Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

Nanocellulose from Agricultural Waste for Neonatal and Biomedical Implant Applications

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Cite this paper as: Chetan Singh Chouhan, Hitin Dagur, Ravi Kant Rahi, (2025) Nanocellulose from Agricultural Waste for Neonatal and Biomedical Implant Applications. *Journal of Neonatal Surgery*, 14 (32s), 90-101.

ABSTRACT

Nanocellulose, a nanoscale form of cellulose derived from plant biomass, has emerged as a promising sustainable material owing to its exceptional properties such as high mechanical strength, large surface area, biocompatibility, biodegradability, and surface chemistry. This review explores the extraction of nanocellulose from various agricultural residues including wheat straw, rice husk, sugarcane bagasse, corn stalks, and coconut husk using eco-friendly methods such as acid hydrolysis, enzymatic treatment, and mechanical disintegration. Emphasis is placed on optimizing extraction processes to yield biomedical-grade nanocellulose while minimizing environmental impact. The application of nanocellulose in biomedical implants, particularly for neonatal use, is discussed with a focus on its roles in tissue engineering scaffolds, wound healing matrices, and drug delivery systems. Its structural similarity to natural extracellular matrices, along with non-toxicity and minimal immunogenicity, makes nanocellulose a highly favourable material for sensitive clinical applications. Additionally, functionalization of nanocellulose surfaces enables antimicrobial, anti-inflammatory, and regenerative enhancements tailored to neonatal care. This review highlights the dual benefits of agricultural waste valorisation and the development of advanced green biomaterials, positioning nanocellulose as a next-generation component in biomedical implants while addressing sustainability and health care innovation.

Keywords: *Nanocellulose, Agricultural Residues, Biomedical Implants, Neonatal Applications, Biocompatibility, Tissue Engineering, Drug Delivery, Sustainable Biomaterials*

1. INTRODUCTION

The escalating global demand for advanced materials derived from renewable resources has catalysed intense research into sustainable nanocellulose, a nanostructured cellulose variant extracted from diverse biological sources including plant biomass (wood pulp, agricultural residues), bacterial sources (*Gluconacetobacter xylinus*), algae, and tunicates (Klemm et al., 2011). This material class, encompassing cellulose nanocrystals (CNCs), cellulose nanofibrils (CNFs), and bacterial cellulose (BC), exhibits an exceptional combination of physicochemical properties highly relevant to biomedicine. These include remarkable mechanical strength, high specific surface area (often exceeding 100 m^2/g), tunable surface chemistry via hydroxyl group functionalization, inherent biocompatibility, and controllable biodegradability (Habibi et al., 2010; Thomas et al., 2018; Trache et al., 2020). Beyond its performance attributes, nanocellulose's derivation from abundant, renewable feedstocks positions it as a cornerstone material in the transition towards a circular bioeconomy, offering a significant reduction in environmental footprint compared to petrochemical-derived polymers and aligning with principles of green chemistry (Du et al., 2019; Cruz et al., 2021).

The imperative for integrating sustainable biomaterials like nanocellulose into the healthcare sector is underscored by the substantial and growing environmental burden associated with conventional medical materials. Single-use medical devices and packaging contribute an estimated 5–10% of the healthcare sector's overall carbon footprint, generating vast quantities of persistent plastic waste (McGain et al., 2020). Nanocellulose-based systems present a compelling ecological alternative while simultaneously offering versatile functionalities critical for biomedical use, such as the ability to form highly absorbent hydrogels, ultra-lightweight aerogels with high porosity, and biocompatible films or coatings. Its extensive surface area facilitates biofunctionalization with drugs, peptides, or signalling molecules, enhancing its therapeutic potential (Lin &

Dufresne, 2014). However, translating this potential into clinically viable products necessitates the rigorous achievement of biomedical-grade standards. This demands comprehensive control over parameters including sterility (validated methods per ISO 11737), endotoxin levels (typically requiring < 0.5 Endotoxin Units (EU)/mL for implants), absence of cytotoxicity, predictable degradation kinetics, and stringent batch-to-batch consistency to ensure safety and efficacy (Foster et al., 2018; Nair et al., 2021).

These stringent requirements become critically amplified and non-negotiable in the context of neonatal applications, particularly for vulnerable preterm infants (gestational age < 37 weeks). Neonates possess physiologically immature systems characterized by an underdeveloped epidermal barrier, attenuated innate and adaptive immune function, heightened systemic absorption potential through the skin, and an extreme susceptibility to chemical, infectious, and toxicological insults (Stark et al., 2018). Consequently, biomaterials interfacing with this fragile population, whether for wound dressings, transdermal drug delivery systems, tissue engineering scaffolds, biosensors, or protective barriers—demand exceptional biocompatibility, minimal irritation potential, ultra-purity (free from leachable), and precisely tailored degradation profiles matched to their unique physiology. Conventional polymeric materials frequently fall short in meeting these specialized needs due to issues like residual monomers, plasticizers, inflammatory responses, or inappropriate degradation rates (Nair et al., 2021). Nanocellulose's intrinsic properties, including low inherent immunogenicity, structural similarity to extracellular matrix components, and high-water retention capacity, present unique opportunities to address these critical challenges (Bacakova et al., 2019; Domingues et al., 2021).

Therefore, the primary purpose of this comprehensive review is to critically synthesize and evaluate the current scientific advancements, challenges, and future prospects of nanocellulose biomaterials specifically engineered for neonatal biomedical applications. The scope encompasses a detailed overview of nanocellulose fundamentals, including its sources, structural classifications (CNCs, CNFs, BC), key physicochemical properties governing biomedical interactions, and common functionalization strategies. It further explores the imperative for sustainable biomaterials in modern medicine, analysing the lifecycle advantages of nanocellulose and its alignment with environmental sustainability goals.

A critical focus lies on elucidating the specific requirements for biomedical-grade materials and the significant hurdles in achieving this standard for neonatal use, such as identifying sterilization methods (autoclaving, gamma irradiation, ethylene oxide) that preserve nanocellulose integrity, ensuring effective endotoxin removal, navigating complex regulatory pathways (FDA, EMA), and addressing standardization gaps. Finally, the review delves deeply into the existing research landscape and emerging applications of nanocellulose within neonatology, examining preclinical and early clinical evidence for its use in areas like drug delivery, wound management, tissue regeneration, and diagnostics, while rigorously assessing the available safety and efficacy data. By identifying key translational barriers—including scalability of production, the critical need for long-term biodistribution and toxicity studies, and the development of standardized, physiologically relevant neonatal in vitro models—this review aims to outline prioritized research directions to accelerate the safe and effective clinical adoption of nanocellulose technologies for this most vulnerable patient group.

2. SOURCES OF NANOCELLULOSE FROM AGRICULTURAL RESIDUES

Agricultural residues include various types of biomass material obtained after harvesting/processing crops, such as rice straw, wheat straw, corn stover, sugarcane bagasse, banana pseudostems, coconut husk, cotton stalks, and peanut shells. The Food and Agriculture Organisation (FAO) reports that billions of tonnes of agricultural leftovers are generated year, but they are frequently underutilised or disposed of in ways that are damaging to the environment, including open field burning, which causes significant greenhouse gas emissions and air pollution (Kumar et al., 2021; Yustira et al., 2021).

Due to their high lignocellulosic biomass content, consisting chiefly of cellulose, hemicellulose, and lignin, the scientific community has been increasingly directed toward valorization of these residues. Notably, cellulose is one of the main ingredients. Cellulose is a linear polysaccharide in which the basic building blocks β-D-glucose units are connected by β-1,4-glycosidic links, and crystallise. In plant cell walls, it functions as an important structural component, providing rigidity and tensile strength (Klemm et al., 2018). Cellulose makes up 30% to 50% of the dry biomass of agricultural residues, depending on the plant (Zhao et al., 2017; Yusuf & Abdullahi, 2020), making these materials ideal for cellulose extraction.

As the cellulose content varies between different types of agricultural residue due to differences in the species of plant used, time of harvest maturity, climatic conditions, and tissue composition. Rich in cellulose (40–45%), sugarcane bagasse is an industrial by-product of the sugar industry that has been thoroughly studied for the generation of bioethanol and nanocellulose (Sauodi & Hasan, 2021) among other uses. Cereal straw like wheat and rice, yielded in large quantities in Asia and North America, usually contains 45% cellulose and has been reported to have been evaluated in multiple extraction scales (Yustira et al., 2021; Vallejo et al., 2021). The pseudostems of banana, which are usually of no use and left in the banana plantations, represent an underutilized source of cellulose (30–42%) (Yusuf & Abdullahi, 2020). Even less commonly studied residues demonstrate an impressive cellulose proportion, including peanut shells or coconut husk (Kim et al., 2020; Zedin et al., 2022).

Agricultural residues are attractive because their low economic value means that raw material costs will be lower for industries seeking to produce cellulose-based products. Furthermore, the use of these residues is in accordance with the principles of circular bioeconomy—converting waste into value-added materials while decreasing dependency from non-renewable resources (Yuan et al., 2020; Kumar et al., 2021). The cellulosic residue must be treated efficiently as it is surrounded by a lignocellulosic sheath containing lignin and hemicellulose to become available. For example, residues rich in lignin are more difficult to obtain cellulose from, which helps dictate the choice of raw crude materials for processing on an industrial scale (Zhao et al. 2017; Yuan et al. 2020). Additional factors such as post-harvest handling and conditions of storage could influence cellulose yield and quality, potentially via microbial degradation or chemical modifications (Lou et al., 2022; Zedin et al., 2022).

Table 1: Nanocellulose Content Global Availability and Valorisation Potential

Residue	Annual Production	Key Regions	Nanocellulose Yield
Sugarcane bagasse	1.9 billion tons	Brazil, India, Thailand	25–40%
Corn stalks	2.0 billion tons	USA, China, Brazil	30–45%
Rice husk	160 million tons	China, India, Indonesia	15–25%*
Wheat straw	1.1 billion tons	EU, China, Russia	20–35%
Coconut husk	50 million tons	Philippines, Indonesia	10–20%
*Lower due to silica content (Johar et al., 2020; Bello et al., 2021)			

3. EXTRACTION TECHNIQUES OF NANOCELLULOSE

This cellulose is tightly associated with hemicellulose and lignin, forming a complex lignocellulosic matrix which makes it difficult to extract readily for direct use. However, this structure lends rigidity to the plant cell wall but is also a considerable hindrance to an effective cellulose isolation. Therefore, pretreatment, which seeks to disrupt this complex structure, is a necessary step before cellulose extraction, increasing the available surface area as well as reducing cellulose crystallinity to facilitate its extraction for later processing (Yuan et al., 2020; Zedin et al., 2022). Ideal pretreatment, after all, should eliminate most of the lignin and hemicellulose, retain cellulose integrity, avoid producing inhibitors (e.g., furfural), cost-effective, green, and scalable as well. Different pretreatment techniques have been developed and improved over time; however, they can be largely grouped in physical, chemical, physicochemical, and biological methods. These are often utilized in conjunction to increase efficiency overall (Kim et al., 2020; Kumar et al., 2021).

3.1 Physical Pretreatments - Milling, grinding, and ultrasonication are physical methods that reduce particle size and increase surface area. Ball milling and high-energy grinding, for example, are commonly employed in reducing the crystalline structure of cellulose and increasing chemical activity (Lou et al., 2022). While these techniques will not lead to delignification by themselves, they are an important step preceding chemical or enzymatic treatments. Pros: Not involving chemicals, easy. Disadvantages: High energy required, low selectivity.

3.2 Chemical Pretreatments - Chemical methods are most commonly used for cellulose extraction due to their high efficiency in removing non-cellulosic components. In alkaline Pretreatment base agents such as NaOH, KOH or $Ca(OH)_2$ have been reported which disrupt ester bonds and cleave lignin as well as some hemicellulose and leave the biomass more porous (Sauodi & Hasan, 2021). This is particularly effective with soft biomass such as wheat straw and banana pseudostems. For example, NaOH treatment of sugarcane bagasse resulted in a 35–50% increase in the purity of cellulose (Yustira et al., 2021). In acid hydrolysis dilute acids, including H_2SO_4 and HCl, hydrolyze hemicellulose, our cellulose fibers into liberation. Nevertheless, strong acids may degrade cellulose and produce toxic by-products (Vallejo et al., 2021). Trade-off: High delignification vs. susceptibility to sugar degradation. In Oxidative and Organosolv Pretreatments, for example, oxidative agents (e.g., H_2O_2) and organic solvents (e.g., ethanol) help bulks a function of lignin and expose cellulose for easier access. Aim: Organosolv pretreatment is receiving attention as it can fractionate biomass without using acid and in a clean manner (Kumar et al., 2021).

3.3 Physicochemical Pretreatments - Its process involves heat, pressure and chemicals. Examples of these are steam explosion, ammonia fiber expansion (AFEX), and liquid hot water pretreatment. Cell wall disruption and partial removal of lignin and hemicellulose by steam explosion. AFEX employs ammonia to cleave ester bonds and enhance cellulose accessibility with limited sugar loss (Zhao et al., 2017).

3.4 Biological Pretreatments - Using fungi or microbial enzymes to degrade lignin is an ecofriendly option. Most lignocellulosic composites are degraded by white-rot fungi in which lignin is selectively degraded and cellulose is preserved (Yusuf & Abdullahi, 2020). Limitations include long processing time and controlled conditions required where as its Strength are being Environmentally conscious and lower energy input.

3.5 Emerging Green Technologies - Currently, ionic liquids (ILs) and deep eutectic solvents (DES) are being recommended, both are quite effective in being able to solubilizing these components without damaging cellulose. These solvents are recyclable and biodegradable, providing a potential green alternative (Lou et al., 2022; Zedin et al., 2022).

Table 2: Comparative Overview of Pretreatment Methods

Pretreatment Type	Method	Key Function	Advantages	Limitations	Reference
Physical	Milling, Grinding	Increase surface area	Simple, chemical-free	High energy demand	Lou et al. (2022)
Chemical	Alkaline (NaOH, KOH)	Lignin removal	Effective delignification	Waste disposal issues	Sauodi & Hasan (2021)
	Acid (H_2SO_4, HCl)	Hemicellulose hydrolysis	Fast reaction	Corrosive, may degrade sugars	Vallejo et al. (2021)
	Organosolv	Fractionates biomass	Cleaner separation	Expensive solvents	Kumar et al. (2021)
Physicochemical	Steam Explosion, AFEX	Disrupts cell walls	Reduces lignin, scalable	Equipment intensive	Zhao et al. (2017)
Biological	Fungal/Enzymatic	Degrades lignin	Eco-friendly, selective	Slow, controlled environment needed	Yusuf & Abdullahi (2020)
Green Solvents	ILs, DES	Solubilizes lignin/hemicellulose	Recyclable, low toxicity	High cost, needs optimization	Zedin et al. (2022); Lou et al. (2022)

Pretreatment is an essential process to facilitate cellulose extraction from agriculture residues. The choice of the pretreatment method is dependent on type of biomass, desired application, environmental considerations and economic viability. Although chemical pretreatments currently account for most pretreatment technologies owing to their high efficacy, the current focus is on green, sustainable alternatives like biological and solvent-based methods.

4. CELLULOSE EXTRACTION METHODS

Agricultural residues were also used for cellulose extraction where cellulose is systematically separated from lignin and hemicellulose after pretreatment. These residues are structurally complex and contain a crystallized network of cellulose fibrils embedded in psalm of lignin and hemicellulose, which renders direct extraction of cellulose from it challenging (Yuan et al., 2020). Effective methods of cellulose extraction should therefore try to isolate cellulose in purified form, but in non-degrading, unchanged crystalline form. As the chemical approaches yield lower selectivity and economy, the extraction has nowadays matured from pure chemical routes to more environmentally friendly routes, such as enzyme-driven, mechanical and green-solvent based technologies. The choice of a specific method varies according to biomass type, environmental impact, economic viability, intended cellulose purity and scale (Zedin et al., 2022; Kumar et al., 2021).

4.1 Chemical Extraction Methods

For cellulose isolation chemical extraction are one of the most enduring and extensively adopted strategies. This includes several reagent-based treatments that will deconstruct the lignocellulosic matrix and release the cellulose with minimal contaminants. The first line of treatment is alkaline extraction generally sodium hydroxide (NaOH) or potassium hydroxide (KOH). These alkaline agents rupture ester linkages and destruct the lignin-carbohydrate complex to release lignin and hemicellulose. For example, a significant increase in cellulose accessibility after NaOH treatment (at rates ranging from 4 to 10%) of sugarcane bagasse or wheat straw with 50% lignin removal has been observed (Yustira et al., 2021).

The acid hydrolysis is carried out using dilute sulfuric acid (H_2SO_4) or hydrochloric acid (HCl) to eliminate residual hemicellulose and amorphous carbohydrates after delignification. Precise monitoring of acid strength, temperature, and time is essential to prevent degradation of cellulose. Hydrolytic degradation occurs due to overexposure and yield by-products such as furfural and levulinic acid, which could inhibit processes downstream (Vallejo et al., 2021). Bleaching treatments using sodium chlorite ($NaClO_2$), hydrogen peroxide (H_2O_2), or sodium hypochlorite (NaOCl) are commonly used to remove remaining lignin, and increase the whiteness and purity of cellulose. Oxidative pretreatments aim towards the cleavage of chromophores present in lignin that result in bright (>90% purity) cellulose fibers for material and biomedical applications (Kumar et al., 2021). Because of chemical consumption, wastewater generation, and the need for multiple washing and neutralization steps, chemical extraction is not environmentally friendly despite being effective. However, it is a cornerstone of cellulose processing industries due to its scalability and consistency.

4.2 Enzymatic Extraction

Biological extraction stands out as a green, selective method for cellulose extraction. Fungi or bacteria produce lignin-degrading and hemicellulose-degrading enzymes (cellulases, xylanases, and laccases); the method is called microbial method (Yusuf & Abdullahi, 2020). Lignin degradation would be initiated by the application of ligninolytic enzymes (e.g., laccase or manganese peroxidase) to selectively degrade lignin, followed by the application of xylanases to hydrolyze hemicellulose. These enzyme cocktails work synergistically to release cellulose fibers from the lignocellulosic matrix where they are arrested. For instance, high cellulose yield was obtained after 72 h of enzymatic hydrolysis of cornstalks treated with a fungal consortium of *Trichoderma reesei* and *Phanerochaete chrysosporium* (Lou et al., 2022). They are carried out using mild conditions (pH 4.5–6.0, 40–50°C) with low energy input, and cellulose degradation is also minimized. Limitations include long processing periods, high enzyme production costs, and a susceptibility to variation in substrates. Such innovations encompass recombinant enzyme production and immobilized enzyme systems aimed at overcoming these bottlenecks, thus rendering enzymatic extraction a highly promising pathway in utilization of biomass as energy carriers for sustainable biorefinery processes (Kim et al., 2020).

4.3 Mechanical Extraction

Mechanical extraction technique relies on the breakdown of biomass to free cellulose fibres. These techniques are frequently combined with chemical or enzymatic treatment to improve extraction efficiency. Grinding and milling, such as ball milling and hammer milling, are methods to reduce the size of biomass particles and to disrupt the crystalline cellulose structure, thereby increasing the surface area available for subsequent treatments. Mechanical comminution aids in releasing cellulose from the lignin and hemicellulose fraction, but by alone is insufficient to reach high purity levels (Yuan et al., 2020).

Ultrasonication is a non-chemical unit operation that employs high-frequency sound waves to generate cavitation bubbles in the medium that collapse above a critical threshold and burst releasing high amounts of energy that disrupts the plant cell walls and increases mass transfer. Ultrasonication, when supplemented with chemical or enzymatic processes, increases reaction rates, decreases reagent requirements, and enhances cellulose yield (Vallejo et al., 2021). Steam explosion is another classic method, in which biomass is exposed to high-pressure steam that is suddenly decompressed. This results in the physical rupture of the cell wall structure and partial removal of hemicellulose and lignin, allowing for increased accessibility of cellulose. It might not completely purify, but it goes a long way in cutting down the use of harsh chemicals. Mechanical methods are scalable, energy efficient, and can work in all settings, making them especially valuable when combined with hybrid systems that utilize both physical and biochemical means.

Green chemistry approaches offer alternatives over classic chemical extraction. Of these, ionic liquids (ILs) and deep eutectic solvents (DES) have displayed exceptional potential for selective dissolution of lignocellulosic components. Disruption of hydrogen bonding networks by ionic liquids [such as 1-butyl-3-methylimidazolium chloride ([Bmim]Cl)] enables them to dissolve lignin and hemicellulose while leaving cellulose intact. Due to their tunable chemical structure, they offer selective fractionation options and are thus suitable for different biomass types (Zedin et al., 2022). Deep eutectic solvents, which consist of a hydrogen bonding donor and acceptor (e.g., choline chloride and lactic acid), have similar properties to ILs but are biodegradable, nontoxic, and cheaper. It has been shown in studies that DES can separate cellulose with more than 90% purity from wheat straw, corn husks, and rice hulls with no toxic waste (Kumar et al., 2021). These advantages notwithstanding, there are challenges involved in solvent recovery, recyclability, and processing economics. But the biorefinery platforms with green solvents are an environmentally conscious approach for cellulose separation.

5. CHARACTERIZATION OF EXTRACTED NANOCELLULOSE

Characterization of extracted cellulose is a crucial point to evaluate the process efficiency, purification degree, and the functional properties of the cellulose obtained from seaweeds. This is particularly relevant for agricultural residues, which vary significantly in their macro-structure, micro-structure, and extraction response (Hosseini Koupaie et al., 2019). Its precise characterization is also essential to assess the appropriateness of cellulose for various industrial sectors, including bioplastics, composites, papermaking, pharmaceuticals, and biofuels (Kaur et al., 2022). Characterization is generally carried out by a collection of spectroscopic, microscopic, thermal, and structural techniques delivering complementary information about the cellulose morphology, crystallinity, functional groups, and chemical composition.

FTIR spectroscopy, which is used to identify the functional groups, is one of the most often used techniques to verify the chemical structure of cellulose. A complete or partial disappearance of typical peaks in the extracted cellulose, ascribed to phenolic and/or lignin (e.g., assignment of aromatic skeletal vibrations at 1510 cm^{-1}) and hemicellulose (e.g., carbonyl groups at 1730 cm^{-1}) evidenced efficient removal of non-cellulosic matter (Nasution et al., 2021). The wide band in the region of 3300–3500 cm^{-1} is representative of –OH stretching vibrations observed for cellulose. The peak around 2900 cm^{-1} is from –CH stretching. The evidence of a strong band at 1050 cm^{-1} (C–O–C stretching) indicates the presence of cellulose backbone structures (Putro et al., 2020). Comparison of FTIR spectra, pre- and post-extraction, shows the chemical purity and validates the removal of interfering compounds.

XRD is critical for investigation of CrI of separated cellulose. According to the Segal technique, native cellulose typically forms the cellulose I polymorph, which has peaks at 2theta=14.8°, 16.4°, and 22.6°. Upon extraction, the increase crystallinity suggests the efficient removal of amorphous hemicellulose and lignin (Putro et al., 2020; Hosseini Koupaie et al., 2019). The mechanical strength, biodegradability and chemical reactivity of cellulose is significantly influenced by its crystallinity. For reinforcement materials, high crystallinity values (>60%) are desired, however, amorphous cellulose is favored in enzymatic hydrolysis in bioethanol production (Tang et al., 2020).

Thermogravimetric Analysis (TGA) gives a clue about the thermal stability and the decomposition behavior of the cellulose that is being extracted. It usually shows three phases of weight loss: (i) moisture loss (~ 100 °C), (ii) significant degradation of cellulose (250–350 °C) and (iii) char formation (> 400 °C) (Reddy et al., 2020). These results suggest that the onset decomposition temperature is higher and residual mass is lower, which indicates purer cellulose, as lignin and hemicellulose decompose in a lower and wider temperature range. Therefore, thermal analysis provides indirect evidence for successful removal of lignin/hemicellulose and verifies suitability (e.g., in biocomposites or as packaging).

The surface morphology and fiber structure of the cellulose can be observed by SEM. Agricultural biomass typically has a fused, dense, and heterogeneous surface before extraction because of the lignin and hemicellulose connection. After extraction, SEM images indicate that there are loosened, individualized, and fibrillated cellulose fibers having rougher textures and diminished particle size (Ali et al., 2020). Additionally, morphological differences reflect the efficiency of pretreatment and extraction protocols and potential applications in composites where interfacial bonding between fibers and matrix strongly relies on surface area and texture.

Generally, the elemental composition of cellulose is determined by CHNS/O elemental analysis or EDX (Energy Dispersive X-ray Spectroscopy). Increases in carbon and oxygen content coupled with decreases in nitrogen and sulfur content suggest reductions in protein and lignin content. Additionally, compositional analysis can be performed using wet chemistry techniques for quantification of α-cellulose, hemicellulose, and lignin contents (Kaur et al., 2022). Surface Charge and Zeta Potential technique is used to create characterization of the surface charge and colloidal stability of cellulose suspensions, which is particularly important for nanocellulose таких. The negatively charged surfaces (~–20 to –40 mV) enhance the dispersion stability and interaction with charged biomolecules (Tang et al., 2020).

6. APPLICATIONS OF NANOCELLULOSE

Biodegradability, abundance, biocompatibility, and mechanical robustness of cellulose extracted from agricultural residues have attracted considerable interest. The increasing focus on sustainability and circular bioeconomy has spurred investigation into the use of biomass-derived cellulose in a variety of fields–industrial, biomedical, packaging, and environmental (Klemm et al., 2018; Mohite et al., 2021). Additionally, extracted cellulose displays unique properties like high crystallinity, tunable surface chemistry, and polymer compatibility that could be utilized to develop various eco-friendly and value-added products.

Cellulose has been used in paper and pulp industries, and agro-widest cellulose provides an ecofriendly alternative to present wood sources. Cellulose obtained from biomass (rice husk, wheat straw, and sugarcane bagasse) is an excellent raw material to use in the production of packaging paper, cardboard, and moulded fibre because of its fibre morphology and tensile strength (Reddy et al., 2020). Additionally, agricultural cellulose can be modified to also manufacture coated and barrier papers with enhanced water resistance and mechanical strength (Panaitescu et al, 2021). Cellulose can be turned into fibres such as viscose rayon and lyocell. Cellulose, when modified, where that of cotton stalks or banana pseudo stem in most cases, are also being explored for textile purposes due to spinnability, dyeability and breathability (Singh et al., 2021). As a reinforcement in bio composites, cellulose fibres improve strength, modulus, and thermal properties. Cellulose sourced from agricultural residues has been used to reinforce polymer matrices (e.g., PLA, PHA), making them lightweight and biodegradable composites suitable for automotive parts, construction panels, furniture (Nasution et al., 2021; Asem et al., 2022).

Membranes, beads and sponges made from cellulose have been engineered to remove heavy metals, dyes, and organic pollutants from wastewater. For example, Cellulose isolated from agro-wastes are chemistrically treated or functionalized with groups such as carboxyl, amine or sulfonate to improve their adsorption abilities and selectivity (Tang et al., 2020). Agro-cellulose is one of the most promising bio-upcycled products for bioplastics where it is used as the matrix or filler material. These plastics are compostable and prevent microplastic pollution, providing a realistic alternative to polyethylene and polypropylene (Guragain et al., 2022).

Second-generation bioethanol is produced from cellulose, a chief feedstock. Agro-waste cellulose pre-treatment the yield of ethanol, butanol or hydrogen through enzymatic hydrolysis and fermentation. High fermentable sugar content and renewability makes it suitable for integrated biorefinery models (Kaur et al., 2022). In recent years, cellulose has become a focus for energy storage and is used in much of the research on electrodes, separators, and gel electrolytes for supercapacitors and lithium-ion batteries, owing to its high surface area, mechanical integrity, and ionic conductivity (Jiang et al., 2021)

Additive Manufacturing includes biodegradable cellulose-based inks tailored for 3D printing. Sensors and Electronics includes Owing to their piezoelectric and dielectric properties, cellulose nanofibers are being employed in flexible electronics, strain sensors, and wearable devices. This high oxygen and oil barrier make them suitable for eco-packaging (Panaitescu et al., 2021). Recent progress in green extraction, functionalization and nanotechnology increase the range of relevant applications of cellulose derived from agricultural residues. Thus, the conversion of agro-waste into cellulose-based high-performance materials has been serious eco-sustainable models to further the foresight for innovative industrial transformation.

7. USE OF NANOCELLULOSE IN NEONATAL BIOMEDICAL APPLICATIONS

Nanocellulose derived from agricultural residues has gained considerable attention as a sustainable and biocompatible material suited for neonatal biomedical applications. Agricultural by-products such as rice husks, wheat straw, sugarcane bagasse, and corn stalks represent abundant and renewable sources for nanocellulose extraction through environmentally friendly methods including acid hydrolysis and mechanical fibrillation (Perera et al., 2023; Norrrahim et al., 2021). These residues are often discarded or burned, leading to environmental issues, but their valorization into nanocellulose provides an eco-friendly alternative that aligns with the principles of circular bioeconomy.

Neonates, particularly those born prematurely, possess delicate and immature skin barriers that are highly susceptible to irritation, infection, and damage caused by invasive procedures or conventional synthetic biomaterials. Nanocellulose exhibits unique physicochemical properties such as high mechanical strength, excellent water retention, and surface modifiability, which contribute to its superior biocompatibility and functionality in neonatal care (Dufresne, 2022). These characteristics enable the development of neonatal medical devices and dressings that are gentle, protective, and capable of supporting the natural healing process without eliciting adverse immune responses.

One of the primary applications of nanocellulose in neonatology is in advanced wound management. Nanocellulose membranes produced from bacterial cultures using agricultural waste as a substrate have demonstrated the capacity to maintain a moist wound environment, which is essential for tissue regeneration (Fortea-Verdejo et al., 2023). These membranes exhibit flexibility and conformability to the contours of fragile neonatal skin while preventing dehydration and bacterial infiltration. Antimicrobial agents such as silver nanoparticles or natural bioactive compounds can be integrated into nanocellulose matrices to provide localized infection control, a critical factor in preventing sepsis in neonatal intensive care units (Czaja et al., 2020).

Nanocellulose-based hydrogels also serve as promising vehicles for controlled drug delivery tailored to neonatal physiology. Due to their large surface area and capacity for chemical functionalization, these hydrogels facilitate sustained release profiles of antibiotics, analgesics, and nutrients, which are critical for neonates with immature metabolic pathways (Pereira et al., 2022). The ability of nanocellulose to protect encapsulated drugs from premature degradation enhances the safety and efficacy of pharmacotherapy in this vulnerable population, minimizing systemic toxicity and improving therapeutic outcomes.

Medical devices such as catheters and implants benefit from nanocellulose coatings derived from agricultural biomass. These coatings demonstrate significant anti-biofilm activity, reducing the incidence of device-associated infections, which are a major cause of neonatal morbidity (Picheth et al., 2017). Chemical functionalization with antimicrobial moieties further enhances these properties while maintaining the material's biocompatibility. Such coatings also offer mechanical protection and reduce inflammation around implant sites, facilitating better integration and reducing the risk of rejection.

Recent technological innovations have expanded the role of nanocellulose in the development of flexible biosensors designed for neonatal monitoring. Nanocellulose-carbon composite sensors are capable of real-time, non-invasive measurement of physiological parameters such as hydration, glucose levels, and pH, all of which are vital for monitoring neonatal health status (Ilyas et al., 2023). The biodegradable nature of these sensors also addresses environmental concerns associated with disposable medical devices.

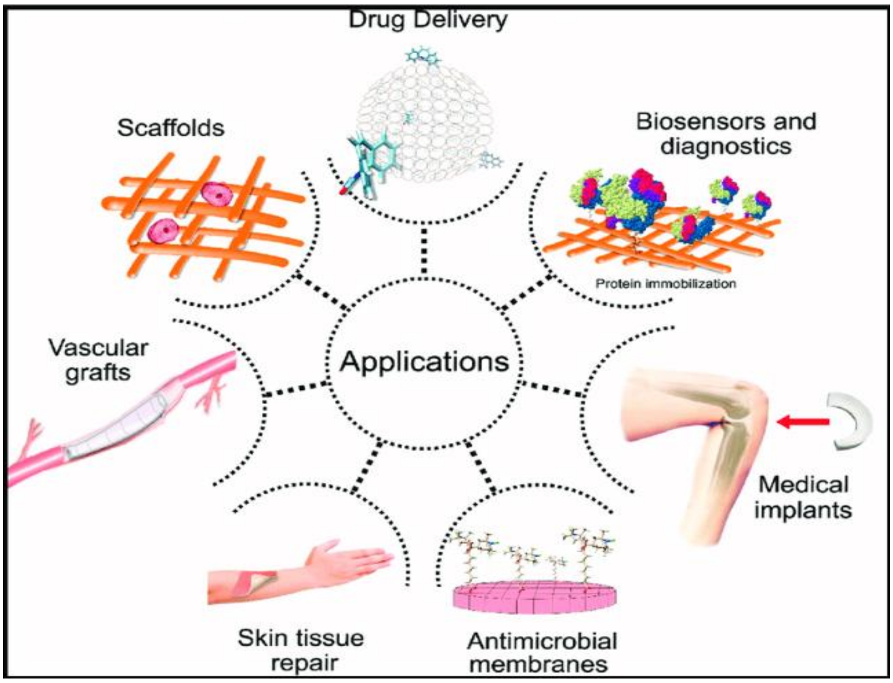

Figure: 1 Applications of nanocellulose in biomedical.

In tissue engineering, nanocellulose composites have been formulated as bioinks for 3D bioprinting applications aimed at fabricating neonatal tissue constructs. These bioinks demonstrate suitable rheological properties and cytocompatibility, allowing for the printing of scaffolds that support cell growth and differentiation. This technology holds potential for reconstructive therapies addressing congenital defects and wound healing in neonates (Santos et al., 2021).

Challenges to clinical translation include the need for rigorous purification protocols to eliminate endotoxins and contaminants, ensuring reproducibility and compliance with medical-grade standards. Long-term biocompatibility and biodegradation studies specific to neonatal models are necessary to confirm safety. Scalable production methods and regulatory approvals remain critical for the integration of agricultural residue-derived nanocellulose into neonatal clinical practice.

Table: 3 Biomedical Applications of Nanocellulose

Application	Nanocellulose Type	Function	Advantages	Challenges	Example	Citation
Wound Dressings	BNC, CNF-AgNPs	Moisture retention, barrier to microbes	Biocompatible, healing support	Limited antimicrobial unless functionalized	*Biofill®*, *XCell®*	Portela et al., 2019
Tissue Engineering	CNF, BNC	Scaffold for tissue growth	ECM mimicry, strong, porous	Needs bioactivity enhancement	Cartilage scaffold	Jorfi & Foster, 2015
Drug Delivery	CNC, CNF	Controlled drug release	Targeted, biocompatible, sustained release	Limited hydrophobic drug compatibility	Antibiotic hydrogel	Lin & Dufresne, 2014; Bacakova et al., 2019
Implants	BNC, CNF	Coating, integration support	Reduces immune rejection,	Long-term in vivo testing needed	Cardiovascular devices	Jorfi & Foster, 2015

			durable			
Antimicrobial Systems	CNF, CNC	Sustained antimicrobial release	Broad activity, non-toxic with optimized dosage	Potential toxicity with silver overload	CNF-Ag wound pad	Mahendiran et al., 2021
Biosensors	CNF, BNC	Enzyme/antibody immobilization	Sensitive, flexible, green sensing platforms	Electrical properties need enhancement	Glucose sensor	Ribeiro et al., 2019
Ophthalmic Drug Delivery	BNC	Controlled ocular drug delivery	Transparency, comfort, compatibility	Drug penetration limitations	Eye drop hydrogels	Bacakova et al., 2019
3D Bioprinting	CNF-alginate	Bioink for printing tissues	Structural fidelity, cell viability	Requires vascularization and bioactivity	Printed cartilage	Markstedt et al., 2015

8. CONCLUSION

Nanocellulose has demonstrated significant potential as a multifunctional biomaterial in the biomedical domain due to its unique physicochemical properties, including high mechanical strength, high surface area, excellent biocompatibility, and the ability to be chemically modified. As discussed in this review, nanocellulose exists primarily in three forms, cellulose nanocrystals (CNCs), cellulose nanofibrils (CNFs), and bacterial nanocellulose (BNC), each offering distinctive advantages that cater to a wide array of biomedical applications. From wound dressings and drug delivery systems to scaffolds for tissue engineering, antimicrobial surfaces, and biosensors, the versatility of nanocellulose is increasingly recognized for its capacity to mimic or support biological systems with minimal toxicity and environmental impact. The high-water retention capacity and structural similarity of BNC to natural extracellular matrices make it particularly promising for tissue regeneration and wound healing applications. CNCs and CNFs, owing to their ease of surface functionalization and mechanical stability, are well-suited for advanced drug delivery platforms and diagnostic biosensors. Furthermore, innovations in 3D bioprinting are increasingly leveraging nanocellulose-based bioinks for the fabrication of patient-specific tissue constructs. These developments not only reflect the adaptability of nanocellulose but also highlight its role in enabling precision medicine and personalized healthcare approaches.

Despite the encouraging progress, several challenges remain in the path toward clinical translation. These include the limited intrinsic bioactivity of nanocellulose that necessitates functionalization with bioactive molecules, scalability issues in industrial production, and a lack of long-term in vivo studies to assess biodegradation and chronic immune responses. Regulatory concerns and standardization of nanocellulose production processes also hinder its broader acceptance in the biomedical industry.

Overall, the integration of nanocellulose into biomedical technologies represents a paradigm shift towards sustainable, biocompatible, and high-performance materials. Continued interdisciplinary research, encompassing materials science, molecular biology, and clinical medicine, is essential to overcome existing limitations and fully harness the capabilities of nanocellulose. With advancements in fabrication techniques and biofunctionalization strategies, nanocellulose is poised to become a cornerstone material in next-generation biomedical devices and regenerative therapies.

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