hydrolysis followed by grafting of the NC and composite matrix production. Some examples of silane commonly applied are: hexamethyldisilazane (HDMS), N-(β -aminoethyl)- γ -aminopropyl-trimethoxysilane, 3-isocyanatepropyltriethoxysilane, 3-glycidoxypropyltrimethoxysilane, trichloromethylsilane, (3-glycidylpropyl) triethoxysilane, trimethoxyoctadecylsilane, 3-(trimethoxysilyl)propylmethacrylate, triethoxyvinylsilane, 3-aminopropyltriethoxysilane (APTES), and 3-aminopropyltrimethoxysilane (APTMS) (Neves et al. 2021; Ghasemlou et al. 2021).

Analogous to alkali treatment, silylation is one of the most established chemical modifications to develop an affinity with nonpolar matrices, increase hydrophobicity and absorption capacity (oils, dyes, and metallic compounds), as well as improve the mechanical and reinforcement properties of the composite. Moreover, the silylation process is recognized for its eco-friendly properties as it entails a low-waste approach, leading to minimal generation of by-products or unreacted materials (Ghasemlou et al. 2021; Chen et al. 2023). Despite all these potential benefits and several applications, this process can promote the disintegration of NC in solution, depending on the DS. To avoid a loss of morphology of the NC, it is necessary to evaluate the extent of the degree of silylation. Values lower than 0.6 are preferred, as the morphological shape of the NC is mostly preserved. In some cases, this also occurs when the silylation is between 0.6 and 1. However, with a higher DS (>1), the biopolymer loses crystallinity, therefore other techniques should be adopted. Acetylation is an alternative process, nevertheless, it is more complex and expensive. To overcome this disadvantage, different reaction conditions and structural properties of silanes were evaluated (Ghasemlou et al. 2021). The reaction temperature was one of the parameters studied. CNCs (1 wt%) modified with APTES (10%, w/w, in a proportion of 1:4) presented different performances when exposed to several reflow temperatures: 60, 70, 80, 90, and 100 °C. The superior evidence of the stretching bands attributed to the Si-CH_3 , Si-O-Si , Si-O-C , and NH bonds was obtained during the synthesis performed at 80 °C. Moreover, an extensive reduction in the band of OH groups was found at this temperature since these groups were replaced by carboxylic groups, indicating that the CNCs were modified. For these reasons, 80 °C was the optimal temperature, and an effective silylation reaction was obtained (Indarti and Wanrosli 2020). Shahriari-Khalaji et al. also analyzed the influence of APTES concentration (3, 6, and 9%) and reaction time (1, 2, and 3 h) on BNC modification. It was confirmed that increasing APTES concentration (9% for 1 and

i) Hydrolysis (pH = 4)**ii) Condensation****iii) Grafting with Nanocellulose****Fig. 11** Chemical process involved in the modification of NC with silanes

2 h) showed a higher yield when compared with APTES at 3 and 6% (3 h). Fibers were produced on the surface with three times the diameter of the inner ones, indicating that the chemical modification only occurred on the BNC surface. A reduced reaction period and the concentration of the coupling agent could have influenced this performance. Incorporating pullulan nanofibers and zinc oxide NPs produced by electrospinning as a reinforcement, a BNC-based material with the desired properties for the final application was obtained. The resulting composite, categorized as an optimal bioactive dressing, demonstrated improved mechanical properties. In addition, the permanence of hydrophilicity due to the presence of zinc oxide NPs-pullulan nanofibers, its excellent antimicrobial activity against *Escherichia coli* and *S. aureus* (log reduction >5), hemocompatibility, and biocompatibility (L929 fibroblasts), further enhances its suitability for use in dressing applications. Furthermore, the developed composite exhibited a considerably reduced healing process time of 12 days compared to the Comfeel[®], commercial wound dressing, which required 23 days (Shahriari-Khalaji et al. 2021).

This chemical process is mostly applied to instill hydrophobic properties in NC-based composites. Nonetheless, the high affinity between NC and a wide range of reinforcement matrices promotes improved mechanical, physicochemical, and biological properties. In this regard, silylated NC exhibits wide-ranging numerous fields, namely, biomaterials, adhesives, food industry, coatings, biomedical, nanocomposites, water treatment, and optical devices. Modified NC can also be applied as a biosorbent of heavy metals, dyes, and oils. Chen et al. evaluated a silylation treatment of CNFs/PVA (1:1 w/w) with ethyltrimethoxysilane (ETOS) at room temperature (2 h), followed by freeze-drying (−60 °C for 48 h). The aerogel produced is to be applied to remove oil and control chemical spills in wastewater. The modification avoided the collapse of the aerogel structure, keeping it hydrophobic and structurally stable. After 40 compression cycles, there was a 20% absorption loss, indicating possible reuse. Moreover, the modified nanocomposite showed a selective ability to absorb gasoline and chloroform in an aqueous solution, capturing them in its structure 50–110 times its weight (Chen et al. 2023). From another perspective, NC was modified with APTES (2%, 75 °C, 7 h) to remove formaldehyde, a volatile and toxic organic compound, in urea-formaldehyde adhesives commonly applied in the wood industry. This silylation process was effective since the concentration of nitrogen and silicon increased, which is characteristic of the silane structure. The final composite, unlike the unmodified NC, was able to remove formaldehyde up to 39% (Kawalerczyk et al. 2022). The application in drug delivery systems was also analyzed. Moghaddam et al. used CNCs silylated with APTMS and L-lysine amino acid (carrier) loaded with anticancer drugs (curcumin and methotrexate). When applied to the modified CNCs, the composite showed improved anticancer efficiency in breast cancer cells (MCF-7 and MDA-MB-231), and a controlled release system of both drugs was achieved. Therefore, the developed composite was classified as biocompatible, proving that the silylation promoted the bonding of the bioactive compounds onto the CNCs surface (Moghaddam et al. 2020).

Table 4 Surface modification of the NC through the silylation process

NC type	Other components	Modification method	Properties	Application	References
BNC	Pullulan and ZnO NPs (eletrospun fibers)	APTES + grafting	Hydrophilic (38°) Antimicrobial (log reduction >5, <i>S. aureus</i> and <i>E. coli</i>) Release of ZnO NPs Hemocompatibility Nontoxic (L929 cells) Promotes wound healing (in vivo, 12 days) Good mechanical properties in wet state (elongation at break 29%; tensile strength 0.28 MPa; and Young's modulus 1.25 MPa)	Wound dressing	Shahriari-Khalaji et al. (2021)
CNF	PVA	APTES	Hydrophobic (148°) Oil absorption (50–110 times of their own weight) High compression recovery Thermal stability Good reusability (absorption loss rate of 20% after 40 squeezing cycles) High porosity (98.4%) Low density (10.8 kg/m ³)	Packaging	Chen et al. (2023)
n.d.	Urea-formaldehyde resin	APTES	Formaldehyde-scavenging ability (modified NC contribute to the decrease in the amount of hazardous emission from the urea-formaldehyde adhesive)	Urea-formaldehyde adhesive	Kawalerzyk et al. (2022)
CNC	L-lysine containing curcumin and methotrexate	APTMS	Controlled release Anticancer (MCF-7 and MDA-MB-231 cells) Biocompatibility Hemocompatibility	Cancer therapy	Moghaddam et al. (2020)
CNC	PLA	APTES	Increased crystallinity Thermal stability Reduced air permeability (7.5 µm/pa.s) Increased tensile strength (53.9%) Increased elongation at break (61.5%)	Packaging	Jin et al. (2020)

n.d. – not defined

In addition, CNCs are the type of NC that present the most advantageous mechanical properties. However, increasing the dispersion of CNCs in the polymer matrix promotes interfacial adhesion and improves the affinity with apolar matrices. Thus, Jin et al. silylated CNCs with APTES and incorporated PLA as a reinforcing matrix to facilitate the dispersion of NC. While the thermal and mechanical properties were improved, the achieved dispersion and increased interaction between silane and PLA resulted in a significant 87% reduction in air permeability. Moreover, an excessive concentration of NC + APTES adversely impacts the mechanical properties of the composite. These agglomerations promote the reduction of the contact area between the reinforcement matrix (PLA), originating rough and not very porous surfaces. However, the correct dosage of APTES promoted the compatibility between CNCs-PLA and the production of a composite with mechanical properties suitable for packaging applications (Jin et al. 2020). The above mentioned silylation processes are summed up in Table 4.

Silylation is a simple, cost-effective, and environmentally friendly process. The selection of the silane (type and concentration) and modification approach (temperature, time, and process) enables the production of nanocomposites with tailored properties.

Graft Copolymerization

Graft copolymerization comprises the anchoring or covalent bonding of polymers onto a base or backbone polymer, in this case, NC. The grafting polymerization may occur as: grafting-onto, grafting-from, and grafting-through. In grafting-onto, pre-synthesized polymer chains, called graft polymers, are attached or grafted onto the base polymer. This process typically involves functionalizing the base polymer with reactive groups or sites, which can then react with or chemically bond to the graft polymers. Grafting-from involves initiating the growth of polymer chains directly from the base polymer. It starts by anchoring initiators or initiator sites onto the base polymer. These initiators then initiate the polymerization of monomers, which become grafted onto the base polymer. Grafting-through, also known as macro-monomer grafting, involves incorporating polymerized monomers into the base polymer structure. The base polymer monomers containing the grafted polymers are polymerized within the base polymer matrix, resulting in the growth of the base polymer (Ghasemlou et al. 2021; Sanchez-Salvador et al. 2018; Rana et al. 2021).

To fall within this classification, grafted monomer must be distinct from the base polymer. When the grafted polymer monomers are identical, a graft homo-polymer is obtained. Whereas, when the grafted polymers contain two or more distinct monomers, a graft copolymer is generated. The major advantage of copolymers is their inherent different chemical structures and properties according to the type and ratio of monomers used. Thus, the tailored composition of the copolymers and their intrinsic heterogeneous composition widens the spectra of their properties, making copolymers highly valuable for advanced functionalizations. These functional groups can introduce specific chemical reactivity, provide self-healing properties,

stimuli-responsiveness, enhance compatibility with materials or surfaces, enable cross-linking, or facilitate the attachment of bioactive molecules.

Copolymer grafting onto NC involves attaching or bonding copolymer chains onto its surface. The grafting process can be achieved through a plethora of methods, including chemical reactions and physical interactions. However, during the copolymer grafting of the different types of NC the commonly used grafting methods are grafting-from and grafting-onto, due to the abundance of OH groups at the NC surface, which can be readily used as initiators (Navarro et al. 2016). Moreover, NC surface may be functionalized to provide distinct and stable groups for less favorable grafting reactions onto OH groups. A successful copolymer grafting onto NC was reported using: radical polymerization, controlled/living polymerization, ring-opening polymerization, and click chemistry.

Radical polymerization is known for its simplicity and versatility, and it comprises the following steps: initiation, propagation or growth, and termination. Initiation occurs when the radical initiator generates free radicals by undergoing homolytic cleavage. These free radicals are highly reactive species with unpaired electrons, which ensue the propagation step, where the generated radicals react with monomer molecules. The reactive radical attacks a monomer molecule, removing a hydrogen atom or an electron from the monomer and forming a new radical at the growing end of the polymer chain. This process is repeated, resulting in the sequential addition of monomers to the polymer chain. Termination may unfold through combination or disproportionation. Termination by combination implies that two growing radicals react with each other, and termination by disproportionation occurs when a growing radical reacts with a dormant radical, resulting in the formation of a stable molecule. Graft-on CNFs free radical copolymerization using potassium persulfate as initiator achieved the polymerization of sodium allyl sulfonate (hydrophilic) and trifluoroethyl methacrylate (hydrophobic) monomers. The grafted copolymers provided amphiphilic properties to the CNFs, to be used as an enhanced oil recovery agent to improve the extraction of oil from underground reservoirs (Guo et al. 2019).

Controlled or living polymerization encompasses several methodologies that ensure a defined growth of the polymer chains, with the ability to tailor the polymerization process. This control allows the production of polymers with narrow molecular weight distributions, uniform chain lengths, and specific end-group functionalities. Typically, living polymerizations comprise three stages: (i) initiation, (ii) activation and polymerization, and (iii) deactivation and reversible control. The crucial features of living polymerization are the formation of the dormant polymer species at the end of chains, allied to a rapid activation-deactivation process in comparison to the polymer growth (Satoh 2015). Polysaccharides may be used as macroinitiators for the transition of inorganic and organic transfer agents (reversible addition-fragmentation chain transfer (RAFT), metal catalysts (atom transfer radical polymerization (ATRP)), and mediated controlled radical polymerization by partial substitution of their OH groups (Ghasemlou et al. 2021; Navarro et al. 2016). Using single-electron transfer-living radical polymerization (SET-LRP) CNFs were grafted-from using 2-(3-(6-methyl-4-oxo-1,4-dihydropyridine-2-yl)ureido)ethyl

acrylate and di(ethylene glycol) ethyl ether, to synthesize a gel ink for 3D printing comprising self-healing properties (Dalloul et al. 2023). Another 3D printable gel with electrochemical and magnetic properties was obtained using CNFs grafted-from with stearyl acrylate and cobalt iron oxide NPs through SET-LRP, where 2-bromo-2-methylpropionic acid was used as the initiator (Mietner et al. 2022). CNFs were also grafted-onto using a macroinitiator polymer block composed of methyl acrylate, and a second block acrylic acid N-hydroxysuccinimide ester. The first block hindered the CNFs fibril-to-fibril interaction, and the second was responsible to embed a fluorescent dye, lucifer yellow derivative. This luminescent probe composite was successfully used as a biomarker for the detection of CNFs uptake by living organisms, as proven by its internalization by *Daphnia magna* (Navarro et al. 2016). Table 5 summarizes some works on graft-polymerization of NC.

Table 5 Graft co-polymerization of NC

NC type	Grafting type/ Polymerization	Monomers	Properties	Application	References
CNF	Grafting-from/ ATRP	Methyl acrylate and acrylic acid N-hydroxysuccinimide ester	Luminescent with no toxicity	Fluorescent biomarkers	Navarro et al. (2016)
CNF	Grafting-from/ free radical	Sodium allyl sulfonate and trifluoroethyl methacrylate	Amphiphilic Decreased water surface and water/oil interfacial tension (27.4 and 1.9×10^{-2} mN/m) Decreased critical micelle concentration value (0.33 g/l) Improved emulsification power	Enhanced oil recovery agent	Guo et al. (2019)
CNF	Grafting-from/ SET-LRP	2-(3-(6-methyl-4-oxo-1,4-dihydropyridine-2-yl)ureido)ethyl acrylate and di(ethylene glycol) ethyl ether	Increased mechanical properties Shear-thinning (printability) Self-healing (80 °C, 5 min)	Gel ink for 3D printing with self-healing properties	Dalloul et al. (2023)
CNF	Grafting-from/ SET-LRP	Stearyl acrylate	Thermal stability Magnetic and electrochemical properties Printability	Gel ink for 3D printing with magnetic and electrochemical properties	Mietner et al. (2022)

It is noticeable that graft co-polymerization in NC is still in its infancy, with a handful of recent references describing the polymerization of non-homopolymers. Notwithstanding, the advantages of their application are obvious. The successful use of interesting grafting methodologies using homopolymers is certainly paving the path for the more complex and interesting co-polymers, such as ring-opening polymerization of CNCs and BNC, as bio-reinforcement and aroma protection, respectively (Xiao et al. 2021; Vismara et al. 2019).

Other Chemical Methods

There are additional strategies to modify NC's surface chemically besides the ones already mentioned in this chapter. In this section, other techniques, such as non-covalent modification via surfactants and covalent modifications through sulfonation, amination, amidation, carbamation, carboxymethylation, and fluorination are going to be briefly described.

Non-Covalent Modification Via Surfactants

Non-covalent modification consists in surfactant adsorption that bears an opposite charge from NC, thus interacting through electrostatic attractions, van der Waals forces, or hydrogen bonds (Lunardi et al. 2021). There is a plethora of surfactants, with different overall charges (positive, negative, nonionic, or amphiphilic), which will have different affinities toward NC or already modified NCs, affecting its surface electronegativity (Zhu and Lin 2019). Furthermore, the ratio NC:surfactant, surfactant concentration, and pH will also influence the interactions between them. Surfactant surface modification is generally used to improve NCs dispersibility, for water purification processes (Ivbanikaro and Adeniyi 2023), and also for drug delivery (Lunardi et al. 2021).

Sulfonation

Sulfonation is a chemical process to covalently bond sulfate groups to cellulose, creating the commonly named sulfate half-esters (Ghasemlou et al. 2021). This is commonly achieved by H_2SO_4 hydrolysis, producing CNCs, which will provide a negative charge to the NC surface. The sulfonation reaction conditions, such as time, temperature, and acid concentration, will affect the sulfate moieties at CNCs surface, making the H_2SO_4 hydrolysis somewhat challenging. Nevertheless, the anionic charge will create electrostatic repulsion, which will stabilize the colloidal suspensions, making these CNCs excellent dispersants (Raza and Abu-Jdayil 2022). Thus, sulfonated CNCs are often used in the production of conductive inks (Feng et al. 2021; Feng et al. 2022). Furthermore, sulfonated NCs can be applied as intermediaries to covalently bond other organic molecules, such as aminoacids, to instill antiviral properties (Hu et al. 2023).

Amination and Amidation

For the surface modification of NC via either amination or amidation, NC needs an oxidation process as pretreatment. In the amination process, the NC OH groups are oxidized, generally through periodate oxidation, into aldehydes (generated at C2 and C3). Afterward, the NH groups (primary, secondary, or tertiary) react with the aldehyde groups (Qiao et al. 2021; Padrão et al. 2020). In the case of amidation, NC OH groups are also oxidized, commonly via TEMPO-mediated oxidation, which will convert the OH groups to carboxylic units. With the addition of an NH and a coupling agent, the amide bond is formed through a carbodiimide-mediated reaction (Ghasemlou et al. 2021). Both TEMPO and periodate oxidation can be consulted in more detail in section “Oxidation” of this chapter.

Depending on the pH, aminated NCs can be used to absorb anionic dyes and metals (very acidic pH) or cationic metals (slightly acid or neutral pH), in water remediation (Qiao et al. 2021). As for amidated NCs, they can be used to synthesize NC composites with different physical (Ghasemlou et al. 2021; Ryu et al. 2019) and chemical (Calderón-Vergara et al. 2019; Majdoub et al. 2021) properties from the original NC.

Carbamation

Carbamation is the chemical process to covalently introduce more reactive groups onto the NC surface. This can be achieved through the usage of isocyanates. Depending on the objective of the modification, different isocyanates are used (Abushammala and Mao 2019). Mono-isocyanates with long alkyl chains are commonly used to hydrofobize NC's surface. Di-isocyanates can be utilized in three different synthesis pathways, since they will have one free isocyanate group to react with other molecules, after the other one is bonded to the NC. In the first route, a two-step reaction can be performed, where the di-isocyanate reacts first with the NC, and then an organic molecule capable of reacting with the isocyanate group is added to the functionalized NC. In the second route, also a two-step reaction, firstly the organic molecule is covalently bonded to the di-isocyanate, which then is bonded to the NC in the next step. This route is preferred over the first one since it is more efficient, and it will prevent both ends of the di-isocyanate to react with NC OH groups. The third route involves a one-pot reaction, where the di-isocyanate, the NC, and the targeted organic molecule are cross-linked at the same time, this process being often used for the synthesis of polyurethanes.

Carboxymethylation

Carboxymethylation is generally used as an oxidative pretreatment of NC, followed by esterification, amidation, or other processes that require a carboxylic acid group to covalently bond other molecules. It consists in introducing carboxymethyl groups, via etherification of NC's OH groups with monochloroacetic acid, charging NC's surface negatively (Almeida et al. 2023). Similar to what occurs in sulfonation, the negative charge at NC surface will create electrostatic repulsions, improving NC's dispersibility and water retention. TEMPO-mediated oxidation is usually preferred

over carboxymethylation due to monochloroacetic acid toxicity (Raza and Abu-Jdayil 2022). Nevertheless, this process facilitates nanofibrillation of lignocellulosic fibers, which can be utilized as stabilizing agents (Kumar et al. 2019) or in encapsulation processes (Kadry 2019).

Fluorination

Through fluorination, NC can be converted into a hydrophobic nanocomposite suitable for different water treatment applications, including efficiently removing heavy metals, dyes, and oils. The incorporation of fluorine groups into the NC structure leads to a reduction in adhesion and surface tension. Additionally, the high electronegativity of fluorine enables the formation of stronger covalent bonds between the fluorinated NC and the reinforcing matrix (for more details, check section “Silylation”), enhancing the overall performance of the composite material (Iqbal et al. 2022).

Fluorination is commonly employed with silanes/organosilanes modification, identified as fluorosilicone, to attain a long-lasting superhydrophobic effect (Zhan et al. 2023). Nevertheless, it is crucial to explore alternative techniques due to the potential disadvantages of fluorinated materials. These disadvantages include toxicity, limited sustainability, and potential environmental harm (Iqbal et al. 2022).

Physical Modifications of NC

Several physical techniques can be used for the surface modification and functionalization of NC, including heat treatment, gamma radiation, and plasma treatment.

Heat Treatment

Heat treatment can change the fiber structure and improve hydrophobicity. Thermal annealing (100–150 °C, 1 h) of CNCs incorporated into Nafion membranes, led to a small decrease in water uptake capacity, protonic conductivity, ion exchange capacity, and hydration number of the films (Hambardzumyan et al. 2022). Heat treatment of 2,2,6,6-tetramethylpiperidiny-1-oxy radical-oxidized CNFs (TEMPO-CNFs) films at 100 °C, 150 °C, and 200 °C with a 3 h duration each. These treatments influenced the optical and mechanical properties, as the color changed from transparent (room temperature and 100 °C) to yellow (150 °C), and light brown (200 °C). Near-complete UV-blocking ability was verified for samples treated at 150 °C and 200 °C. Discoloration due to thermal treatment has been attributed to the carbonyl and carboxyl functional groups of pure cellulose, which can initiate the formation of chromophores, especially in oxidized cellulose nanomaterials such as TEMPO-mediated. Besides, the formation of hydrophilic groups caused by thermal degradation is also implied in the contact angle measurements, which showed a considerable decrease in films treated at 200 °C (WCA of 35°). A reduction in strength and strain was noticeable at higher temperatures (Niskanen et al. 2022).

Gamma Radiation

Different types of radiation, such as gamma, UV, and microwave, can be employed to achieve surface modification of NC. Gamma radiation is used for sterilization but can also be applied to induce physical or chemical modifications. During exposure to gamma radiation (high-energy-ionizing radiation), the surface of this biopolymer becomes ionized through the collision of the atoms present in the NC and the radiation rays at the atomic and molecular levels. Subsequently, reactive radicals and ions are produced through water hydrolysis, performing as initiators to facilitate subsequent surface chemical modifications (e.g., oxidation, grafting, and cross-linking). The preferential formation of the radical in the CH group, rather than the OH group, can be attributed to the electropositivity associated with the former (Fig. 12). This process is widely employed for reinforcing hydrophobic composites for several applications, including biomedical (antimicrobial materials, drug delivery, wound dressing, tissue engineering, and skin substitutes), nanocomposites, water treatment, and packaging. Nevertheless, degradation of NC may occur depending on the dosage and exposure time. The mechanical properties undergo alterations when subjected to high ionizing radiation, with evidence suggesting that values exceeding 15 kGy decrease this particular property (Barsbay and Güven 2019).

The application of gamma radiation as a physical surface modification takes a prominent position due to the low degree of complexity and the fact that it does not require chemical and toxic products (e.g., solvents, cross-linking agents, and initiators). Ishak et al. evaluated the production of a gelatin/CNCs hydrogel cross-linked by gamma radiation, applied in drug delivery. The gamma radiation improved the composite's mechanical properties, which was classified as a green process. The suitability of gamma radiation for sterilization allows for flawless integration within the given application (Wan et al. 2021). Therefore, within the biomedical field, an assessment was conducted on a hydrogel/wound dressing formulation composed of CNFs, poly(acrylic acid), and graphene oxide. This formulation aimed to enable the noninvasive detection of urea in sweat through a color shift. Applying gamma radiation-induced cross-linking at 25 kGy considerably enhanced the compressive properties of the nanocomposite. In addition, the incorporation of graphene oxide

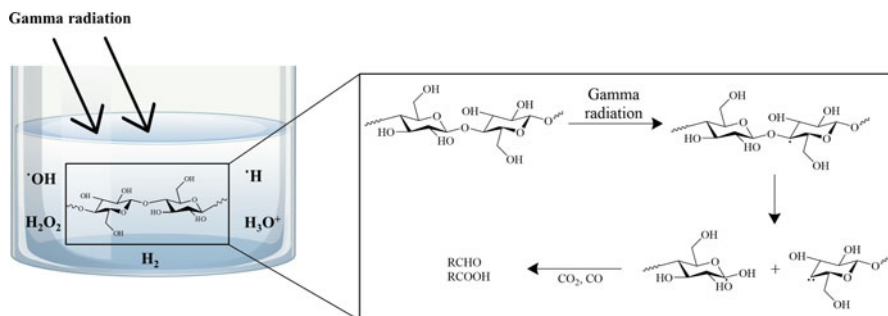


Fig. 12 Process involved in the physical modification of NC with gamma radiation

facilitated the detection of urea, providing an alternative to the invasive methods typically employed for this purpose (Passornraprasit et al. 2022). Moreover, gamma radiation modification can enhance or augment a polymer's antioxidant properties by enabling radical scavenging. Thus, Criado et al. successfully produced a CNCs composite with antioxidant properties by inducing the formation of aldehyde groups during treatment, employing different doses of gamma radiation (10, 20, 40, and 80 kGy). Furthermore, the composite's hydrophilic nature remained unaffected due to the substantial generation of carboxylic groups during the physical modification process. These improvements can find applications in food preservation packaging (Criado et al. 2017). This type of modification can occur during the production of NC, namely, Al-Hagar and Abol-Fotouh analyzed gamma radiation's influence on BNC's production yield. After 240 h of incubation, a yield of 475% was found when exposed to a lower dosage dual radiation (0.5 kGy). Applying gamma radiation enhanced the proliferation rate of the bacteria and their production efficiency (Al-Hagar and Abol-Fotouh 2022). Table 6 summarizes some works carried out on surface modification of the NC through the gamma radiation process.

Table 6 Surface modification of the NC through the gamma radiation process

NC type	Other components	Gamma radiation dose	Properties	Application	References
CNC	Gelatin and riboflavin	30 kGy	High swelling ($\approx 1000\%$) Controlled release of riboflavin ($\approx 72\%$ in 12 h) Noncytotoxic (L929 cells)	Drug delivery systems	Wan et al. (2021)
CNF	Poly (acrylic acid) and graphene oxide	25 kGy	High swelling (≈ 74 g/g) Good adhesion Good mechanical properties Laser absorptivity (52.8°) Urea detection (40–80 mM)	Urea sensing patch	Passornraprasit et al. (2022)
CNC	–	80 kGy	Hydrophilic (34°) Antioxidant (equivalent to $80 \mu\text{M}$ of ascorbic acid)	Packaging	Criado et al. (2017)
BNC	–	0.5 kGy	Porous ($0.19 \text{ cm}^3/\text{g}$) High absorption capacity (116 g/g) Tensile strength (61 MPa) Elongation at break (4.4%) Young's modulus (19 MPa)	Increase BNC production	Al-Hagar and Abol-Fotouh (2022)

Overall, the application of gamma radiation for modification purposes can serve multiple purposes, such as: (i) improving the yield of the BNC fermentation process, (ii) increasing properties that are not inherent to NC, and (iii) performing as a preliminary process through the production of initiators that will facilitate subsequent chemical processes, namely, grafting and cross-linking.

Plasma Treatment

Plasma treatment is an eco-friendly, cost-effective, and efficient fast-growing technique for the surface modification and functionalization of cellulose materials. This technique allows for controlled surface modification while preserving the bulk properties of the polymers. Plasma is generated by applying high-voltage electrical discharges to a gas where its molecules are ionized or excited, resulting in a reactive media, mainly composed of electrons, ions, atoms, free radicals, and excited molecules. Here, chemical reactions occur without harmful catalysts or chemicals, thus being a fast and solvent-less modification. It overcomes the drawbacks of polluting, time-consuming, and complex chemical modification methods (Salimi et al. 2019; Bangar et al. 2022; Oberlintner et al. 2022; Matouk et al. 2020). The interactions of the plasma with the surface of polymeric materials can result in different effects, including (i) surface etching or cleaning; (ii) formation of functional groups; (iii) deposition of a coating layer by plasma polymerization of a precursor; and (iv) graft-polymerization (Matouk et al. 2021) (Fig. 13). In plasma functionalization, several different inert or reactive gases can be used, which affect the amount and type of surface functional groups formed on the polymer surface (Żywicka et al. 2023).

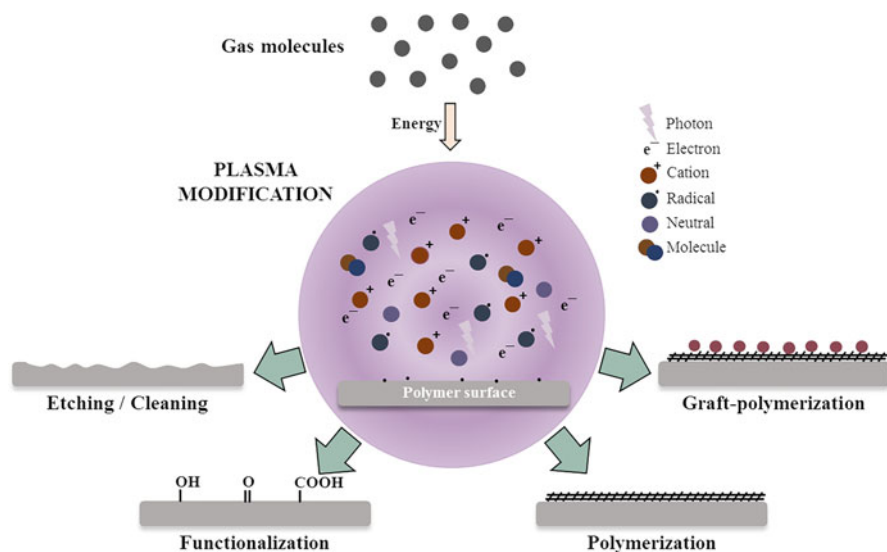


Fig. 13 Plasma-assisted surface modifications

The high inherent wettability of NC often hinders its use in several applications, including transportation and food-industry-related packaging. Therefore, Oberlintner et al. increased the CNFs surface hydrophobicity by exposing CNFs films to tetrafluoromethane (CF_4) plasma (Oberlintner et al. 2022). Within 10 s the films were converted from hydrophilic (initial WCA of 46°) to hydrophobic ($\text{WCA} > 90^\circ$) and it reached a plateau after 30 s of exposure with a WCA of 130° . These results are owed to the nanoporosity induced by plasma, which affected the surface tension between the water and the CNFs and the fluorine groups formed on the NC fibers' surface.

Argon is the most common inert gas used in plasma treatment due to its properties such as good thermal conductivity and low electron affinity, ionization energy, and rate of electrode erosion (Żywicka et al. 2023). Matouk et al. functionalized CNCs films employing dielectric barrier discharge plasma using different gaseous precursors: argon/methane (Ar/CH_4), argon/ammonia (Ar/NH_3), and argon/silane (Ar/SiH_4) (Matouk et al. 2020). The results showed that plasma did not affect the quality of the CNCs films in terms of crystallinity, and the wettability can be changed by altering the elemental chemical composition and/or roughness of the CNCs, depending on the gas mixture. The exposure to Ar/NH_3 plasma increased the CNCs films' hydrophilicity due to the formation of polar groups and increased surface roughness. In contrast, the exposure to Ar/CH_4 plasma led to a hydrophobic surface due to the creation of CH_xO_y coating on the CNCs film surface and the decrease of the surface roughness. Meanwhile, exposing the CNCs films to Ar/SiH_4 plasma yields a superhydrophobic coating due to the formation of SiO_2 groups on the CNCs film surface. The authors propose the application of these CNCs films in the development of packaging where the outer layer can be treated by Ar/CH_4 or Ar/SiH_4 plasmas to enhance the oxygen barrier and resist water, and then it can be made more hydrophilic by exposing it to Ar/NH_3 plasma to allow printing. In another work, the surface hydrophilicity of CNCs was reduced using plasma treatment to improve their dispersion in polar organic solvents (Matouk et al. 2021). A cylindrical atmospheric pressure dielectric barrier discharge was employed to functionalize CNCs using three different gas mixtures: Ar/CH_4 , Ar/SiH_4 , and an Ar/CH_4 followed by Ar/SiH_4 . The plasma treatment did not affect the CNCs' crystallinity but the hydrophobicity was improved after the Ar/SiH_4 plasma treatment (WCA of 150°), which enhanced its dispersibility in polar solvents.

Plasma-induced polymerization is different from the plasma surface treatment. While in the latter one, the plasma changes the chemical structure of several outermost molecular layers on the organic material, in plasma polymerization a nanometric polymeric film is deposited on the surface (Bangar et al. 2022). The ionized and excited molecules and radicals produced by plasma can be used to polymerize a wide range of monomers on NC surfaces. Alanis et al. functionalized CNCs utilizing monomers of different natures: caprolactone, styrene, and farnesene, which were successfully grafted on the CNCs by plasma-induced polymerization (Alanis et al. 2019). The polymer chains grow through a mechanism of free-radical polymerization that is initialized by the species created on the plasma-exposed surface. The modification did not alter the natural rod-like structure of the CNCs. Meanwhile, when

employed as a reinforcement additive in the polymer matrix acrylonitrile-butadiene-styrene (ABS), the modified CNCs significantly enhanced the impact resistance of ABS (114%), confirming the improvement of the compatibility.

The use of BNC mainly focuses on biomedical applications as it is nontoxic, biocompatible, and presents a porous three-dimensional structure that closely mimics the inherent complexity and hierarchical structure of native tissues (Aditya

Table 7 Surface modification of the NC through plasma treatment

NC type	Other components	Gas or monomer (flow rate, time)	Properties	Application	References
CNF	Glycerol	CF ₄ (80 sccm, 30 s)	Hydrophobic (130°)	Packaging	Oberlintner et al. (2022)
CNC	–	Ar/CH ₄ (200 sccm, 18 min), Ar/NH ₃ (200 sccm, 60 min), and Ar/SiH ₄ (5100 sccm, 3 min)	Hydrophobic (100°, Ar/CH ₄) Hydrophilic (8°, Ar/NH ₃) Hydrophobic (150°, Ar/SiH ₄)	Packaging	Matouk et al. (2020)
CNC	–	Ar/CH ₄ , Ar/SiH ₄ , and Ar/SiH ₄ /CH ₄ (0.5 L/min, ≈ 6 s)	Hydrophilic (80°, Ar/CH ₄) Hydrophobic (150°, Ar/SiH ₄) Hydrophobic (140°, Ar/SiH ₄ /CH ₄)	n.d.	Matouk et al. (2021)
CNC	ABS	Styrene, caprolactone, or farnesene (1 h)	High impact resistance (4.0 ft-lb/inch)	n.d.	Alanis et al. (2019)
BNC	–	Ar (240 s)	High specific surface area (156.3 m ² /g) High porosity (0.308 cm ³ /g) Biocompatibility and cell adhesion (HaCaT cells)	Skin tissue engineering and wound healing	Kutová et al. (2021)
BNC	–	Ar (10 sccm, 10 min)	Excellent antimicrobial and antiviral (>99% - <i>S. aureus</i> , <i>E. coli</i> , and phage Φ6) Noncytotoxic (L929 cells) Viral filtration efficiency (>99%)	Filters for surgical masks and respirators	Żywicka et al. (2023)

n.d. – not defined

et al. 2022). To improve the cell adhesion on BNC membranes, Kutová et al. studied the effect of the drying method (air-drying or lyophilization) of BNC and subsequent modification with argon plasma on the adhesion and growth of human keratinocyte cells (HaCaT cell line) (Kutová et al. 2021). Their results showed that lyophilized samples maintained their nanostructure, and had higher porosity and specific surface area when compared with air-dried samples. After the plasma modification, the WCA decreased, and the porosity and specific surface area increased for all samples. Furthermore, the cell culture experiments revealed that the modification with argon plasma for 240 s markedly accelerated the formation of typical HaCaT keratinocytes islands and the continuous growth of cell layers on both samples.

In a recent work carried out by Zywicka et al., low-pressure argon plasma was used to functionalize BNC previously homogenized and lyophilized for the production of sustainable filters that can be used as masks (Żywicka et al. 2023). The argon plasma-modified BNC maintained adequate airflow resistance (6 mbar at an airflow of 95 L/min) and showed excellent antimicrobial properties (>99%) and viral filtration efficiency with >99% reduction in the activity of phage $\Phi 6$, which is explained by the presence of ROS on the surface of argon-modified BNC. No cytotoxicity was observed using L929 murine fibroblasts and the effect was maintained for over 12 months of storage. These filters offer a bio-based, biodegradable, sustainable, and safe alternative to existing materials used in face masks and respirators. Table 7 summarizes some works carried out on surface modification of the NC through plasma treatment.

Conclusion

Technological revolutions focused on the advanced development of sustainable and green materials are warranted to cope and mitigate climate change, which will ultimately leave our planet barren and inhospitable. Therefore, bio-based materials capable of outperforming conventional (and more polluting) materials are on a critical high demand. NC must have a privileged place in this revolution, not only due to its inherent properties but also, in particular, due to the recent developments for its modification. This chapter further underscores the importance of NC modification for the expansion of cutting-edge functionalities as well as multifunctional materials. The encompassed modifications were divided into chemical and physical modifications. Esterification and silylation of NC via multiple reactions were mainly focused on the hydrophobization of NC. This hydrophobization widens the range of application of NC, potentiating the barrier and loading properties of NC. Thus, novel biomedical applications and food industry applications may be successfully implemented, such as wound dressings, hydrophobic drug delivery, and active packaging. Oxidation of NC is a straightforward and intensively applied methodology to obtain, pretreat, activate and functionalize NC, usually through the use of nontoxic chemicals and mild conditions. Oxidation further improves hydrophilicity of NC, improving dispersibility, enhancing mechanical properties, and may be used as an initiator for a wide palette of subsequent modifications, namely, amination and

amidation. Graft copolymerization, where the graft polymers are composed of more than one monomer, distinct from the NC (base polymer), represents a promising area of research, with several methodological challenges due to their relative novelty. Moreover, the obtained complex composites display interesting activities that should be further explored. The physical modifications possess an important advantage, which is the absence of chemicals, and subsequent generation of wastewater. Nevertheless, it should be highlighted that the (sometimes intensive) energy required for these modifications should be copulated to a renewable energy system. Physical modifications improve hydrophobicity and reactivity of NC. Furthermore, gamma radiation is able to improve the mechanical and swelling properties of NC and simultaneously sterilize it. One of the most promising physical modifications, due to the enormous scope of functionalization potential, is plasma-induced polymerization, which is still yet considerably unexplored, in particular in NC applications. Interestingly, an application that is nearly transversal to all modifications is the development of food packaging, which is in line with United Nations Sustainable Development Goal 2 (SDG 2), which comprises the improvement of food safety and extended shelf life.

Finally, it should be highlighted that the number of works focused on CNFs is increasing in comparison to CNCs. This may be due to the CNFs simple production methodology and superior properties in comparison to CNC. Nevertheless, the sustainability and outstanding properties of BNC should be further explored in future applications, as this highly relevant NC has not yet gained considerable prominence.

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