Journal of Science and Technology
ISSN: 2456-5660 Volume 7, Issue 06 (August 2022)
www.jst.org.in *DOI:https://doi.org/10.46243/jst.2022.v7.i06.pp1-19*

NANOCELLULOSE-AN EMERGING RESOURCE FOR FUTURE TECHNOLOGY: A REVIEW

Su.Renugaa*, M.Rajamehala, A.Muthu Kumara Pandian, M.VijayPradhap Singh, M.Rajasimman

* Department of Education, DMI-St.John The Baptist University Malawi

-Department of Biotechnology, Vivekanandha College of Engineering for Women, Tiruchengode, Tamilnadu

-Department of Chemical Engineering, Annamalai University, Chidambaram

Email Id: rajamehala@gmail.com, renugaasu@gmail.com

To Cite this Article
Su.Renugaa, M.Rajamehala, A.Muthu Kumara Pandian, M.VijayPradhap Singh, M.Rajasimman, **NANOCELLULOSE-AN EMERGING RESOURCE FOR FUTURE TECHNOLOGY: A REVIEW"**",*Journal of Science and Technology, Vol. 07, Issue 06,-August 2022, pp1-19*

Article Info

Received: 19-06-2022 Revised: 8-07-2022 Accepted: 13-08-2022 Published: 23-08-2022

ABSTRACT

In recent times, with development of nanoscience, nanocellulose gain importance in both research and mechanized areas due to its various properties. Usually fragmentation of naturally occurring polymers or bacterial action helps to produce nanocellulose. Nanocellulose is a natural polymer extracted from the lignocellulosic biomasses. They possess the combined cellulose properties with the landscapes of nanomaterials and provides innovent place for material science and its applications. It is an area with increasing interest due to its unique properties and functions. It has various application in environmental and biomedical fields due to its excellent surface chemistry and biological properties. Nanocellulose is a sustainable raw material with different application. In this review the classification, Isolation, sources, extraction methods, pretreatments, condition and nano cellulose's mechanical properties were described. In addition, current application in tissue engineering, environment, surgical implants, oil and gas, cosmetics, drug deliveries by nanocellulose were discussed.

KEYWORDS: *Nanocellulose, Lignocellulosic biomasses, Surface chemistry, Physical and biological properties, Extraction methods, Applications in biomedical and environment.*

INTRODUCTION

Nanotechnology is one of the greatest developing fields of science. Nanotechnology and nanoscience deals with the study of extremely small things which ranges in nanometer across all other fields of science. Nowadays with development of nanotechnology and nanoscience, cellulose is the most ancient and essential natural polymer on earth (Kumar et al., 2017). Recently the more attention was given to the different form of cellulose using nanotechnology. Cellulose is a naturally occurring biopolymer (Van de Ven, Godbout., 2013). They are natural polymers which act as sustainable raw materials and renewable materials in various industries. Nanocellulose is a derivative form of cellulose with atleast one dimension in nanometer range. Nanocellulose has significant cellulose properties such as hydrophobicity, broad chemical modification capacity. It also has the formation of semi crystalline fibre morphologies. Nano

cellulose has a large surface area. This large surface area made nano cellulose to have efficient interactions with surroundings like water, organic and inorganic polymeric compounds, nano particles and living cells. Nanocellulose, a distinctive and favorable natural material extracted from native cellulose, has gained much consideration for its use as biomedical material, because of its remarkable physical properties, special surface chemistry and excellent biological properties (biocompatibility, biodegradability and low toxicity). The plant fibers are extracted and it was converted into smaller rudimentary constituents has classically been a challenging process with high energy demands, thereby limiting cellulose nanofiber application advancement. More recently, there was an attention on energy-efficient fabrication methods, whereby fibers are pretreated by various physical, chemical, and enzymatic methods to reduce energy consumption. In these recent developments, plant-based nanocellulose production has much importance, which deals with green chemistry and biomaterial sciences for environment.
Not only plants acts as source for nanocellulose, it can also be acquired from microorganisms, algae, tunicates and some animals. Plants source mainly includes wood pulp, which contains large amount of cellulosic materials in its parenchyma tissue. Algae are generally regarded as green energy, which used to synthesize nanocellulose. Algal based nanocellulose has many remedial activities in environment. The extraction and production of nanocellulose includes several pretreatments. Nanocellulose has its application in different fields, mainly in environmental and biomedical science (Carreño et al., 2017). In this review the extraction, production of nanocellulose and its application in different fields were discussed.

CLASSIFICATION OF NANOCELLULOSE

Based on size and structure nanocellulose (Cellulose nanomaterials) can be categorized into two major groups: nano-objects and nanostructures (Jorfi, Foster., 2015). The extracts or products obtained from native cellulose which usually found in plants, animals, bacteria in nano scaled structure materials is regarded as nanocellulose (Lin, Dufresne., 2015). Commonly, the family of nanocellulose can be categorized into three types, (1) Bacterial cellulose , which is also called as microbial cellulose, (2) Cellulose nanocrystals (CNC), which is also referred to nano crystalline cellulose, cellulose (nano) whiskers, rod-like cellulose microcrystals; (3) cellulose nanofibrils (CNF), which is also referred to as nano fibrillated cellulose (NFC), micro fibrillated cellulose (MFC), cellulose nanofibers.

CELLULOSE NANO FIBRES (CNF)

Cellulose nanofiber (CNF) can be regarded in different terms, suchas nanofibrillated cellulose (NFC), nanofibrillar cellulose, nanofibrous cellulose (Kargarzadeh et al., 2017). The difference in structure made possible to study about CNFs. CNFs is consist of stretched masses of elementary nanofibrils and also with alternating crystalline and unstructured (amorphous) domains (Huang et al., 2018). Before turning into CNFs, the plant cell wall, which is made of complex cellulose structure, are subjected to mechanical integration strongly. Depending on the disintegration capacity, the diameter ranges from 10 to 100 nm (Razalli et al., 2017). A very large number of mechanical techniques are there to produce cellulose nanofibers from feed stocks. To our knowledge, the only cellulose material which is produced using enzymatic synthesis by bottom up approach is bacterial cellulose. It is one of the unsoiled forms of cellulose synthesized by non-photosynthetic organisms over enzymatic polymerization of organic substrates such as sugar and glycerol. The BC and other plant gleaned CNFs are differed in the absence of definite functional groups (except alcohol) and polymers (lignin, hemicellulose, and pectin) in BC (Kunusa et al., 2018). Therefore, BC is known for its high pureness in CNF form as well as high water-holding capacity and crystallinity (80–90%) among the various types of CNFs (Kaushik, Moores., 2016).

CELLULOSE NANOCRYSTAL (CNC)

CNC also stated in different terms as: nano crystalline cellulose (NCC) and cellulose nano whisker (CNW). Due to high crystalline CNC is less flexible. Crystalline regions isolated from CNF provide an elongated rod like shape to CNCs, which is one of the main reasons of less flexibility . Starting with removal of amorphous regions in CNFs for isolation of crystalline region enables a series of changes and provides characterization of CNC today (Pelissari, Sobral, Menegalli., 2014). Conventionally, CNC can be produced using concentrated acid through acid digestion as one of the pre-treatment methods. CNCs are mainly extracted by chemical treatments. Moreover, CNC can be obtained by several post-treatments and purification.

BACTERIAL NANOCELLULASE

Most of the commercial products are produced from bacterial cellulose. Strains such as *Gluconacetobacter xylinus, Komogataeibacter xylinus, Komogataeibacter medellinensis* are the best bacterial species are used to produce bacterial nanocellulose which has high efficiency in cellulose production. Some special mechanical properties are seen along with stress strain behavior that usually takes after tender tissue in dried BNC. BNC has tensile strength of about 2MPa. BNC stress break is similar to that of steel. Therefore it is well suitableto use as a strengthening factor for materials like polymers, papers and steels. Proper to the high modulus of elasticity in combination with a big internal loss agent, BNC also is a better material for loudspeaker membranes and headphone. Its nearly produce about 500–1500 tons per year per producer in the traditional fermentation industries. Bio cellulose swindles are typically cultivated for two weeks at temperatures of 23 to 32^{0}Cin plastic pans or bins normally in the surrounding environmental conditions. One plastic jar contain about 500 grams of broth culture that yields nearly 1.5g dry biocellulose.Bacterial cellulose have high water content in the form of stable hydrogels. Bio cellulose is mainly used in, the food and cosmetics industries. Bacterial cellulose is traded worldwide. BNC usage in different fields like medical, Pharmaceutical (Jozala et al., 2016), environmental and some advanced technical applications , usually troubled by poor feedstock qualities, varying culture conditions, high impurities and also due to less stability of the materials. The highly purified BNCs are used in R&D departments of various fields in life science (Stanisławska 2016).

SOURCES OF NANOCELLULOSE

Cellulose is the first material to be extracted from the source, later nanocellulose is produced. Cellulose can be obtained from various sources like algae, bacteria, plants and tunicates till today. The sources of nanocellulose also determine the energy consumption during the extraction in addition to its structural properties. Therefore source shows a key role in nanocellulose extraction. It is necessary to know the suitable cellulosic material in order to know the extraction techniques. It is established based on final nanocellulose properties and applications. Additionally, raw materials, extraction techniques, processing the environmental impact associated with the sourcing, extraction, processing are taken into considerations, which is used to fabricate products for environmental applications.

TABLE.1 : SOURCES OF CELLULOSE MATERIALS

SOURCE MATERIALS GROUP	SOURCE NAME	REFERENCE
HARD WOOD	Eucalyptus, Balsa, White Birch (*Betula verrucosa*), Oak, Elm, Maple, Aspen.	(Wei et al., 2017)
SOFTWOOD	Pine, Juniper, Spruce, Hemlock, Yew, Larch, Cedar	(Qu et al., 2019)
AGRICULTURAL RESIDUES	Oil palm, Hemp, Jute, Agave, Sisal, Straw of triticale and soybean, Coconut husk, Sugarcane bagasse, Corn leaf, Sunflower, Bamboo Canola, Wheat, Rice, pineapple leaf and coir, Peanut shells, Vegetable wastes especially Potato peel, Tomato peel, Garlic straw residues, Mulberry fiber.	(Ferreira et al., 2018)
ANIMAL	Tunicates, Chordata, *Styela clava, Halocynthia roretzi Drasche.*	(Trache et al., 2020)
BACTERIA	*Gluconacetobacter Salmonella, Acetobacter, Azotobacter, Agrobacterium, Rhizobium, Alkaligenes, Aerobacter, Sarcina, Pseudomonas, Rhodobacter, Komagataeibacter medellinensis, Gluconacetobacter xylinus, Gluconacetobacter medellinensis.*	(Wang et al., 202)
ALGAE	*Cladophora, Cystoseria myrica, Posidonia oceanica*	(Huang et al., 2018; Ruan et al., 2016)

ALGAE

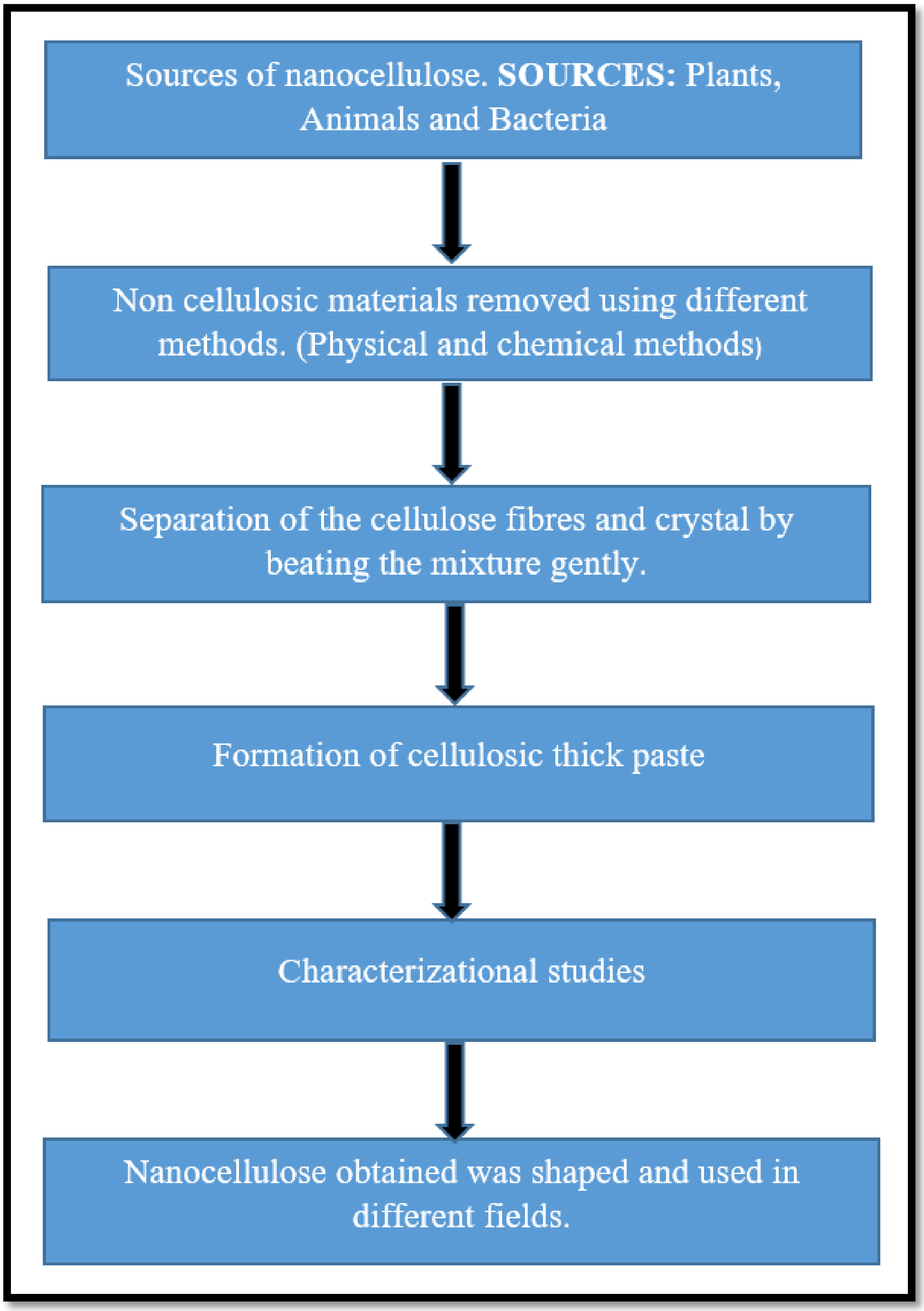
Mostly nowadays in order to get sustainable environment, utilization of green energy is higher. The main weapon of green energy is algae (Huang et al., 2018). Current trends on artificial photosynthesis like CO_2 fixation and water splitting uses algae as a major source. Nowadays algal nanocellulose are used to synthesize fabricates, membranes and adsorbents for environmental remediation.Scientific name of green algae is *Cladophora*, is also known as *Shiogusa*, which is a seaweed in Japan. It is used for extraction of nanocellulose. This green algae has its application in resolving problems regarding water pollution in seaside areas. The findings of Nicolai and Preston's, noted that there is a difference in cell wall characteristics of different species of algal cell wall. It is also found that *Cladophorales* algae found highly crystalline. This highly crystalline characteristic of this *Cladophora* Algae has high inertness of cellulose. This inertness reduces the proneness to chemical treatments than conventional plant cellulose (Ruan et al., 2016). It is also tested and proven that this filters are used to trap the virus particles in efficient manner (El-Safty et al., 2015). This cellulose is also used in adsorbing the Palladium (II) ions in short time with 80% capacity. Algae as a source of nanocellulose also reduce greenhouse gases by absorption. The production of algal nanocellulose is inexpensive (Uzyol, Saçan., 2017).

BACTERIA

Nowadays major research is on bacterial nanocellulose production using different microbial hosts. Bacterial cellulose has high purity, it does not contains other polymers. The production of bacterial cellulose takes nearly two weeks. The nanocellulose produced from microbes has high crystallinity than plant derived nanocellulose. The most common microbial species used for nanocellulose production are *Acetobacter xylinum, Gluconacetobacter xylinus* or *Komagataeibacter medellinensis* (Nechyporchuk et al., 2016) and *Gluconacetobacter medellinensis.* The production of BNC involves placing the bacterial strain in a solution, which consists of required nutrients for the microbe including carbon source. Cellulose with high crystallinity produced from bacterial source than plants. The solution was oxygenated at low pH at temperature of about 25- 29^0 C. BNC was obtained when the secreted exopolysaccharides comes into contact with air. Later BNC was subjected to membrane purification which involves removal of bacterial residues by heating with 0.1M sodium hydroxide for 10 to 20 minutes. BNC have 15-35 GPa of young modulus, 200-300 MPa of tensile strength and 1.5-2 % of elongation. BNC is a white, artificial leather, highly hydrated and have high flexible membrane.These are mainly noted for its adsorbent, catalyst and membrane. It is used for exclusion of heavy metal ions, dye degradation and membrane distillation due to its catalytic and adsorptional properties. Nowadays, the main goal is produce bacterial cellulose in short period of time.

PLANTS

Plants are the major source for cellulose. Mainly parenchyma tissue has high amount of cellulose. Nano cellulose production using plants is one of the easiest method compared to other sources. Plant cellulose fibres are used as main sources for nanocellulose fabrication. Bast fibres, core fibres, grass and fibres of seed, reed, leaf and other fibres are the major source of plant fibers used for nanocellulose extraction. Agricultural wastes also utilized for nanocellulose production. Wood pulps are the most common type of plant fibre used for cellulose fabrication. It is used for itshighpurity in cellulose, long-lasting and flexible networks, and good physical properties compared with other plant sources. Nanocellulose extracted from wood pulp is used as catalysts for the reduction of 4-nitrophenol and it also acts as membrane filters for bacteria, virus, and heavy metal ion removal. Bleached birch fibres which are extracted from *Betula verrucosa* and *B. pendula* were also considered to fabricate dicarboxylic acid fluffy nanocellulose and also used in the treatment of municipal wastewater (turbidity removal and oxygen demand) in efficient manner. Nanocellulose from cotton plantsalso produced by mercerization along withacid treatment, washing, and filtration. It is also used for heavy metal removal (Cadmium, Chromium) (Taleb et al., 2016) and dye degradation.



PREPARATION TECHNIQUES OF NANOCELLULOSE

Cellulose is isolated from the untreated pulp which mainly composed of hemicellulose, lignin, oils, waxes, later it is converted to nanocellulose. In order synthesis cellulose nanofibers and cellulose nanocrystals, the cellulose pulp which is purified already is processed. Breaking of cellulose fibres into nano size fragments is required to yield CNF/CNC by top down approach. But most of the bacterial cellulose nanofibers are produced by electrospinning technique (bottom-up process) (Rajinipriya et al., 2018).Normally, the production techniques involves several processes to produce nanocellulose based on its morphology, crystallinity, and surface chemistry. There were series of biological, mechanical and chemical pretreatments in nanocellulose synthesis. These techniques were discussed briefly.

TABLE.2 METHODS AND PRE-TREATMENTS FOR NANOCELLULOSE PRODUCTION

METHODS	PRE-TREATMENT TECHNIQUES	REFERENCE
Chemical methods	Using dilute acids, concentrated acids, organic acids, Alkaline, Ionic liquids, Organic solvents, Deep eutectic solvents etc.,	(Rabemanolontso, Saka.,2016; Bhutto et al., 2017; Chen et al., 2017; Hassan et al., 2018; Satlewal et al., 2018)
Physical methods	Mechanical splintered, High intensity ultrasonication, Microwave radiation, Gamma radiation.	(Singh et al., 2014; Rodriguez et al., 2017; Rezania et al., 2020; Liu, Kong.,2019)
Physiochemical methods	Wet oxidation, Hydrothermolyis, Steam explosion, Ammonia fibre explosion, Ammonia recycle percolation.	(Karimi, Taherzadeh., 2016; Zhao et al., 2020)
Biological methods	Microbial enzymes and Combined bioprocessing techniques.	(Behera et al., 2014)

CHEMICAL TREATMENT

Acid hydrolysis is one of the efficient methods to synthesis nanocellulose. It involves hydrolysis of the source with mineral acids by removing crystalline regions of semicrystalline cellulosic fibers. Primarily the polysaccharides which bound to the surface of the fibres are removed. Similarly rod like crystalline cellulose is produced by the cleavage and destruction of amorphous regions. By this kind of pretreatments hemicellulose, fats, wax, pectins and lignin in the impure cellulose are removed.

ALKALI PRETREATMENT

Usually the external surface of fiber cell wall contains fats, wax, and lignin in high amount. It was removed by alkali pretreatment. It helps to break the linkage between carbohydrates and lignin by disrupting the lignin structure. Cotton mercerization is one of the treatment in which plant material treated with caustic Sodium hydroxide. Similarly, 17 to 18% of Sodium hydroxide is used to remove the impurities. In this purification method lignin, hemicellulose, pectins are removed by solubilization of lignin. Alkali pretreatment is a sensitive method. This process is carefully handled in order to avoid the cellulose degradation. Nanofibers are extracted from the surface through hydrolysis from the fibre surface along with alkaline solution.

OXIDATIVE PRE-TREATMENT

Oxidative pretreatment involves application of TEMPO radicals. Usually presence of OH-groups results in clumping. It was resolved by TEMPO radicals. These pretreatments involve surface modification. It involves introduction of carboxylate and aldehyde functional groups into solid native celluloses under aqueous conditions. Usually oxidation takes place at the surface of microfibril. It became negatively charged. Repulsion of the nanofibers due to negative charge, thus easing fibrillation.

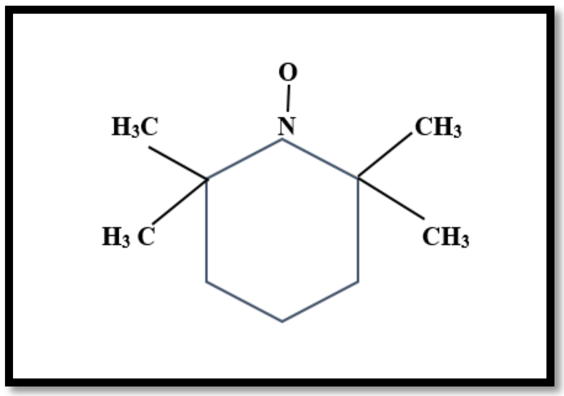


Fig 1. (2, 2, 6, 6-Tetramethylpiperidin-1-oxyl) or (2, 2, 6, 6-tetramethyl piperidin-1-oxidany) or TEMPO. **(**Shibata, Isogai., 2003**)**

ENZYMATIC PRE-TREATMENT

Cellulose cannot be easily degrades by single enzyme. Degradation of cellulose is achieved by using a set of cellulose. Cellulase enzyme is categorized into A- type and B - type. This A and B type Cellulase enzymes ae regarded as cellobiohydrolases. Similarly Type C and D are called as endoglucanases. Cellobiohydrolases degrades crystalline cellulose. Degradation of cellulose by endoglucanases needs some disorder in its structure. The contacts between these two enzymes are usually high to facilitate the disintegration of MFC. Enzymatically pretreated cellulose nanofibers have promising structure, high molar mass, larger aspect ratio when compared to other nanofibers produced by pulp fibers from acid hydrolysis. In nature, a single enzyme cannot be used to degrade cellulose, butby a set of cellulases. These enzymes can be categorized as A- and B- type cellulases, C and D- Type cellulases. The former is termed as cellobiohydrolases, and the later is called as C- and D-type cellulases, or endoglucanases. Highly crystalline cellulose is degrading by cellobiohydrolases, whereas endoglucanases generally needs some disorder in the structure to degrade cellulose. In order to facilitate MFC disintegration, these enzymes shows high synergistic effects. The enzymatically pretreated cellulosic wood fibers gives rise to MFC, which shows a more favorable structure, having a higher average molar mass and a larger aspect ratio, than nanofibers produced by subjecting pulp fiber to strong acid hydrolysis.

ACID HYDROLYSIS

Journal of Science and Technology
ISSN: 2456-5660 Volume 7, Issue 06 (August 2022)
www.jst.org.in *DOI:https://doi.org/10.46243/jst.2022.v7.i06.pp1-19*

Acid hydrolysis mainly involves removal of amorphous region to produce nanocrystalline cellulose. Degradation of polysaccharides into simple sugars using acid solutions from cellulosic, hemicellulosic and search materials is called as acid hydrolysis. Flax like lignocellulosic fibers contains 20% to 40% hemicellulosic materials. Hemicellulosic materials mainly contain pentoses and hexoses, which are heteropolysaccharides. This process reduces sugar into monomers. Hemicellulose are more prone to oxidation and degradation reactions than cellulose. In alkaline and acid medium hydrolysis of glycosidic bond is faster at lower Ph. Nanocrystals are produced using Hydrochloric and sulphuric acid by acid hydrolysis. Sulphuric acid gives stable structure to nanocrystals over a wide range of pH values. Hydrochloric acid gives neutral nanocrystals with limited distribution in water. The most important parameter is reaction time, which have to be considered during hydrolysis (Vanderfleet et al., 2019) . Long reaction time will provide complete digestion of cellulosic hemp fibres. Short reaction time results in clumping of fibres and high dispersibility in water.

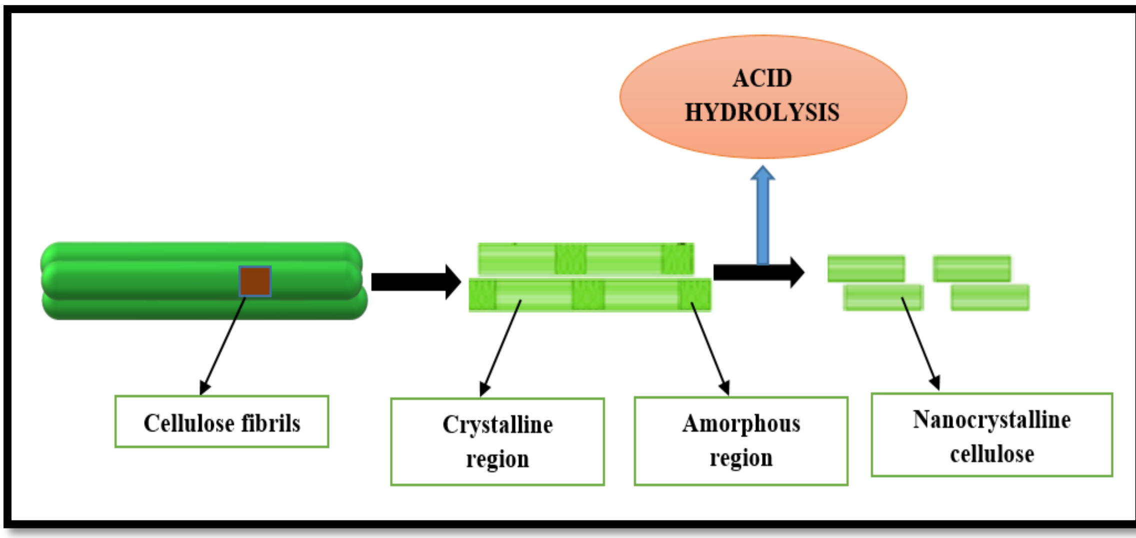


Fig 2. NANOCRYSTALLINE CELLULOSE BY ACID HYDROLYSIS** (Rajinipriya **et al., 2018)

MECHANICAL TREATMENT

Mechanical process is used to produce purified form of nanocellulose. Nano fibrils lies between 50 to 1000 nm in diameter and several micrometers long when produced using mechanical process. Before extraction of Nanofibres, they possess reinforcing ability. Nano composite sheet is formed by pressing it with PVA by cell wall extraction from parenchyma tissue. The primary and secondary cell wall contains more nanofibres which was extracted by mechanical pretreatments followed by chemical pretreatments. This is generally regarded as chemo-mechanical pretreatments. It does not degrade the cellulose in primary and secondary cell wall. This chemo mechanical methods involves yielding of nanofibrils in efficient manner. It produces nanofibrils in diameter range of 5 to 50 nm. The exclusion of non-cellulosic compounds from the crude mixture of cellulose is done by chemical retreatments. Generally the mechanical methods include the following techniques: Homogenization, Grinding, Cryocrushing, micro fluidization and Sonication etc.

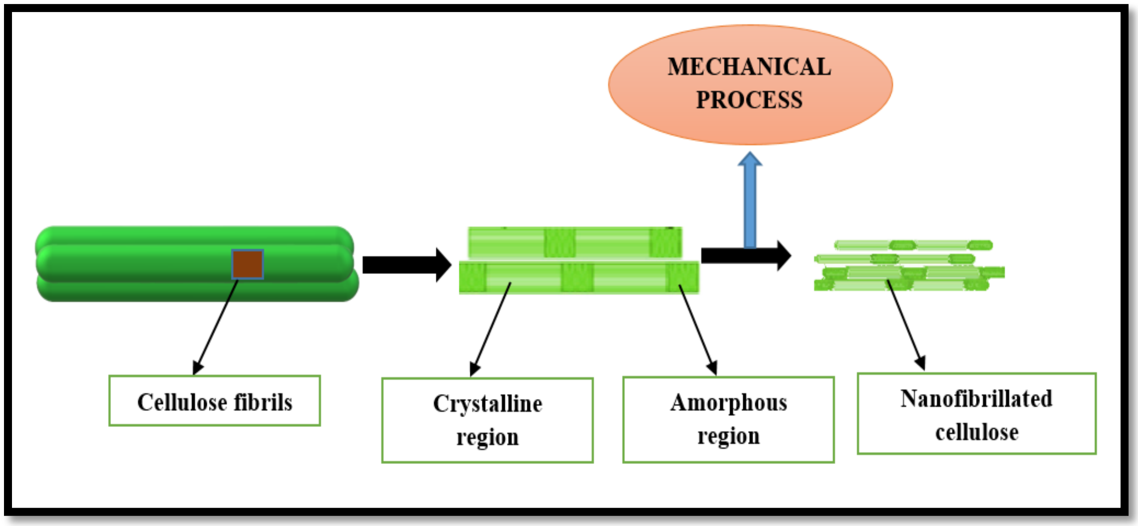


Fig 3. NANOFIBRILLATED CELLULOSE BY MECHANICAL PROCESS (Rajinipriya et al., 2018)

REFINING AND HIGH-PRESSURE HOMOGENIZATION

Nano fibrillated cellulose nowadays available as commercial products from different companies. It depends on mechanical treatment using defining and high pressure homogenizing process steps. It is based on mechanism that using a disk refiner, dilute fibers are send through a gap between rotor and stator disks. These disks have bars and grooves that fitted with on the surface. Here the fibres are subjected to cyclic stress repeatedly. This mechanical treatments increase the bonding strength by changes inmorphology and size of the fibres resulting in clustered form.

GRINDING

Researcher's uses grinders with some modification in their structure which mainly possesses specifically designed disks to produce nanocellulose fibers. It is a mechanical pretreatment in which the slurry is passed between the static and rotating grind stone. This rotating grind stone spins at 1500 rpm. It results in production of fine fibres by obtaining sharing forces. Due to high shear forces, cell wall structure of the pulp get disrupted (Wang et al., 2012). It results in production of nanocellulose fibers and crystals from the sources. Bacterial cellulose also underwent this mechanism at minimum rpm speed. Bacterial cellulose produced by experiencing less shear forces on it **(**Missoum et al., 2013**)** .

CRYOCRUSHING

The production of nanocellulose under freezing condition and also application of high shear forces is called as cryo crushing. Cryocrushing mainly uses liquid nitrogen as a freezing agent. Primarily the cell wall becomes freezed, results in formation of ice crystals in cell wall. Now this frozen crystal of cell wall was subjected tohigh shear forces. The high pressure on frozen cell wall results in liberation of cellulose materials. Nearly the nanocellulose materials obtained by this method have the diameter range of 5-80 nm. Before high pressure fibrillation, the cryo crushed nanocellulosic materials were distributed in water suspension using disintegrator. Cryocrushing is also used to extract nanocellulose fibres from soya bean stock.

SONICATION

Sonication is one of the extraction method for nanoparticles which is also used in homogenization, catalysis, dispersion etc. It uses sound waves to agitate particles in a solution. The conversion of electrical signal into physical vibration to break substances using sound waves is generally regarded as sonication. In sound spectrum, Ultrasound has the range of 20 KHz to 10MHz. It is because of conversion of mechanical or electrical energy into high-frequency sound energy by transducer. A very strong mechanical oscillating power was produced by High-intensity ultrasonication (HIUS) waves bycavitation. When the molecules in a liquid absorb ultrasonic energy, it results in the formation, expansion, and implosion of microscopic gas bubbles. The temperature was nearly $5000^{o}C$ and pressure of about 500 atm was experienced at implosion site. It was due to violent shock waves generation in cavitation bubble and surrounding area. Nano cellulose was produced by using HIUS energy in Batch method. When there is increase in power the nano fibrillation and crystallization is high. Similarly when the power is high the temperature is around $91^{0}C$. The cellulose concentration also depends on the dimension of the fibres obtained by this method.

MICROFLUIDIZATION

Microfluidization is one of the homogenization techniques which usually takes place at constant pressure, which is used for production on nano cellulose fibers. Microfluidizer has high shear processors. The slurry is passed through a z – shaped pump where it experiences high shear forces. The pressure was nearly about 276 MPa. There will be a series of check valves which allows the recirculation of the slurry. It is needed to increase the degree of fibrillation. It is used to produce fine nanoparticles with multiphase applications. High pressure causes disruption of cellwall of the source, results in release of cellulosic materials. Microfluidization is used in nanoemulsions, cell disruption, nanodispersions, nanocellulose production (mainly from algal source) and nano encapsulation **(**Missoum et al., 2013**)**.

APPLICATIONS

DRESSING MATERIALS

Nano cellulose is used as dressing material in the form of patches or large lobes. It is biocompatible, sterile, porous, and flexible. It allows wounds to breathe heal and formation of layers and scars are prevented in the form of water jackets. They reduce pain, and protect the skin from infection. It reduces loss of body fluids. It can also be used as defensive clothing for employees of emergency services (fire-fighters, soldiers) as they frequently exposed to burns when in contact with the fire (Shah, Brown., 2005; Ślęzak et al., 2016). The major disadvantage is it requires high cost.

OIL AND GAS

Cellulose nanocrystals are used in the oil and gas industry which includes drilling, cements and spacer fluids. Here nanocellulose acts as thickening agents, stabilizers, reinforcing agents and proppants (ceramic balls). Nanocellulose is mainly used in oil and gas industries for their thermal stability and its rheological properties (Molnes et al., 2016; Heggset et al., 2017).

COSMETICS, PHARMACEUTICAL, FOOD, PACKAGING, ENVIRONMENTAL APPLICATIONS

The promising stabilizing capacity, Inertness of chemicals and non-toxicity increase the possibility of CNCs in cosmetic, pharmaceutical and food products. It has verified a biomedical application which includes drug delivery; tissue engineering, biosensors, and bio adhesives (Roman., 2015).CNCs also contain surface sulfate ester groups as it is not in pure cellulose forms. It gives some important properties such as colloidal stability and functional handles for chemical modification.

NANO-SCALE DRUG CARRIERS USING NANOCELLULOSE

Nanocellulose acts as drug carriers. Nano cellulose have different bioactive functions and dealings in cell cultivation media and antibacterial as well as antiviral effects (Zoppe et al., 2015). In drug formulation, nanocelluloses were proven as effective excipients including tablet binders and fillers, film coatings, or as tablet matrices. Greater bulk density, improved flow ability, easy fragmentation of particles and rearrangement, reduced elastic recovery and a greater tensile strength was found in BNC powder. Thus tablets and capsule process formation was increased by using nanocellulose materials. The BNC film qualitywas proposed for the coating of solid dosage as it has tensile strength, elongation and elasticity modulus. The supramolecular 3D nanostructure has the ability to hold a high quantityof active ingredients. Thus these properties results in the development of nanocellulose. It facilitates nanocellulose based drug delivery system. Mostly high bio compatibility, hemocompatibility and renewability made nano cellulose as an effective drug carrier. Nowadays few nanocellulose drug carriers are under clinical trials.

Nanocellulose drug carriers are categorized into three: planar hydrogels, CNFs, CNCs. Planar hydrogels were used in the form of fleeces, membranes, coatings, films. It was used in its wet, dried or semi dried native manner for the entrapment of active ingredient

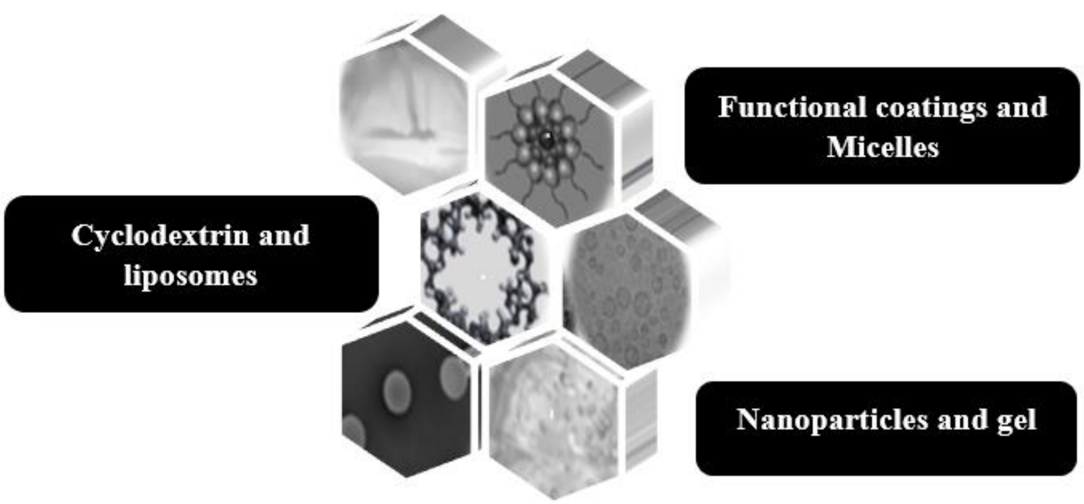


Fig 4. STRATEGIES BASED ON THE COMBINATION OF NANOCELLULOSE AND FURTHER CARRIERS TO ACCOMPLISH THE CONTROLLED FAST AND PROLONGED RELEASE OF DRUGS. (Kulkarni et al., 2012**)**

anocellulose was greatly utilized in biomedical field for its malleable structures and features. Different fields like physics, chemistry, life sciences and engineering assists in designing of nano biomaterials from both biological and synthetic materials which had wide application in biomedical fields. (Kim et al., 2019; Pires et al., 2019). In general, CNCs shows non-toxicity or less toxicity, better structural stability, various physical and chemical properties, huge surface to volume ratio, biocompatibility and bio degradability, which has great potential in many fields (Karimian et al., 2019; Jorfi, Foster., 2015). The CNCs posses less immunogenic response and usually has less toxicity. It is stated that these nature of CNCs with no environmental threats, enables to assist in cell proliferation by using it as tissue culture medium (Ilyas et al., 2018). However, it is reported that, in some cases CNCs involved in creating oxidative stress in cells and some inflammatory responses. These kind of obstacles can be conquered by its nanometric size and its better surface chemistry. So the toxicity can be influenced by CNCs in various manners (Thomas et al., 2018). CNCs have great impact on cell toxicity and immunogenicity, which can be possible by functionalizing specific functional groups or bestowing electrical charges in its physiochemical features (Bacakova et al., 2019).CNCs have good structural stability, colloidal stability and increased surface to volume ratio. In addition, CNCs were utilized for loading charged and neutral drugs as it has negative charge on its surface, which further proceed to control the active compounds and involved in transportation mechanism in target cells (George, Sabapathi 2015; Grishkewich et al., 2017; Tan. et al., 2019). In some cases, CNCs cannot be utilized in its original form, since it possess low drug loading capacity and hydrophobic nature. In order to increase efficiency in binding properties of hydrophobic drugs, huge modifications were bring to its surface by introducing reactive chemical groups in CNCs backbone (Salimi et al., 2019). After such modifications, it is necessary to maintain the structural stability and there is a need to increase CNCs efficiency in drug delivery system. CNCs can be utilized for efficient drug delivery in target cells. In order to target prostate and cancer cells, a complex of CNCs, cyclodextrin and curcumin were developed. An anti-proliferative effect was exposed to targeted cancer cells by this complex rather than using curcumin alone (Ntoutoume et al., 2016). CNC based hydrogels have better surface structure with open pores and high surface to volume ratio, enable easy drug delivery and good bioavailability. These kind of intense studies were illustrated in peer literatures (Du et al., 2016; Shojaeiarani et al., 2019).

TISSUE ENGINEERING APLLICATIONS

Nanocellulose materials persuade the requirements of Tissue culture techniques. Comparatively, nanocellulose material exhibit competent biodegradability, biocompatibility, high sustainability, water retention properties with better mechanical characteristics, also enables differentiation, cell proliferation and cell adhesion, which assist in Tissue culture technology (Abitbol et al. 2016; Mokhen, John.,2020) CNCs have become an auspicious material assisting in cartilage, bone, nervous system, hepatic, muscular, vascular and several ophthalmic healing process by altering its physical and chemical features. Different polymeric matrices requires nano cellulose as supporting material and it has better compatibility with chitosan, collagen, gelatin and also other biological materials, which was commonly used in Tissue engineering. In bone tissue engineering, CNC/chitosan/alginate/ hydroxyapatite scaffold was fabricated by freeze drying method. It reveals that cell proliferation, cell adherence were enhanced. Further, the physical and mechanical features of scaffolds was greatly increased when CNC was incorporated with other biological materials (Shaheen et al., 2019). Bone tissue scaffold with high feasibility was synthesized by cross-linking hydrazine with nanocellulose. This illustrates that, after implantation it exhibits good flexibility, porosity and aids in bone growth (Osorio et al., 2019; Moohan et al., 2020). In addition, nowadays nanocellulose materials were utilized as an effective wound dressing material and assists in wound healing, since it was more functionalized with competent features (Miao, Hamad., 2019).

CONCLUSION

Nanocellulose can be synthesized from different lignocellulosic biomass. The sources of nanocellulose include plants (agricultural wastes, wood pulp etc.) animals and bacteria. In this review the isolation, extraction and purification of nanocellulose were discussed. The goal of the present review is to emphasize that nanocelluloses as a prime example of natural sources for pioneering applications in materials science and technology. Nanocelluloses bio toxicity has to be considering for environmental remediation. The research on eco toxicology of nanocellulose materials is still at initial stage. Due to its biocompatibility, bio-degradability, low-cost and easy availability, nano-cellulose finds application in different research fields. In the biomedical field, nano cellulose has rendered it suitable applications in bone regeneration, in circulatory system and tissue engineering. In this regard, the works mentioned in this review indicate how nano cellulose produced from its sources and its application in different fields. However, the beneficial effects of nano cellulose are not limited to this aspect.

The formation of new capillaries is improved by using nanocellulose, which is necessary to provide nutrients and oxygen to the freshly developed bone. In addition to (re)generation of hard tissues like bones, when nanocellulose combined with other substances like alginates, it is also used to generate soft materials like "bionk", which is used for cartilage reconstitution in bio medical. For example, the nano cellulose in gel form is properly able to adhere the colon mucosa and it creates a barricade against water penetration, thus favoring gel durability and drug local delivery. The illustrations of nano cellulose applications here reported strongly support the massive application potential of this material whose applicability included in every field, but is not limited to, the biomedical field. Despite all of these difficulties in nanocellulose production, it is readily available on the market, allowing use of all its outstanding properties.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCE

Abitbol T, Rivkin A, Cao Y, Nevo Y, Abraham E, Ben-Shalom T (2016) Nanocellulose, a tiny fiber with huge applications. Curr. Opin. Biotechnol. 39, 76–88.

Bacakova L, Pajorova J, Bacakova M, Skogberg A, Kallio P, Kolarova, K (2019) Versatile application of nanocellulose: from industry to skin tissue engineering and wound healing. Nanomaterials. 9:164.

Behera S, Arora R, Nandhagopal N, Kumar S (2014) Importance of chemical pretreatment for bioconversion of lignocellulosic biomass. Renew. Sustain. Energy Rev. 36, 91–106.

Bhutto A.W, Qureshi K, Harijan K, Abro R, Abbas T, Bazmi A.A et al (2017) Insight into progress in pre-treatment of lignocellulosic biomass. Energy. 122, 724–745.

Carreño N.L.V, Barbosa A.M, Noremberg B.M, Salas M.S.S, Fernandes S.C.S, Labidi J (2017) Advances in Nanostructured Cellulose-based Biomaterials, Springer International Publishing, Cham.

Chen H, Liu J, Chang X, Chen D, Xue Y, Liu P., et al (2017) A review on the pretreatment of lignocellulose for high-value chemicals. Fuel Process. Technol. 160, 196–206.

Du H, Liu W, Zhang M, Si C, Zhang X, Li B (2019) Cellulose nanocrystals and cellulose nanofibrils based hydrogels for biomedical applications. Carbohyd. Polym. 209, 130–144.

El-Safty S.A, Shenashen M.A, Sakai M, Elshehy E, Halada K.J (2015) Detection and Recovery of Palladium, Gold and Cobalt Metals from the Urban Mine Using Novel Sensors/Adsorbents Designated with Nanoscale Wagon-wheel-shaped Pores. Visualized Exp. e53044.

Ferreira F.V, Mariano M, Rabelo S.C, Gouveia, R. F, Lona L.M.F (2018) Isolation and surface modification of cellulose nanocrystals from sugarcane bagasse waste: from a micro- to a nano-scale view. Appl. Surf. Sci.436, 1113–1122.

George J, Sabapathi S (2015) Cellulose nanocrystals: synthesis, functional properties, and applications. Nanotechnol. Sci. Appl. 8, 45–54.

Grishkewich N, Mohammed N, Tang J, Tam K.C (2017) Recent advances in the application of cellulose nanocrystals. Curr. Opin. Colloid Interface Sci. 29, 32–45.

Hassan S.S, Williams G.A, Jaiswal A.K (2018) Emerging technologies for the pretreatment of lignocellulosic biomass. Bioresour. Technol. 262, 310–318.

Heggset E.B, Chinga-Carrasco G, Syverud K (2017) Effect of acid hydrolysis conditions on the degradation properties of cellulose from *Imperata brasiliensis* fibers. Carbohydr. Polym. 157, 114–121.

Huang L, Zhang X, Xu M, Chen J, Shi Y, Huang C, Wang S, An S, Li C (2018) Preparation and mechanical properties of modified nanocellulose/ PLA composites from cassava residue. AIP Adv. 8, 025116.

Huang X, Wang J, Li T, Wang J, Xu M, Yu W, El Abed A, Zhang X, Beilstein J (2018) Review on optofluidic micro reactors for artificial photosynthesis. Nanotechnol. 9, 30–41.

Ilyas R, Sapuan S, Sanyang M.L, Ishak M.R, Zainudin E. (2018) Nanocrystalline cellulose as reinforcement for polymeric matrix nanocomposites and its potential applications: a review. Curr. Anal. Chem. 14, 203–225.

Jorfi M, Foster E.J (2015) Recent advances in nanocellulose for biomedical applications. Appl. Polym. Sci. 132, 41719.

Jozala A.F, De Lencastre-Novaes L.C , Lopes A.M, De Carvalho Santos-Ebinuma V, Mazzola P.G , Pessoa A, Grotto D, Gerenutti M, Chaud M.V (2016) Bacterial Nano cellulose production and application, Appl. Microbiol. Biotechnol, 100, 2063-2072.

Kargarzadeh H, Ioelovich M, Ahmad I, Thomas S, Dufresne A (2017) Methods for Extraction of Nanocellulose from Various Sources. In Handbook of Nanocellulose and Cellulose Nanocomposites Eds. Wiley-VCH: Weinheim, Germany. 1–49.

Karimi K, Taherzadeh M.J (2016) A critical review of analytical methods in pretreatment of lignocelluloses: composition, imaging, and crystallinity. Bioresour. Technol. 200, 1008–1018.

Karimian A, Parsian H, Majidinia M, Rahimi M, Mir M, Smadi-Kafil H (2019) Nanocrystalline cellulose: preparation, physicochemical properties, and applications in drug delivery systems. Int. J. Biol. Macromol. 133, 850–859.

Kaushik M, Moores A (2016) Review: nanocelluloses as versatile supports for metal nanoparticles and their applications in catalysis. Green Chem. 18, 622–637.

Kim D, Islam M.S, Tam M.K (2019) The use of nano polysaccharides in biomedical applications," in Advanced Functional Materials from Nano polysaccharides, eds N. Lin, J. Tang, A. Dufresne, and M. K. Tam (Singapore: Springer), 171–219.

Kulkarni P.K, Dixit S.A, Sing U.B, Am J (2012) Drug Discov. Dev. 2, 72–86.

Kumar R, Sharma R.K, Singh A.P (2017) Grafted cellulose: a bio based polymer for durable application. Polym. Bull. 1–30.

Kunusa W.R, Isa I, Laliyo L.A.R, Iyabu H.J (2018) FTIR, XRD and SEM Analysis of Microcrystalline Cellulose (MCC) Fibers from Corn corbs in Alkaline Treatment Phys. Conf. Ser. 1028, 012199.

Lin N, Dufresne A (2015) Nanocellulose in biomedicine: Current status and future prospect. Eur. Polym. J. 39, 302–325.

Liu L, Kong F (2019) In vitro investigation of the influence of nanofibrillated cellulose on lipid digestion and absorption. Int. J. Biol. Macromol. 139, 361–366.

Miao C, Hamad W.Y (2019) Critical insights into the reinforcement potential of cellulose nanocrystals in polymer nanocomposites. Curr. Opin. Solid State Mater. Sci. 23, 100761.

Missoum K, Belgacem M.N, Bras J (2013) Nanofibrillated cellulose surface modification: a review. Materials, 6, 1745–1766.

Mokhena T, John M (2020) Cellulose nanomaterials: new generation materials for solving global issues. Cellulose 27, 1149–1194.

Molnes S.N et al., (2016) Nanofluids and their engineering applications. Ind. Crops Prod. 93, 152–160.

Moohan J, Stewart S.A, Espinosa E, Rosal A, Rodríguez A, Larrañeta E (2020) Cellulose nanofibers and other biopolymers for biomedical applications. A review. Appl. Sci. 10:65.

Nechyporchuk O, Belgacem M.N, Bras J (2016) Production of cellulose nanofibrils: a review of recent advances. Ind. Crops Prod. 93, 2–25.

Ntoutoume G.M.N, Granet R, Mbakidi J.P, Brégier F, Léger D.Y, Fidanzi- Dugas F (2016) Development of curcumin–cyclodextrin/cellulose nanocrystals complexes: new anticancer drug delivery systems. Bioorg. Med. Chem. Lett. 26, 941–945.

Osorio D.A, Lee B.E, Kwiecien J.M, Wang X, Shahid I, Hurley A.L (2019) Cross-linked cellulose nanocrystal aerogels as viable bone tissue scaffolds. Acta Biomater. 87, 152–165.

Pelissari F.M, Sobral P.J.A, Menegalli F.C (2014) Isolation and characterization of cellulose nanofibers from banana peels. Cellulose, 21, 417–432.

Pires J.R, Souza V.G, Fernando A.L (2019) Valorization of energy crops as a source for nanocellulose production–current knowledge and future prospects. Ind. Crop Prod., 140:111642.

Qu J, Yuan Z, Wang C, Wang A, Liu X, Wei B (2019) Enhancing the redispersibility of TEMPO-mediated oxidized cellulose nanofibrils in N, N dimethyl formamide by modification with cetyl trimethyl ammonium bromide. Cellulose 26, 7769–7780.

Rabemanolontsoa H, Saka S (2016) Various pretreatments of lignocellulosic. Bioresour. Technol. 199, 83–91.

Rajinipriya M, Nagalakshmaiah M, Robert M, Elkoun S (2018) Importance of agriculture and industrial wastes in the field of nanocellulose and recent industrial developments of wood based nanocellulose. ACS Sustainable Chem. Eng. 6, 2807–2828.

Razalli R.L, Abdi M.M, Tahir P.M, Moradbak A, Sulaiman Y, Heng L.Y (2017) Polyaniline-modified nanocellulose prepared from Semantan bamboo by chemical polymerization: preparation and characterization RSC Adv. 7, 25191–25198.

Rezania S, Oryani B, Cho J, Talaiekhozani A, Sabbagh F, Hashemi B (2020) Different pretreatment technologies of lignocellulosic biomass for bioethanol production: an overview. Energy, 199:117457.

Rodriguez C, Alaswad A, Benyounis K, Olabi A.G (2017) Pretreatment techniques used in biogas production from grass. Renew. Sustain. Energy Rev. 68, 1193–1204.

Roman M (2015) Toxicity of cellulose nanocrystals. Ind. Biotechnol. 11, 25–3.

Ruan C, Strømme M, Jonas L (2016) A Green and simple method for preparation of an efficient palladium adsorbent based on cysteine funtionalized 2,3- dialdehyde cellulose. Cellulose. 23, 2627–2638.

Salimi S, Sotudeh- Gharebagh R, Zarghami R, Chan S.Y, Yuen K.H (2019) Production of nanocellulose and its applications in drug delivery: a critical review. ACS Sustain. Chem. Eng. 7, 15800–15827.

Satlewal A, Agrawal R, Bhagia S, Sangoro J, Ragauska A.J (2018) Natural deep eutectic solvents for lignocellulosic biomass pretreatment: recent developments, challenges and novel opportunities. Biotechnol. Adv. 36, 2032–2050.

Shah J, Brown M.R.J.R (2005) Towards electronic paper. Appl. Microbiol. Biotechnol. 66, 352-355.

Shaheen T.I, Montaser A, Li S (2019) Effect of cellulose nanocrystals on scaffolds comprising chitosan, alginate and hydroxyapatite for bone tissue engineering. Int. J. Biol. Macromol. 121, 814–821.

Shibata I, Isogai A (2003) Depolymerization of cellouronic acid during TEMPO-mediated oxidation. Cellulose, 10**,** 2, 151–158.

Shojaeiarani J, Bajwa D, Shirzadifar A (2019) A review on cellulose nanocrystals as promising biocompounds for the synthesis of nanocomposite hydrogels. Carbohyd. Polym. 216, 247–259.

Singh R, Shukla A, Tiwari S, Srivastava M (2014) A review on delignification of lignocellulosic biomass for enhancement of ethanol production potential. Renew. Sustain. Energy Rev. 32, 713–728.

Ślęzak A, Kucharzewski M, Jasik-Ślęzak J (2016) The characteristics of medical dressings bacterial cellulose membrane. Department of Biology and Biophysics, University of Czestochowa. Department of General Surgery, Medical University of Silesia in Bytom.

Stanisławska A (2016) Bacterial nanocellulose as a microbiological derived nanomaterial. Advances in materials science, vol. 16, 4, 50.

Taleb K.A, Rusmirović J.D, Rančić M.P, Nikolić J.B, Drmanić S.Z, Veličković Z.S, Marinković A.D.J (2016) Arsenic removal by magnetize loaded amino modified nano/ micro cellulose adsorbents: Effect of functionalization and media size Serb. Chem. Soc.81, S316–S323.

Tan T.H, Lee H.V, Dabdawb W.A.Y, Hamid S.B.B.O.A (2019) "A review of nanocellulose in the drug-delivery system," in Materials for Biomedical Engineering: Nanomaterials-Based Drug Delivery, eds A. M. Holban and A. Grumezescu (Radarweg: Elsevier),131–164.

Thomas B, Raj M.C, Joy J, Moores A, Drisko G.L, Sanchez C (2018) Nanocellulose, a versatile green platform: from biosources to materials and their applications. Chem. Rev. 118, 11575–11625.

Trache D, Tarchoun A,F, Derradji M, Hamidon T.S, Masruchin N, Brosse N, Hussin M.H (2020), Nanocellulose: From Fundamentals to Advanced Applications. Front. Chem, 8:392.

Uzyol H.K, Saçan M.T (2017) Bacterial cellulose production by *Komagataeibacter hansenii* using algae-based glucose. Environ. Sci. Pollut. Res.24, 11154–11162.

Van de Ven T, Godbout L (2013) Highly charged nanocrystalline cellulose and dicarboxylated cellulose from periodate and chlorite oxidized cellulose fibers. InTech.

Vanderfleet O.M, Osorio D.A, Cranston E.D (2018) Optimization of cellulose nanocrystal length and surface charge density through phosphoric acid hydrolysis. Philos. Trans. R. Soc., 376, 20170041.

Wang Q.Q, Zhu J.Y, Gleisner R, Kuster T.A, Baxa U, S. E McNeil S.E (2012) Morphological development of cellulose fibrils of a bleached eucalyptus pulp by mechanical fibrillation. Cellulose, 19, 1631–1643.

Wang W, Yu Z, Alsammarraie F.K, Kong F, Lin M, Mustapha A (2020) Properties and antimicrobial activity of polyvinyl alcohol-modified bacterial nanocellulose packaging films incorporated with silver nanoparticles. Food Hydrocoll, 100:105411.

Wei L, Agarwal U.P, Hirth K.C, Matuana L.M, Sabo R.C, Stark N.M (2017) Chemical modification of nanocellulose with canola oil fatty acid methyl ester. Carbohyd. Polym. 169, 108–116.

Zhao C, Shao Q, Chundawat S.P (2020). Recent advances on ammonia based pretreatments of lignocellulosic biomass. Bioresour. Technol, 298:122446.

Zoppe J.O, Johansson L.S, Seppälä J (2015) Manipulation of cellulose nanocrystal surface sulfate groups towards biomimetic nanostructures in aqueous media. Carbohydr. Polym. 126, 23–31.