Cellulose Nanocomposites: Fabrication and Biomedical Applications

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\textbf{A B S T R A C T}

Cellulose is a linear biopolymer which is composed of nanofibrils, thus having a large surface area. This low-cost, low-density, high-specific-surface-area, easily processable polymer is found in nature in the form of plants, bacteria and tunicates. Cellulose has outstanding characteristics including low cytotoxicity, biocompatibility, good mechanical properties, high chemical stability, and cost effectiveness which make them suitable candidates for biomedical applications. The manipulation of cellulose at nanoscale resulted in nanocellulose having exceptional physicochemical properties. Therefore, cellulose nanocomposite is a fascinating area of research which has applications in biomedical fields like wound healing, bone tissue engineering, three dimensional printing, drug carriers, medical implants etc. This review is mainly focused on the developments in the generation of cellulose nanocomposites and their potential applications in the biomedical field.

1. Introduction

As the demand for ecofriendly materials surges, it is expected that biopolymers will drive the industrial needs putting forward sustainable solution for replacing synthetic polymers. Several studies are focused on developing value-added products from natural polymers like chitin, cellulose, alginate etc. In particular, cellulose has found profound applications in biomedical field due to its biocompatibility and biodegradability. Being the most abundant polymer on earth cellulose is widely distributed over a variety of sources, including plants, algae, tunicates, and some bacteria such as Acetobacter xylinum (Blessy Joseph et al., 2018). It is the main component of plant cell wall. Cellulose has the strong affinity to self-associate and form extended structure, by the formation of intramolecular and intermolecular hydrogen bonds, due to the presence of strong interacting hydroxyl groups (Jorfi and Foster, 2015). Cellulose is formed from the repeating units of D-glucose, linked through glycosidic linkages \(\beta(1\rightarrow4)\) (Bezerra et al., 2015). Nanostructured cellulose referred to as nanocellulose comprise properties of cellulose and nanomaterials. Thus nanocellulose having high aspect ratio, improved mechanical properties, renewability, and biocompatibility is used for advanced and novel applications in tissue engineering, drug delivery, wound healing and so on. According to a recent report by global market insights nanocellulose market size was close to 146.7 million dollar (USD) in 2019 and will grow at a compound annual growth rate (CAGR) of 21.4% from 2020 to 2026 (Kiran Pulidindi, 2020). Nanocellulose is generally considered as a potential reinforcing filler for manufacturing composites as they are renewable, possess lightweight and is cost effective. They also find immense applications in drug delivery systems and as scaffolds in tissue engineering. The ubiquitous properties of nanomaterials depend on their source of extractions, processing methods and other environmental factors. Natural biomass like, wood, jute, flax, hemp, fruit waste has been exploited in large scale for nanocellulose extraction (Chirayil et al., 2014; Atiqah et al., 2019; Pai et al., 2020). There are three main classes of nanocellulose (a) cellulose nanocrystals (CNCs) or cellulose nanowhiskers (CNWs) also known as nanocrystalline cellulose (NCC), (b) cellulose nanofibrils (CNFs) or nanofibrillated cellulose (NFC) or microfibrillated cellulose, and (c) bacterial cellulose (BC or microbial cellulose). The review gives a brief...
idea about the research and development pertaining to cellulose nanocomposites, characteristics and their biomedical applications.

2. Types of Cellulose

The four different polymorphs of cellulose are: Cellulose I, Cellulose II, Cellulose III and Cellulose IV. Cellulose I also known as native cellulose exists in parallel sheet without inter-sheet hydrogen bonding. Cellulose II or regenerated cellulose is obtained by soaking native cellulose in alkali. They are prone to more structural changes. However, they are thermodynamically more stable and exist in antiparallel strains with inter-sheet hydrogen bonding. The changes in crystal structure are responsible for difference in properties for Cellulose I and Cellulose II. The Cellulose III is an amorphous form which is obtained by treatment of Cellulose I or Cellulose II with amines. The Cellulose IV is obtained after treatment of Cellulose III with glycerol at very high temperatures (Klemm et al., 2011; Nunes, 2017). Based on chemical nature, cellulose can be classified as cellulose ester and cellulose ether. Cellulose esters are obtained from natural cellulose on reaction with organic acids, anhydrides or acid chlorides. Their use is limited because of its moisture sensitivity and high processing temperature (Edgar, 2004). Cellulose ether is polymers obtained by chemical modification of cellulose soluble in aqueous or organic media. Cellulose acetate, cellulose propionate, cellulose triacetate and cellulose nitrate make up cellulose ether whereas methyl cellulose, ethyl cellulose, hydroxyl propyl cellulose, hydroxyl propyl methyl cellulose and carboxy methyl cellulose make up cellulose ethers (Majewicz et al., 2002).

3. Structure and Properties of Cellulose

Cellulose, one of the main constituents of the plant cell wall is the most versatile biopolymer on the earth. It is a linear polysaccharide, composed of D-glucose units linked via β(1→4) bonds. It is nontoxic, biodegradable and has high tensile strength enabling it to be applicable in diverse fields. Cellulose can sustain its semi-crystalline state of aggregation even in water, unlike other polysaccharides. The important characteristics of cellulose like degradability, chirality, hydrophilicity, chemical variability can be attributed to its molecular structure. Cellulose fibers are crystalline due to superior hydrogen bonds. The hydrogen bonds between hydroxyl group networks, form the cellulose structure which is a significant area of research (Kumar Gupta et al., 2019).

Cellulose structure is formed by the D-glucopyranose units in the 4C1-chair conformation, which shows the lowest energy configuration. The β(1→4) glycosidic bonds connect these structural units causing an alternate turning of the cellulose chain axis by 180°. Inside the cellulose chain, for every anhydroglucose unit (AGU), three hydroxyl groups exist with high reactivity. A primary hydroxyl group is present at C6, and two secondary hydroxyl groups are placed at C2 and C3 carbon atoms in the plane of the ring. The one chain end of the cellulose is nonreducing end involving anomic C atom bonded by glycosidic linkages, and the other chain end is reducing end consisting of a D-glucopyranose unit in equilibrium with the aldehyde function. The strong hydrogen bonding systems in cellulose causes the crystallinity, reactive hydroxyl groups, insolubility in most solvents properties of cellulose. Around carbon atoms, cellulose also possesses hydrophobic regions capable of controlling its properties. Intramolecular as well as intermolecular hydrogen bonds are formed by the interaction of oxygen atom of glucopyranose ring, three hydroxyl groups of AGU and glycosidic bonds with each other within the cellulose chain or with the adjacent chain. These hydrogen bonds create different three-dimensional arrangements. Besides β glycosidic bonds, the intramolecular hydrogen bonds result in the stiffness of the cellulose. From the previous Infrared and 13C spectroscopic studies, it was concluded that the intramolecular hydrogen bonds forms from the interaction of OH group at C2 carbon atom and the oxygen atom of adjacent AGU unit along with those between the oxygen atom of OH group at C6 and adjacent OH groups linked to C2. Therefore, highly viscous solutions are formed from cellulose and it also has a huge tendency to crystallize. The strong interactions between cellulose chains are due to intermolecular hydrogen bonding. Between the neighbouring cellulose molecules, these bonds are formed along the (0 0 2) plane of the crystal lattice of Cellulose I, i.e., native cellulose, usually between the oxygen atom in C3 and the hydroxyl group at C6. The hydrogen bonding, hydrophobic interactions and weak C—H—O bonds cause the assembly of cellulose in layers as shown from the previous x-ray and neutron diffraction experiments. Cellulose I is produced in nature and Cellulose II being allomorph has different hydrogen bonding. In Cellulose II, intermolecular hydrogen bonding exists between the hydroxyl groups of C6 and C2 of another chain, no intramolecular bonding of hydroxyl in C2 and intermolecular hydrogen bonding occurs between C2-OH and C3-OH of next chain. The Cellulose II are densely pack and strongly bond which implies that they are thermodynamically stable and less reactive in comparison to Cellulose I (Lenz, 1994). In general, cellulose is found in two polymorphs, cellulose Iα and cellulose Iβ and both forms occur in bacteria and plants. But, Iα form mainly occurs in
bacteria whereas $I\beta$ form in plants. In these polymorph forms, chains are stacked in parallel bundles. In $I\alpha$ form sheets are directly stacked upon each other, but in cellulose $I\beta$ form stacked sheets are offset between alternating layers. In both polymorphs, hydrogen bonds are formed between intra layer chains, but only van der Waals forces act between sheets (Hangasky et al., 2020).

Cellulose forms the primary component of plant fibers, surrounded by lignin and hemicelluloses. In plant cell wall, cellulose chains are arranged as fibrils which further assemble to form microfibrils possessing diameters of few nanometers. The ordered arrangement of microfibrils is shown in (Fig. 1a). Top down approaches are used for the conversion of cellulose to various macro and nanoscale materials. The CNF, CNW also referred to as CNC or NCC and BC are the different nanostructures of cellulose. Various mechanical, chemical, enzymatic and biological methods are used for the extraction of nanocellulose (Fathi et al., 2019).

The CNFs are colloidaly stable with a diameter of 5-50 nm and length of few micrometers which contain both crystalline and amorphous regions (Chakrabarty and Teramoto, 2018). High aspect ratio of the CNF results in shear thinning and thixotropic behaviour (Nechyporchuk et al., 2016; Yang et al., 2019). Various methods of CNF isolation include high pressure homogenization, grinding, ultrasonication and refining (Azeredo et al., 2017). The CNWs also known as cellulose nanocrystals are needle like or rigid rod like nanowhiskers as shown in Fig. 1b with a width of 5-70 nm and length of 200-500 nm with sulphate group at surface. The morphology depends on the source of cellulose. The characteristic properties of the CNW are ultrahigh strength, high aspect ratio, low thermal expansion, high specific surface area, high bending strength, low density and self-assembling in liquid (Azzam et al., 2010; Klemm et al., 2011). The CNW extends application as emulsifier, filler, stabilizer, thicker in food and pharmaceutical areas (Kian et al., 2018). The BC is a purer 3D network of ultrafine cellulose fibrils with comparatively less amount of carboxyl and carbonyl moieties and with no hemicellulose and lignin (Wondraczek and Heinze, 2014). An important characteristic feature of bacterial cellulose is in situ moldability (Klemm et al., 2001). Other significant properties of the BC are high crystallinity, water absorption capacity and excellent mechanical strength. Polymerization value of the BC ranges up to 10 000 (Yoshinaga et al., 1997). The BC cellulose sheet possesses application in the treatment of wound healing (Czaja et al., 2006). Schematic representation of bacterial cellulose is given in Fig. 1c.

Fig. 1  Cellulose contained in plants or trees has a hierarchical structure from the meter to the nanometer scale, as shown in (a). A schematic diagram of reaction between cellulose and strong acid to obtain nanocellulose is shown in (b). Bionanocellulose cultured from cellulose-synthesizing bacteria is shown in (c) (Miyashiro et al., 2020). Reproduced with permission from Multidisciplinary Digital Publishing Institute (MDPI).

3.1. Properties of cellulose

3.1.1. Solubility

Special procedures must be devised to determine the solubility of cellulose because of the presence of hydrogen bond. Solvents are classified into two types, derivatizing solvents which forms covalent bonds and non derivatizing solvent which interact
physically. Formable stable cellulose derivative can dissolve cellulose as cellulose nitrate is soluble. On a large scale, a mixture of copper hydroxide and ammonia followed by precipitation in dilute sulphuric acid can be used to dissolve cellulose (Heinze, 2015). The most commonly used solvents for cellulose are binary mixtures of organic liquids or inorganic or organic electrolytes. The characteristic features required for dissolution of cellulose are solubility of a sufficient amount of electrolyte in the organic liquid, adequate stability of the electrolyte/solvent complex, cooperative action of the solvated ion-pair on cellulose hydrogen bonds and finally sufficient basicity of the anion (Heinze, 2015). The solubility of cellulose is quick in acetone/triethylcellooctylammonium chloride mixture and dimethyl sulfoxide (DMSO) and tetra-n-butyl ammonium fluoride × 3H2O mixture with no preactivation of cellulose (Gerick et al., 2011).

The ionic liquids used for dissolving cellulose are N-alkylpyridinium halides, especially N-ethylpyridinium chloride and N-benzylpyridinium chloride, benzyl dimethyl(tetradecyl)-ammonium chloride and salts of 1-alkyl-3-methylimidazolium (Swatloski et al., 2002). The solubility in ionic liquids is directly proportional to the length of alkyl chain. However, this effect is not pronounced with the increase in alkyl chain which implies that odd-even effect is observed for short alkyl chains (Erdmenger et al., 2007). Ionic liquids possess certain demerits and more studies need to be carried out. Cellulose is found to dissolve at an aqueous solution of sodium hydroxide at a concentration of 7%–10% below 268 K. Recently, it is reported that cellulose possesses the ability to dissolve in a mixture of aqueous base of urea and thiourea (Zhou and Zhang, 2000; Cai and Zhang, 2005; Cai et al., 2006; Egal et al., 2008). However, the solution is unstable and sensitive to various parameters such as temperature, storage time (Cai and Zhang, 2006).

3.1.2. Mechanical properties

Mechanical properties of cellulose are defined by both crystalline and amorphous regions and are higher than others due to its uniform distribution. Removal of hemicelluloses results in improvement of mechanical properties (Fathi et al., 2019). The amorphous and crystalline region of the CNW elicits unique properties, where the stiffness and elasticity are characterized by crystalline region. Amorphous region is responsible for flexibility and plasticity. However, crystalline region is more compared with other nanostructure resulting in higher stiffness (Lin and Dufresne, 2014). The CNF shows both crystalline and amorphous regions. The Young’s modulus of crystalline cellulose was found to be around 100–200 GPa and modulus of bacterial cellulose was 114 GPa. Therefore, the nanocellulose is used as load bearing material for various substances (Lin and Dufresne, 2014). Li et al. (2013) reported an interesting study utilizing top-down strategy for the preparation of nano-wood by direct chemical treatment of natural wood. Nano-wood comprising of aligned cellulose nanofibrils exhibited high mechanical strength of ~13 MPa. This enhanced mechanical properties are related to the crystalline ordering of the glucan chains of the cellulose fibrils (Li et al., 2018). The mechanical properties of cellulose nanopapers were compared with those of printing paper and multiwalled carbon nanotube (MWCNT) based bucky paper. Nanopapers made from the CNF and bacterial cellulose had much higher mechanical strength than printing paper and bucky paper due to strong inter-network interactions and dense microstructure. The CNF nanopaper had an ultimate strength of (196 ± 22) MPa whereas the BC nanopaper showed a lower tensile strength of (151 ± 21) MPa (Mao et al., 2017).

3.1.3. Chemical properties

Hydroxyl groups linked by hydrogen atoms play a crucial role in forming crystalline and fibrillar packs (Fathi et al., 2019). Based on distinct functional groups such as sulfate, carboxyl, aldehyde, amino, and thiol, cellulose nanocrystals have different charged properties. Cellulose nanocrystals having sulfate or carboxylate groups have negative charge, whereas cellulose nanocrystals with amino groups have positive charge. Homogenous sulphation of cellulose in ionic liquids can tune the properties of cellulose sulphate by altering the amount of sulphating agent. Minor polymer degradation takes place when the reaction is conducted at room temperature (Gerick et al., 2009).

Hydroxyl groups are the most reactive groups. The position of OH group at 2 and 3 is responsible for the solubility of the polymer. In addition, amino cellulose having OH at secondary positions are water soluble whereas esterified polymer derivative are soluble in organic solvent (Heinze, 2015). The distance of the terminal NH2 groups from the cellulose backbone can affect the basicity, and reactivity. Moreover, di- and oligoamines result in various properties such as pH value and charge distribution, control of hydrophilic/lipophilic balance, and redox-chromogenic properties (Jung and Berlin, 2005). Shear thinning behaviour is affected by the carboxylic group. Thus, higher polymerization results in increased shear rate which finally reduces the viscosity (Mondal, 2017).

3.1.4. Biological properties

Biocompatibility is the property of foreign body to remain in harmony with tissue without causing a subtle change (Dugan et al., 2013). Cellulose is an inert broadly biocompatible polymer which remains as such in human digestive system because of the lack of enzyme cellulase (Fathi et al., 2019). There are not many reports on the direct biocompatibility of the CNF and CNW. Among the different nanocellulose, the BC has better biocompatibility compared to CNF and CNW (Helenius et al., 2006). Blood
compatibility is another biological property. It was observed that oral administration of TEMPO-oxidized cellulose nanofibers to mice proved to be a promising hemocompatibility and unique biological activities (Shimotoyodome et al., 2011). Cellulose is non-biodegradable in vivo but studies have shown that oxidized cellulose are potentially degradable (Li et al., 2009; Luo et al., 2013). Low toxicity was reported for the CNF and CNW but no evidence was reported for toxicity regarding bacterial cellulose (Chen et al., 2009; Clift et al., 2011; Pereira et al., 2013).

4. Extraction of Cellulose

For the extraction of the CNF various methods are available. They can be produced using mechanical methods including grinding, high pressure homogenization, cryo crushing with liquid nitrogen etc. In addition, various chemical alkali and enzymatic treatment can be used before mechanical techniques to enhance the inner surface area, rise the accessibility of hydroxyl groups, change crystallinity, break cellulose hydrogen bonds to amplify the reactivity of the plant fibers (Rojas et al., 2015). Depending on the required dimension of the fibers, the cellulose extraction method varies. Cellulose isolation can be done using alkaline procedure, enzyme technology, ultrasound treatment or dilute acid pretreatment. In alkaline procedure, the plant tissue is digested in NaOH solution to remove lignin and hemicellulose. Further it is bleached with a mixture of glacial acetic acid and sodium chloride to remove any remaining part of hemicellulose and lignin. And the obtained fibers are washed with NaOH solution followed by deionized water to acquire a neutral pH. In cellulose extraction using ultrasound treatment, the plant tissue is treated with deionized water and ultrasonic irradiation is carried out. And then plant material is treated with NaOH solution (0.5 mol/L), H₂O₂ in NaOH solution and with NaOH solution (2 mol/L). After this filtration, washing with distilled water, drying steps are done to isolate cellulose fibers. Enzyme technology is applied for cellulose isolation to selectively hydrolyze hemicellulose, lignin portions and sustain the cellulose part. In this method, oven dried bleached pulp is soaked in water, and autoclaved and fungal culture is allowed to grow on the plant fibers for different time duration at room temperature with slow agitation. And then the plant fibers are autoclaved, washed, sheared and cryocrushed. In the cryocrushing step the plant fibers are frozen applying liquid nitrogen and a high shear force is applied to separate microfibrils from the cell wall. Subsequently the fibers are dispersed in a water suspension and filtered resulting in cellulose microfibrils. Dilute acid pretreatment is used for the efficient removal of lignin and hemicellulose in cellulose isolation. Air dried plant material is milled, presoaked in dilute sulphuric acid under continuous agitation, filtered, washed with deionized water and heated in a pressure reactor in dilute sulphuric acid. Later, the reactor was quenched in an ice bath, the slurry was filtered, washed with deionized water and dried overnight. Though hot dilute sulphuric acid pretreatment enhances the digestibility by hemicellulose dissolution and lignin redistribution, the cellulose crystallinity is increased due to annealing and the potency of pretreatment is limited. During pretreatment structural changes of lignin may occur, but the structure of cellulose remains unaffected (Radotić and Mićić, 2016).

Cellulose microfiber extraction consists of three major steps—conventional pulping stage for the removal of lignin and hemicellulose, mechanical separation of fibers into microfibrils using homogenization and acid hydrolysis. For the purification of cellulose from bagasse, firstly the oven dried bagasse was milled and digested in a NaOH solution for the removal of hemicellulose and lignin, followed by bleaching with glacial acetic acid/sodium chloride mixture for further removal of lignin and hemicellulose. And the fibers washed with NaOH solution once followed by repeated washings with deionized water. In order to obtain cellulose microfibers, an aqueous suspension of cellulose fibers was warmed, blended and homogenized resulting in the formation of smaller particles. In homogenization, the dispersion medium was altered from water to t-butanol and the microfibers were freeze dried from liquid nitrogen and a high shear force is applied to separate microfibrils from the cell wall. Subsequently the fibers are dispersed in a water suspension and filtered resulting in cellulose microfibrils. Dilute acid pretreatment is used for the efficient removal of lignin and hemicellulose in cellulose isolation. Air dried plant material is milled, presoaked in dilute sulphuric acid under continuous agitation, filtered, washed with deionized water and heated in a pressure reactor in dilute sulphuric acid. Later, the reactor was quenched in an ice bath, the slurry was filtered, washed with deionized water and dried overnight. Though hot dilute sulphuric acid pretreatment enhances the digestibility by hemicellulose dissolution and lignin redistribution, the cellulose crystallinity is increased due to annealing and the potency of pretreatment is limited. During pretreatment structural changes of lignin may occur, but the structure of cellulose remains unaffected (Radotić and Mićić, 2016).

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Extraction of cellulose from plant fibers can be done using different mechanical and chemical methods and acid hydrolysis, bleaching and alkalization can be used to extract the nanoscale cellulose from cellulose. In a recent study, cellulose was extracted from raw areca fibers using hydrogen peroxide and formic acid in lower concentration. To obtain areca fibers from areca fruit, the collected areca empty fruits were immersed in double distilled water for five days. And to extract cellulose from areca fibers, the areca fibers were washed with detergent and then dried in an oven. The raw fibers were dewaxed using ethyl alcohol followed by washing with double distilled water and drying. The fibers were suspended in 10% NaOH followed by 10% H₂O₂ and autoclaved for one hour and washed with distilled water. Subsequently, the fibers were soaked in a mixture of formic acid and hydrogen peroxide and the mixture was kept in a water bath resulting in delignified fibers. The delignified fibers were washed with formic acid followed by repeated washings with double distilled water. And then the fibers have undergone treatment with H₂O₂ and NaOH was used to obtain the suitable pH. Finally, the white suspension was collected, filtered and...
washed repeatedly resulting in cellulose extraction (Ranganagowda et al., 2019). The extraction of cellulose from sisal fibers was conducted using chemical processes such as acid hydrolysis, alkaline extraction, bleaching and chlorination. And the nanocellulose, which has applications as nanofillers in matrices, was produced by means of acid hydrolysis of the extracted cellulose. Cellulose extraction was carried out using the following procedures—repeated washings of sisal fibers with distilled water, drying in oven, chopping (preconditioning steps), boiling in a mixture of ethanol and toluene (dewaxing step), filtering, washing with ethanol and drying. Subsequently, two different procedures were carried out for cellulose extraction. In the first procedure, the fibers were treated with NaOH in ethanol followed by H$_2$O$_2$ under continuous agitation, followed by treatment with NaOH-Na$_2$B$_4$O$_7$·10H$_2$O under continuous stirring and treatment with HNO$_3$, washing with ethanol, distilled water, and again washing with ethanol and drying in the oven. In the second procedure, the sisal fibers were treated with sodium chlorite, sodium bisulphate solution (delignification) and then treatment with NaOH solution, filtering, washing with distilled water and drying in a vacuum oven steps were performed to obtain cellulose. From these celluloses, the CNF were produced using acid hydrolysis of sulfuric acid solution under continuous stirring (Morán et al., 2008).

From jute fiber waste, nanocellulose was produced using high energy ball milling technique. Small segments of jute fibers were initially chemically treated to remove hemicellulose and lignin. Mercerization with sodium hydroxide solution, acid treatment with sulphuric acid and alkali treatment using NaOH solution were carried out. And then, ball milling technique was used for grinding of fibers. According to the milling conditions (dry/wet, milling time), the particle size and morphology of jute nano particles were changed (Abbasi and Baheti, 2018). Cellulose nanofibers were isolated employing supercritical carbon-dioxide (SC-CO$_2$) from kenaf fibers, and the process assisted by mild oxalic acid hydrolysis. The fibers had a diameter of 10–15 nm and BET surface area of 10.362 m$^2$/g. The authors propose SC-CO$_2$ method as a non-toxic and economically feasible method for the isolation of the CNF. The crystallinity is a significant parameter that influences the thermal and mechanical properties and was determined using X-ray diffraction analysis. As seen in Fig. 2, intense peak was obtained for SC-CO$_2$ cellulose nanofibers.

Fig. 2 The XRD of raw kenaf fiber, alkali treated kenaf fiber, bleached kenaf fiber, and SC-CO$_2$ extracted CNFs (Atiqah et al., 2019). Reproduced with permission from MDPI.

5. Fabrication of Cellulose Nanocomposites

Nanocomposite is defined as two-phase material where one phase has nanometer size range (Zhu et al., 2017). The impressive properties of cellulose make it a promising candidate for fabrication of cellulose nanocomposites (Pandey et al., 2013). The hydrophilic nature of the cellulose is one of the challenging factors in the fabrication process. Organic solvent based nanocomposites can be prepared by dissolving freeze dried cellulose suspension in a mixture of dimethylsulfoxide and N,N-Dimethylformamide with slight amount of water by sonication. Homogenous dispersion of hydrophobic polymer matrix can be achieved by surface functionalization of the surface hydroxyl group (Wang et al., 2007). Among the different types of techniques for processing of cellulose nanocomposites, the methods such as electrospinning, cast drying, freeze drying, vacuum assisted filtration, wet spinning, layer by layer assembly and several micropatterning techniques are the predominant methods (Sharma et al., 2019).

5.1. Electrospinning

Electrospinning is a widely used technique for the manufacture of nanofibers and has been used for the synthesis of the BC based composite nanofibers. Prior to electrospinning, the BC can be treated with strong acids to create nanosized whiskers that are smaller in length. After that the nanowhiskers can undergo blending with suitable polymers to go through electrospinning to form nanocomposites. Previous studies have proven that the electrospun composite nanofibers possess high mechanical properties because of the ability of the BC whiskers to embed and align inside the nanofibers (Qiu and Netravali, 2014). It has been reported that, using electrospinning method, the CNF matrices were coated with cellulose nanocrystals with desirable orientation by uniaxial alignment. And this orientation can improve the mechanical properties and thermal stability of the CNFs.
a material having no cytotoxic effect, these can have applications as a tissue engineering scaffold (Sharma et al., 2019).

5.2. Solvent casting

Cellulose nanoparticles are usually produced in the form of an aqueous suspension and this can be mixed with the aqueous solution of hydro polymer and the resulting mixture can be casted and evaporated to obtain nanocomposites as solid films (Kalaiselvam et al., 2011). Various studies have reported the preparation of cellulose nanofiber reinforced starch (Anglès and Dufresne, 2001; Liu et al., 2010), silk fibroin (Noishiki et al., 2002), poly(oxyethylene) (Azizi Samir et al., 2004; Azizi et al., 2006), polyvinyl alcohol (Zimmermann et al., 2005), hydroxypropyl cellulose and soy protein isolate (Wang et al., 2006).

Bacterial cellulose can be grounded to form smaller lengths, still sustaining a high aspect ratio and dispersed into resins to obtain nanocomposites. This process is simpler than the acid hydrolysis method used to create nanowhiskers, and the ground bacterial cellulose/resin mixture can be casted to synthesize BC-based fibrous membrane-like nanocomposites having good mechanical characteristics. The improved mechanical properties result from the homogenous dispersion of nanowhiskers (Qi and Netravali, 2014). Paralikar et al. (2008) developed barrier membranes using polyvinyl alcohol (PVOH), the CNC and poly(acrylic acid) (PAA) via casting/evaporation technique. The CNCs and PAA were used as filler and crosslinking agents respectively in which the PAA gave water resistance capacity to the PVOH. To produce the stock solutions of the PAA and PVOH, the powder form was dissolved in deionized water and stirred in an oil bath, and the obtained solutions were blended with the CNC dispersion. And the resulting solution was sonicated prior to casting to disperse the agglomerates. Then a known volume of blended solution was poured into flat bottom dishes to regulate the thickness of the composite membranes. After air drying, the membranes having different weight percentages of CNC, PAA and PVOH were heated in oven to produce the final barrier membranes. In cast drying technique, by using different coating procedures such as bar coating or spray coating by complete solvent evaporation, the colloidal mixture is allowed to deposit on the clean substrate surface to produce solid films (Sharma et al., 2019). Polylactide (PLA)/cellulose nanocomposite can be fabricated by mixing PLA and modified CNW by solution casting. Modified CNW can be prepared by in situ polymerization of the CNW and lactic acid. Prior to solution casting, the PLA was dried in oven for 20 h and mixed with modified CNW in presence of dichloromethane solution at 25 °C for 12 h. The mixture was casted into films, evaporated, and dried completely at 50 °C in vacuum oven for 24 h (Chai et al., 2020). The fabricated nanocomposites exhibit enhanced mechanical properties by acting as a nucleating agent (Qian et al., 2018; Kian et al., 2019; Chai et al., 2020). Solvent casted CNW nanocomposite wet films were prepared with the carboxyl methyl cellulose having enhanced strength (Oksman et al., 2016).

5.3. Freeze drying

Freeze drying/lyophilization method is the removal of water that sustains nanocomposites in aerogel suspensions or solutions and hence can be used to synthesize bio-nanocomposites aerogels from cellulose. In this technique, initially the freezing of samples is conducted to remove small molecular solvents via sublimation. Freeze drying process enables the regulation of pore size and aerogel particle distribution. In addition, by varying the size of the container used, the orientation and shape of the aerogel can be optimized. For the production of aerogels, the ice-template method is mostly conducted by noticing the crystal growth formation resulting in nanostructure assembly. Chazeau et al. (2020) investigated the plastic behaviour of poly(vinyl chloride) (PVC) reinforced by the CNW and the nanocomposites were processed using freeze drying. The cellulose whiskers extracted from tunicates were obtained as an aqueous suspension in which the electrostatic repulsions between sulphate groups incorporated during sulphuric acid treatment prevented the sedimentation of whiskers. And the cellulose whisker suspension was mixed with the aqueous suspension of the PVC, formed by emulsion polymerization and freeze dried. By hot mixing process, the produced freeze-dried powder, di-ethylhexyl phthalate (DOP) and stearic acid based lubricant were mixed together and the mixture was hot-pressed by compression molding to create the nanocomposite sheets.

5.4. 3D printing

Incorporation of nanomaterials into the host matrices of polymers using 3D printing can offer a number of advantages in nanocomposite manufacture like modification of conventional material properties, customized geometries, reduced delay between design iterations and increased parts integration and can be done in two ways. Matrix material can be 3D printed with stoppages for batch printing and addition of nanomaterial can be done automatically or manually. Otherwise the nanomaterial can be added to the host matrix initially and then the 3D printing of the mixture can be done for nanocomposite fabrication (Campbell and Ivanova, 2013). For the production of biomaterials for biomedical applications including regenerative medicine and tissue engineering, the newly developed 3D printing technique can be utilized. This method consists of the layer by layer
printing of different biopolymers such as polysaccharides and proteins as bio-inks and extrusion of melts for the synthesis of hierarchical three-dimensional nanostructures in the nanocomposites. Cellulose nanomaterials can be either used as a substrate or ink constituent for 3D printing (Li et al., 2017; Joseph et al., 2020). Studies have been carried out regarding the fabrication of cellulose nanocomposite as an adhesive bandage to aid wound healing process, using 3D printing method. In the same study, electrode printed with silver ink has been incorporated onto the bandage to note the temperature of the wound. In addition, 3D printing technique was used for printing of cartilage making use of alginate/hyaluronic acid and the CNF to use for stem cell culture for integrating in-situ physiological environment. The 3D printing can also have applications in the making of nanocellulose derived protective clothing and textiles (Tenhunen et al., 2018). Sultan and Mathew (2019) researched about the synthesis of porous cubic scaffold with uniform pore structure using 3D printing of the CNC based hydrogel ink with sodium alginate and gelatin. The developed 3D scaffolds have shown porosity and compression modulus values similar to those needed for cartilage regeneration applications. In order to control the pore size and compression modulus of scaffolds, the hydrogel ink composition and 3D processing can be changed. Hence, fabrication of scaffolds according to the specific needs of patients can be done using this process (Sultan and Mathew, 2019). Nanocellulose hydrogel preparation using 3D printing technology has been investigated recently. Kajsa et al. (2015) recorded the printing of different pieces using CNF/alginate dispersion. Thereafter, the molds obtained by printing were soaked in a CaCl$_2$ solution. Using 80% CNF/20% alginate mixture, 3D structures having improved storage modulus, compressive strength and shear modulus were printed as seen in Fig. 3.

Fig. 3  a) 3D printed small grids (7.2 mm × 7.2 mm) with Ink 8020 after cross-linking; (b) Shape of grid deforms while squeezing; and (c) it is restored after squeezing. (d) 3D printed human ear and (e and f) sheep meniscus with Ink8020. Side view (e) and top view (f) of meniscus (Kajsa et al., 2015). Reproduced with permission from American Chemical Society

The CNW nanocomposites-polyvinyl alcohol filaments containing various amounts of the CNW for bone engineering application was fabricated where 10% CNW is used as functional additive to improve the 3D printing performance (Wang et al., 2018). The 3D printing of the CNW nanocomposite hydrogel via stereolithography is used in tissue engineering applications (Palaganas et al., 2017)

6. Cellulose Nanocomposites Applications

The biodegradability and cyto/hemocompatibility of nanocellulose and bionanocomposites have given rise to their essential usage in the biomedical field. The nanocellulose reinforced polymer composites play a significant role in the biomedical applications such as drug delivery, tissue engineering, antibacterial and disease diagnostics (Khattab et al., 2017).
6.1. Wound healing

Wound healing is a complex process which needs effective therapies to facilitate the tissue regeneration activity. Antimicrobial biomolecules having healing capabilities are functionalized on to polymeric matrices to form wound dressing materials. Recently, studies have been carried out about the production of cellulose containing nanofibrous meshes for wound dressing applications (Teixeira et al., 2020). Díez et al. (2011) successfully generated nanocellulose-nanosilver composites by dipping a film composed of nanocellulose into a solution of silver nanoclusters protected by poly(methacrylic acid) (PMMA). This binding is explained by the hydrogen bonding of the PMMA, containing silver nanoclusters with the nanocellulose. The adsorption of silver clusters onto the nanocellulose is supported by the large surface area of nanofibrils of cellulose. These silver particles can act more bactericidal in its surrounding in a five-fold larger surface area than the area of the nanocellulose film. In brief, the surface functionalization of nanofibrillated cellulose with metal nanoclusters can be a promising wound healing tool because of its antibacterial properties.

In a similar study, Barud et al. prepared silver containing BC based nanocomposites for antibacterial applications like wound healing by soaking BC pellicles into silver triethanolamine (TEA) solution (Barud et al., 2008). Antimicrobial silver particles having an average diameter of 8 nm were homogeneously distributed on to the surface of nanofibers.

Silver nanoparticles were incorporated into nanofibrillated BC (Ag/BC) by photochemical reduction process using UV radiation. The composites were analyzed for antibacterial activity by disc diffusion method (Pal et al., 2017). The $10^{-2}$ mol/L sample of Ag/BC showed the highest level of activity against Gram-negative bacteria Escherichia coli as seen in Fig. 4.

![Fig. 4](image-url) Photographs of antibacterial performance of Ag/BC pellicles with three chosen samples at different Ag concentrations. (a) $10^{-2}$ mol/L; (b) $10^{-3}$ mol/L; and (c) $10^{-4}$ mol/L. (d, e) Photographs taken with disk-shaped BC and Ag/BC at $10^{-2}$ mol/L AgNO$_3$ concentration to calculate the inhibition zone (Pal et al., 2017). Reproduced with permission from American Chemical Society.

The fabrication of bacterial nanocellulose (BNC)-grafted poly(acrylic acid) (AA)-graphene oxide (BNC/P (AA)/GO) composite hydrogel using electron beam irradiation has been done by Chen et al. (2019). Assessment of the bio adhesiveness, mechanical properties, water vapour transmission rates (WVTRs), biocompatibility, water retention abilities and water sorptivity of composite hydrogel was done and concluded that swelling capacity, water retention ratio, bioadhesion and WVTR properties were improved while maintaining their mechanical characteristics. Also, the BNC/P(AA)/GO composite hydrogels were biocompatible and have shown a obvious increase in cell attachment and proliferation. The study indicates that BNC/P(AA)/GO composite hydrogel has potential applications as a wound dressing material. Yuan et al. (2020) examined the activity of oxidized bacterial cellulose and chitosan with collagen (OBC/COL/CS) nanocomposite for rapid internal hemostasis using a rat liver injury model. Collagen was attached to use its functional features including improved hemostasis and promotion of wound healing and to develop a novel nanocomposite. The study concluded that the OBC/COL/CS nanocomposite had suitable mechanical strength, in vivo biodegradation, antimicrobial properties, in vivo hemostatic efficacy, blood cloting
capability, better adhesion of erythrocytes and platelets, ultrafast ceasing of bleeding and hence it can be used as a procoagulant agent and hemostat to control internal bleeding and to promote excellent wound healing.

6.2. Bone tissue engineering

Wan et al. (2006) formed hydroxyapatite (HAp)-bacterial cellulose (BC) nanocomposites and from the Fourier transmission infrared studies it was found that the HAp crystals with low crystallinity synthesized on the bacterial cellulose possess carbonate, similar to natural bone apatites. Therefore, these porous three dimensional network structures can be used in bone tissue engineering research fields in future.

Fang et al. (2009) studied the osteoblastic differentiation of human bone marrow derived stromal cells (hBMSC) on the BC-HAp nanocomposite scaffolds. It was clear that the hBMSC on the developed BC-HAp nanocomposites was able to show improved cell adhesion and activity than those on the plain BC, due to the favored pore size and enhanced inorganic components of BC-HAp composites. Also, the in vitro biocompatibility of BC-HAp nanocomposites was revealed and hence its application as a bone tissue engineering material was proved in the study. Saska et al. (2012) prepared a novel nanocomposite combining BC and type I collagen (COL) and assessed it for in vitro bone regeneration. The BC-COL composites with a high surface area and well interconnected pore structure can accelerate the cellular attachment and tissue regeneration process. The introduction of collagen has changed the crystallinity of BC membranes and decreased the elastic modulus of the composite. Till day 10 and 14, the cell proliferation on BC and BC-COL membranes were similar. But on day 17, high alkaline phosphatase activity (ALP activity) and total protein content of cells on BC-COL was observed confirming the bone mineralization and osteoblast phenotype formation in vitro. Hence, BC-COL can be a promising material for bone tissue engineering. The study demands the functionalization of BC-COL nanocomposite with other proteins that boost bone formation for bone engineering applications.

The development of nanocomposite scaffolds using BC with HAp and Fe₃O₄(Ferrate) nanoparticles by ultrasonic irradiation has been previously reported. Torgbo and Sukyai (2019) evaluated the physicochemical characteristics of BC-Fe₃O₄-HAp nanocomposites and it was observed that the nanoparticles were uniformly distributed in the BC matrix. By introducing nanoparticles into the BC matrix, swelling ability of the BC was decreased and the degree of porosity of the matrix was maintained as 80%. The results showed that the produced nanocomposite scaffold was biocompatible with the osteoblast MC3T3-E1 cell line and non-toxic to mouse fibroblast L929 cells. Also, the mechanical properties of the composite were improved and matched to those of trabecular bone in humans. Nanoparticle incorporation also caused a reduction in crystallinity of the scaffold which helped in the timely biodegradation of the material when used for restoration of bone tissue. Although in vivo studies are required for further researches, the study concludes that the composite scaffold can be used in bone regeneration because of its capability for cell attachment, differentiation and proliferation.

6.3. Lenses

Tummala et al. (2019) analyzed the biocompatibility of the polyvinyl alcohol (PVA)-CNC composite hydrogel in the form of a contact lens with HCE-2 (human corneal epithelial) cells. The cell response to hydrogels were evaluated by seeding HCE-2 cells on the hydrogels with and without simulated tear fluid (STF) pre-conditioning. The composites were incubated with the STF; protein elution and quantification was carried out to determine the protein adsorption on the surface of hydrogel. It was confirmed that the PVA-CNC hydrogels had affinity towards protein adsorption because of the interactions between negatively charged CNCs in the nanocomposite and positively charged lysozyme. The metabolic activity or integrity of corneal epithelial cells were not affected by the presence of hydrogels. The adherence of viable corneal cells to the lenses were observed which has exhibited typical epithelial morphology unaffected by the STF pre-conditioning. In total, the study has led to the conclusion that PVA-CNC hydrogels can have applications in medical field as an ophthalmic biomaterial.

6.4. Cellulose nanocomposites for tissue engineering

Bacterial cellulose and bacterial cellulose-chitosan membranes (BC-Ch) obtained by freeze drying were evaluated for wound healing by Lin et al. (2013), and the histopathology studies showed that neovascularization or new blood vessels were observed on 7th day. Keratin formation was more integrated in BC-Ch treated wounds. Capillary formation and epithelialization increased in wounds treated with bacterial cellulose by day 14. The repaired dermis was similar to normal skin in case of BC-Ch group.

The BC-polydopamine matrix was impregnated with silver nanoparticles (AgNPs) to form BC-PDAg nanocomposite scaffold (Jiji et al., 2020). The antimicrobial activity of the scaffold was evaluated against gram positive and gram negative bacteria. The BC scaffolds did not show any activity against gram negative and positive strains. The BC-PDAg showed antibacterial effect
against both the strains. The in vivo efficiency was evaluated in rat models. The groups treated with the BC-PDAg showed improved re-epithelialization and increased formation of granulation tissue. Polycaprolactone (PCL) is a synthetic biodegradable polymer, extensively studied for tissue engineering. However, the polymer is hydrophobic that limits biological interactions. In order to modify the cell responses, 3D printed the PCL was coated with the CNF. The contact angle decreased drastically after coating with the CNF. Consequently, cell proliferation was also higher in the CNF modified scaffold than untreated ones. The study demonstrated that the CNF was able to improve cell attachment and proliferation for tissue engineering applications (Rashad et al., 2018).

6.5. Nanocellulose for mechanical reinforcement

The scientific community has been searching for cost effective and environmental friendly reinforcing agents that can be used in industry. It is quite well known that nanocellulose acts as an excellent reinforcing material. The use of natural polymers like cellulose has paved way for development of low density materials, which are having huge demand for commercial applications. Chang et al. (2010) showed that incorporation of cellulose nanoparticles into starch matrix (5 wt% cellulose nanoparticle) exhibited significant improvement in mechanical properties. The tensile strength increased from 3.15 MPa to 10.98 MPa when the nanoparticle concentration was varied from 0 wt% to 5 wt%. This could be due to the good interfacial interaction between starch matrix and cellulose nanoparticles (Chang et al., 2010). Biomass from hemp stalks was used for extracting micro and nanofibers of cellulose due to their outstanding mechanical and crystalline properties (Abraham et al., 2016). The 7.5 wt% CNC and CNF acted as effective reinforcement for polyvinyl alcohol polymer matrix. Based on the period of hydrolysis two types of the CNCs were used; CNC15 and CNC30, CNC treated at hydrolysis time of 15 min and 30 min respectively. The impregnation of CNC15, CNC30 and CNF increased the tensile strength by 26.3, 13.4 and 48.6%, respectively, compared to neat PVA matrix. The cellulose microfiber (CMF) composite showed decreased mechanical properties and this might be because of the non-uniform dispersion. The enhancement in mechanical properties is due to the high aspect ratio of the CNC and CNF that enables effective dispersion and interaction of PVA chains and nanocellulose (Kassab et al., 2020).

Cellulose nanofibres isolated from banana fibres were used to reinforce natural rubber (NR). Both Young’s modulus and strength enhanced upon increasing CNF (Abraham et al., 2013). The addition of crosslinking agents (Zn based compounds and Sulphur) facilitated the interaction between cellulose and rubber. The possible mechanism behind betterment of mechanical properties was explained by the formation of 3D network between NR, CNF and Zinc metal. Phomrak and Phisalaphong (2017) reported the preparation of bacterial cellulose-rubber composite (NRBC) employing latex aqueous micro dispersion process. The mechanical characteristics of neat NR film were very low when compared with the composite containing bacterial cellulose. The Young’s modulus and tensile strength of the nanocomposite was 4128.4 and 75.1 MPa, respectively. It was further suggested that the NR chains might have been immobilized by the nanocellulose network resulting in the superior properties compared with neat film. Recently, the same group fabricated NRBC films where lactic acid was used as crosslinking agent (ANRBC). The films degraded within three months in soil and also exhibited enhanced mechanical properties when compared with the NRBC films. Lactic acid modification improved the interfacial interactions between NR and BC in the composite (Phomrak and Phisalaphong, 2020). A typical immiscible system, polylactic acid/Natural rubber blend was prepared by solvent casting and extrusion followed by compression moulding. Cellulose nanocrystals were investigated as compatibilizers for the system. Three different types of fillers were used in this study, one unmodified (CNC), long alkyl chain grafted CNC (C18-g-CNC) and PLA grafted CNC (PLA-g-CNC). The preferential localization of fillers affects the compatibility which was analyzed in the study. Unmodified CNC moved to the PLA phase, thus there was no obvious effect in mechanical properties. Long alkyl chain grafted CNC had affinity for the NR phase and resulted in decrease in Young’s modulus. Although the PLA grafted CNC were localized in the PLA phase, the tensile strength could be retained with a slight increase in Young’s modulus. Thus PLA grafted CNC having small PLA chains acted as effective nucleating agent (Bitinis et al., 2013). Xu et al. (2013) reported the reinforcing effect of cellulose nanofibrils and cellulose nanowhiskers on poly ethylene oxide (PEO) matrix. Both CNF and CNC were obtained from the same source bleached dry lap eucalyptus pulp. Comparing the mechanical properties of CNF and CNC, it could be seen that CNFs resulted in higher strength and modulus than CNCs because of the higher aspect ratio and fiber entanglement of CNF. However, a lower strain-at-failure was obtained for PEO/CNF composite films due to their relatively large fiber agglomerates (Xu et al., 2013). The particle morphology, preparation technique, dispersion, and orientation of the CNC or CNF, interfacial interactions, and mechanical test methods are the major factors that can affect the mechanical characteristics of the nanocomposites. It was found that, at low loading level, the mechanical characteristics of the nanocomposites were improved due to the good dispersion, the larger aspect ratio and percolated network of nanoparticles, and compatibility of the CNC or CNF within the polymer matrix. And at high loading levels, the mechanical properties of the nanocomposites were enhanced, because of surface modification and cross-linking resulting in better interfacial interactions (Yu and Yan, 2017).
Saba et al. (2017) studied the effect of CNF filler on the dynamic mechanical analysis (DMA) of epoxy composites as a function of temperature. Compared to the pure epoxy, the storage modulus of CNF/epoxy nanocomposites were increased. The enhancement in stiffness of the epoxy nanocomposites was attributed to the high stiffness of the CNF filler which can constrain the epoxy polymeric chain movement by the better dispersion of the filler. In this study, 0.75% CNF/epoxy nanocomposites showed the highest storage modulus than the other filler loadings. The uniform dispersion and improved reinforcing effect of 0.75% CNFs in epoxy composites resulted in the increased value of storage modulus. And this could promote the physical interactions through hydrogen bonds between the polar groups of epoxy matrix and surface hydroxyl groups of the CNFs filler than other nanofiller loadings. Further increase in the CNF concentration to 1% caused accumulation of filler particles and a large number of voids in the polymer network resulting in reduced value of storage modulus (Saba et al., 2017).

Siqueira et al. (2013) synthesized bionanocomposites by reinforcing cellulose nanocrystals (obtained from Luffa cylindrica fibers) into the PCL polymeric matrix. Both chemically modified (using n-octadecyl isocyanate to improve filler/matrix interactions) and unmodified CNCs were used for nanocomposite fabrication and the mechanical characteristics of the composites were tested. The study revealed that the neat PCL film possessed a low elastic modulus and ductile behaviour at room temperature. And the unmodified CNCs/PCL nanocomposites have shown a slight increase in tensile modulus and a reduced strain at break. This can be attributed to the high aspect ratio of L. cylindrica CNCs. In addition, the increased rigidity of the bionanocomposites could be partially attributed to the increase in the degree of crystallinity of the matrix. The chemically modified PCL nanocomposites displayed improvement in stiffness with the increase in tensile modulus. Also, the strain at break of nanocomposites was increased and strength at break was maintained compared to the mechanical data of unmodified CNCs/PCL nanocomposites. The high value of tensile modulus resulted from better adhesion between filler and matrix causing a higher homogeneity and formation of hard domain ensued by chain tangling effect between PCL matrix and surface modified CNCs. And the strain at break was increased due to the breaking of hydrogen bonds between CNCs enabling a higher extension of the material (Siqueira et al., 2013).

7. Surface Modification of Nanocellulose

The main limitation while using nanocellulose for functional applications is its hydrophilicity. The presence of number of functionalities within cellulose structure enables ease of surface modification. Several approaches have been suggested like surface modification by covalent interactions, using chemical and enzymatic moieties etc. The PCL/CNF- nanocomposite materials were compounded and processed by Vilela et al. (2019). The CNF used was modified with latex nanoparticles comprising of hydrophilic (P [DMAEMA-co-MAA]) and hydrophobic (PMMA or PBMA). Based on degree of polymerization, a variety of latex types were used PBMA-176 (a) PBMA-176 (b) PBMA-705 (c) PMMA-176 (d) PMMA-705 and (e) PMMA-1410. For samples with unmodified CNF, agglomeration of nanocellulose was visible and there was poor interaction between the polymer matrix and the CNF. However, in the samples containing modified CNF, a better dispersion of CNF was seen and this further increased with increase of CNF-latex composition from 1.0 to 5.0 and 7.5 wt% as seen in Fig. 5. It was also concluded as the increase in degree of polymerization (DP) also has a significant effect on interfacial adhesion.

Silane modification of bacterial cellulose was employed for improving interfacial adhesion between poly(lactic acid) (PLA) and BC (Somord et al., 2018). This method includes preparation of stacked, self-reinforced PLA-BC films and further preparation of nanocomposite by hot compaction. Tensile testing indicated that the tensile modulus and strength improved gradually with increasing modified-BC content (1 wt% and 10 wt%), especially for modified BC films. The measure of permeability of films to water vapour is an important parameter for industrial applications that is analyzed by water vapour permeation rate (WVPR). With increasing BC and modified BC a reduction in the WVTR of the nanocomposite films was observed, that could be due to increased tortuous diffusion path created by bacterial cellulose. To enhance the biological properties of BC for soft tissue engineering, fibroblasts were bioengineered on the surface of BC to produce extracellular matrix (ECM) proteins. Un-modified BC (NM-BC) had a lower contact angle of 38°. The formation of cell derived proteins results in an increase in contact angle to 59° for modified BC (Mod-BNC). The proteins mask the hydroxyl groups and replace them with non-polar amino acids. The cell viability studies were done using sodium 3′-[1-[(phenylamino)-carbony]-3,4-tetrazolium]-bis(4-methoxy-6-nitro)benzene-sulfonic acid hydrate (XTT) assay. Cell viability was higher in modified BC groups than in unmodified ones. This is suggested to be due to increased cell numbers as well as enhanced mitochondrial activity. Fibroblasts showed spindle like morphology when grown on modified BC and they also occupied more volume than the unmodified group (Osorio et al., 2019). Fernandes et al. (2013) reported the production of Bacterial cellulose using Gluconacetobacter xylinum microbial strain. The BC was modified by introducing amino alkyl groups by silane chemical grafting. The unmodified membranes didn’t show any antibacterial activity whereas the modified membranes exhibited activity against E. coli and S.
The antibacterial activity was due to polycationic nature of the BC scaffolds (Fernandes et al., 2013). The mechanical properties of pristine CNF aerogel and silane modified aerogels were evaluated (Hasan et al., 2019). The modified aerogels exhibited a compressive stress of 210.12 KPa, whereas the compressive stress was 102.10 KPa for unmodified CNF aerogel (Fig. 6). This increase in compressive stress is due to the presence of cross-linked Si—O—Si bonds of polysiloxane in the modified cellulose aerogels.

8. Conclusions

In the last few decades, the number of attempts made by researchers on the production of biomaterials for various applications has increased tremendously. Biomaterials such as cellulose find use in panoply of applications since they are abundantly available, sustainable, renewable, biodegradable and biocompatible. However, there are many concerns regarding the use of organic solvents for extraction of cellulose. This need to be overcome by the use of cost effective, green solvents or finding alternative routes for extraction. The problem of hydrophilicity is another major issue with cellulose and surface modification is a promising strategy to circumvent this. The demand for solvent free processing methods is also witnessed recently. There has been an increased social awareness in promoting environmentally friendly materials, which paves way for more research based on cellulose. While industrial applications are considered, researches need to come up with more business friendly methods for the sustainable application of cellulose, especially for large
scale processing.

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