





Review

# Recent progress in nanocellulose-based biocomposites for bone tissue engineering and wound healing applications

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## Abstract

Nanocellulose (NC) is considered as promising biomaterial owing to its stiffness, renewability, high strength, and biodegradability. NC is classified into three types such as cellulose nanocrystals (CNCs), bacterial nanocellulose (BNC), and cellulose nanofibers (CNFs), and they differ with each other in terms of size, mechanical behaviour, morphology, and crystallinity. The development of biocomposites with nanocellulose as reinforcing agent has gained much attention among researchers owing to their promising applications in various sectors. The thermal, mechanical, and biodegradable properties of both synthetic and natural polymers can be enhanced by reinforcing them with nanocellulose. The fabrication of NC-based biocomposites can be achieved by employing different techniques such as solution casting, resin impregnation and melt compounding methods. The porosity, tensile modulus, tensile strength, MVTR (moisture-vapour transmission rate), biocompatibility, hydrophilic, water retention ability, bio-adhesiveness and hemocompatibility are the essential properties of tissue engineering scaffolds and wound dressing materials, and these properties can be optimized by reinforcing them with NC. This review intends to focus on the reinforcing effect of NC on the physicochemical and thermo-mechanical characteristics of NC-based biocomposites. This review also aims to summarize the utilization of NC-based biocomposites in tissue engineering scaffolds and wound dressing applications.

## Graphical abstract



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## Introduction

Cellulose is an abundantly available biopolymer because it is a major constituent in the cell walls of plants, and it is also produced by many bacteria in its pure form (Seddiqi et al., 2021). The renewability, sustainability, flexibility, stiffness, considerable thermo-mechanical properties, low density, and good water resistance are the various advantages of cellulose, which make it a promising green material (Andrade et al., 2015; Hao et al., 2020; Verma et al., 2024). Cellulose derivatives like cellulose acetate, ethyl cellulose, hydroxyethyl cellulose, and cellulose sulfate have also been used in the biomedical field (Bahari Golamkaboudi et al., 2024). Cotton and wood are the main sources of cellulose owing to their high cellulose content. Agricultural biomass waste such as bagasse, rice straw, palm, wheat straw, banana fronds, bamboo stalks, mulberry bark, potato tubers, and hemp bark are the other sources of cellulose (Omidi & Habibi, 2024). Lignocellulosic biomass (LB) is derived from agricultural residues of plant and plant-based materials, and it is composed of lignin (aromatic polymer), hemicellulose, and cellulose (Zoghlami & Paës, 2019). Lignin serves as a binder that holds the hemicellulose and cellulose fibers together in plant cell walls (Mili et al., 2022). The cellulose can be derived from the lignocellulosic biomass by removing the non-cellulosic contents like hemicellulose and lignin using various chemical, physical, and enzymatic treatments. The obtained cellulose fibrils from LB are composed of crystalline and amorphous structures with size ranging from 3 to 100 $\mu$ m in diameter and 1–4mm in length (Lavoine et al., 2012). The bacterial cellulose is a kind of cellulose derived from the bacterial strains (Almihyawi et al., 2024). Interestingly, nanostructured cellulose (nanocellulose) finds applications in various fields such as catalysis, biosensing, flame retardants, tissue engineering, drug delivery, packaging, pharmaceutical, protective coatings, biomedical scaffolds, and water purification owing to their biocompatibility, long-lasting nature, tunable surface chemistry, anisotropic shape, good optical, and mechanical properties (Kargarzadeh et al., 2018; Khalil et al., 2012; Khiari, 2017; Menon et al., 2017; Moon et al., 2011; Nicu et al., 2021). Nanocellulose (NC) has been obtained from natural sources using enzymatic, mechanical and chemical treatments. The mechanical, thermal and biodegradable properties of natural and synthetic polymers can be improved by incorporating NC as reinforcing agents into them. The fabrication of NC-based biocomposites has gained much attention among researchers due to their promising applications in various sectors and low environmental impact. Nanocellulose possesses excellent mechanical properties and higher surface area at the nanoscale compared to cellulose by retaining inherent biodegradability and

biocompatibility, which allows NC a promising candidate for various therapeutic applications, including wound healing, tissue engineering and drug delivery owing to its superior ability to deliver substances and interact with cells more precisely than larger cellulose fibrils. NC also facilitates superior cell adhesion and efficient drug release owing to its high surface area and smaller size than cellulose. The use of NC in the treatment of neurological diseases probably supports the neural tissue-derived cell's activity and also improves proliferation. NC undergoes slightly faster degradation than cellulose due to its smaller size, which facilitates efficient tissue regeneration while using it as a scaffold. NC as a drug carrier promotes controllable and sustainable drug release owing to its higher surface area than cellulose. A brief overview of the extraction of NC from natural sources and structural confirmation of NC-based biocomposites using various analytical techniques has been discussed initially. This article also summarizes the influence of NC as reinforcement on the physicochemical and mechanical properties of natural/synthetic polymers. It also highlights the essential characteristics of NC-based biocomposites as scaffolds in bone tissue engineering and as wound dressing materials for wound healing.

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## Section snippets

### Extraction of nanocellulose from natural sources

Nanocellulose can be derived from cellulose by various enzymatic, chemical, and mechanical treatments. The tensile strength of NC (10GPa) is higher than cast iron, and it possesses a higher strength-to-weight ratio nearly 8 times than stainless steel (Phanthong et al., 2018). NC is categorized into nanofibrillated cellulose or cellulose nanofiber, nanocrystalline cellulose or cellulose nanocrystal, and bacterial cellulose (Li et al., 2018). They differ from each other in terms of properties, ...

### Structural analysis of NC-based biocomposites

The structure of the biopolymer reinforced with NC can be investigated by analysing the interaction of cellulose NFs with the biopolymer matrix using FTIR spectroscopy. The peak area and the position of the absorption peaks in the FTIR spectrum of biopolymers are generally altered after incorporating cellulose NFs into the biopolymer matrix due to their chemical or physical interactions, and these inferences are used to conclude the structure of the biocomposites. X-ray diffraction analysis is ...

### Effect of NC on the physicochemical and mechanical properties of NC-based biocomposites

Wang et al. (2021) extracted CNFs from the jute fibers by TEMPO-mediated oxidation method and also obtained different lengths of CNFs by varying the sodium hypochlorite solution concentration. While treating the CNFs with different concentrations of NaOCl solutions (20g), the CNFs with a diameter in the nanorange of 5 to 10nm and different lengths ranging from a few hundred nanometers to a few microns were obtained. The oxidation rate of hydroxyl groups on C6 in the cellulose also increased ...

### Bone tissue engineering applications