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Review

Nanocellulose-enabled drug delivery: focus on advances in essential oil encapsulation and *in silico* modeling

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Abstract

Nanocellulose is a natural polymer derived from cellulose that comes in three main forms: nanocrystalline cellulose, nanofibrillar cellulose, and bacterial cellulose. It has exceptional properties, including a high specific surface area, non-toxic nature, excellent mechanical properties, low thermal expansion, and high biodegradability, making it a material of choice for pharmaceutical applications. On the other hand, essential oils are volatile compounds that degrade quickly, and their encapsulation would be of great interest. However, in this review presenting the application of nanocellulose in the pharmaceutical field, we explore the potential of this biomaterial in the encapsulation of essential oils, paying particular attention to the computational methodologies used in this field.

Key words
Nanocellulose, drug delivery systems, encapsulation, essential oils, *in silico* study.

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1. Introduction

Nanocellulose, derived from renewable sources such as plants, bacteria, and certain algae, has attracted growing interest in recent decades due to its unique physicochemical properties and broad biomedical potential. There are three main forms: nanocrystalline cellulose, nanofibrillar cellulose, and bacterial cellulose (1). This nanomaterial is characterized by a large specific surface area, modifiable surface chemistry, exceptional water retention capacity, and remarkable mechanical strength (2). In addition, nanocellulose is biocompatible and biodegradable, making it a prime candidate for applications in the pharmaceutical and biomedical industries.

The pharmaceutical industry is researching nanocellulose more and more as a flexible drug delivery platform. When used as an excipient in solid oral forms, it can improve stability, compressibility, and disintegration (3). Its ability to form hydrogels, films, and nanocomposites opens the door to its use in dressings, transdermal patches, and controlled-release systems (4). Its potential is further increased by functionalizing its surface, which makes it possible to target medicinal drugs precisely and create systems that are responsive to stimuli (temperature, pH, and enzymes) (5).

Nanocellulose is becoming a new-generation biomaterial for contemporary medications because of its availability, low toxicity, and adaptability (6).

Presenting recent developments in the application of nanocellulose in the pharmaceutical industry, this article attempts to highlight the potential and interest of this biomaterial in the encapsulation of essential oils, natural compounds with strong antimicrobial and antioxidant activities, but their direct use is limited due to volatility, poor solubility, and instability during storage. To overcome these challenges, encapsulation techniques have been developed, with nanocellulose emerging as a promising carrier (7) (8). Particular attention is paid to the computational methodologies used in this research (docking, density functional theory (DFT) and molecular dynamics (MD)… etc.), with the aim of highlighting the main results and assessing the extent to which these approaches have proven effective, either by corroborating experimental data or by providing new insights.

2. Nanocellulose sources and types

Nanocellulose is a renewable material primarily derived from cellulose, which is found in wood, plants, and certain types of algae, and is even produced by bacteria. Depending on their origin and production process, there are three main types of nanocellulose (figure 1, table 1). Cellulose nanocrystals, which are generally extracted by acid hydrolysis, are rigid and highly crystalline. Cellulose nanofibrils are obtained through mechanical, chemical, or enzymatic treatments and have a flexible structure composed of both amorphous and crystalline areas (9). Bacterial nanocellulose is a high-purity material produced by certain bacteria, such as Gluconacetobacterxylinus (10). This diversity gives nanocellulose a wide range of mechanical, optical, and functional properties, making it a promising material for many industrial and technological applications.

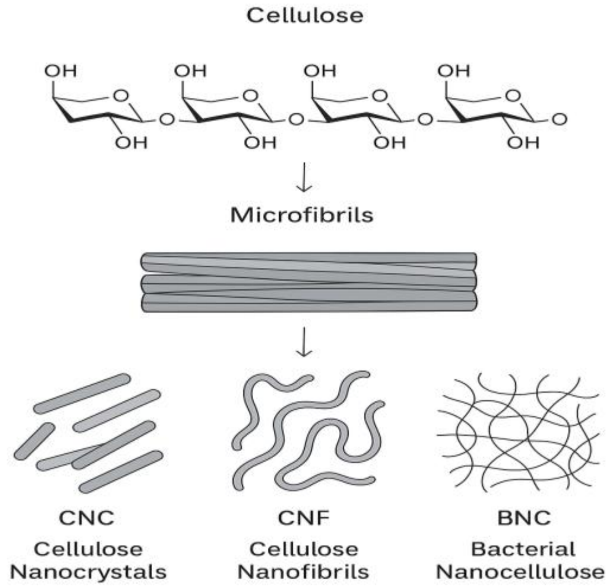

Figure 1. Structure and types of nanocellulose

Table 1. Origin, sources, production process and application of the different types of nanocellulose.

Type of nanocellulose	**Main sources**	**Production methods**	**Typical application**
Cellulose nanocrystals	Wood, plant fibers (cotton, hemp, flax)	Acid hydrolysis (commonly with H_2SO_4 or HCl)	Reinforcement of composite materials, optical films, inks, nanosensors
Cellulose nanofibrils	Wood, plant fibers	Mechanical, enzymatic or chemical fibrillation	Biodegradable packaging, barrier coatings, hydrogels, technical papers
Bacterial nanocellulose	Bacteria (*Gluconacetobacterxylinus* and others)	Bacterial fermentation in nutrient media	Biomedical applications (wound dressing, implants, artificial tissues), filtration membranes, flexible electronics)

3. Properties relevant to pharmaceutical applications

The pharmaceutical industry is investigating nanocellulose as a drug delivery carrier for the targeted, extended release of active components. It is also used to create intelligent dressing matrices that speed up the healing process. The potential applications of this material include biomedical implants, where it can provide both biological tolerance and mechanical support. Lastly, nanocellulose is notable for its functional adaptability. It can be chemically altered to increase its affinity for specific medications or tissues, leading to a new class of efficient, environmentally friendly pharmaceutical treatments.

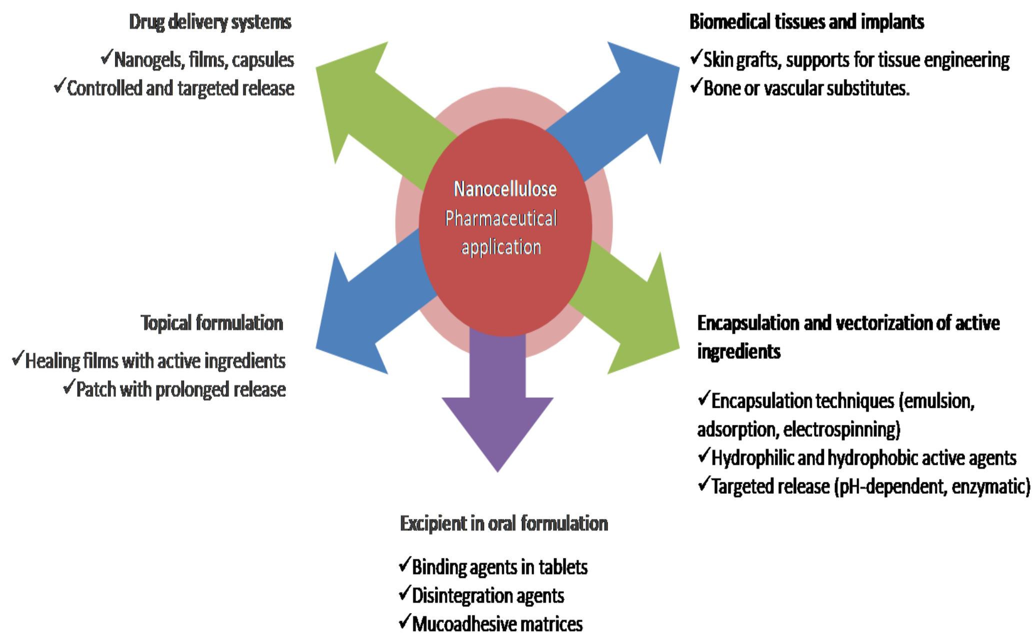

Figure 2. Pharmaceutical applications of nanocellulose

4. Nanocellulose for drug delivery and active ingredients encapsulation

Nanocellulose is becoming increasingly popular in the pharmaceutical sector, especially for medication delivery, due to its distinctive properties. Its tolerance, biocompatibility, and low toxicity make it a material of choice for delivering therapeutic molecules. This nanomaterial has a large surface area, enabling it to deliver a large number of active molecules, whether water-soluble or fat-soluble (11). Nanocellulose is chemically modifiable, which allows it to be better adapted to the nature of the drugs being delivered. In addition to its ability to form hydrogels that ensure the prolonged release of therapeutic molecules (12), it can also be combined with nanoparticles as a thin film to produce solutions for oral, transdermal, or ophthalmic administration (13).

Furthermore, the exceptional mechanical stability of nanocellulose guards against drug degradation. The moisture required for delicate applications is maintained by its excellent water retention capacity. For instance, it facilitates healing in medicated dressings by serving as a matrix for localized, targeted release. Additionally, nanocellulose increases the bioavailability of poorly soluble substances by facilitating their dispersion. Finally, it is an innovative and sustainable alternative to the synthetic polymers commonly used in pharmaceutical formulations because it is renewable and biodegradable (4).

The encapsulation of active ingredients using nanocellulose represents an innovative approach to improving therapeutic efficacy and treatment safety. Thanks to its adsorption capacity and free hydroxyl groups, nanocellulose can trap or bind various bioactive compounds, ranging from small hydrophobic molecules such as curcumin or ibuprofen to protein macromolecules (14).

Nanocrystalline and nanofibrillar celluloses are particularly suitable for the formation of nanocapsules, films, or hydrogels. Bacterial cellulose, on the other hand, is better suited for forming encapsulation matrices for antimicrobial or anticancer agents, as it offers protection against premature degradation and ensures targeted delivery to the site of action. Encapsulation in nanocellulose also improves the physicochemical stability of fragile molecules such as antioxidants, vitamins, and enzymes.

5. Essential oil encapsulation advantages

Encapsulation is an inventive method for enhancing the stability, efficacy and safety of essential oils. Encapsulation is an inventive method for enhancing the stability, efficacy and safety of essential oils. When exposed directly to the environment, these volatile chemicals rapidly lose their bioactive properties and become susceptible to oxidation, heat and light (15). Encapsulation shields essential oils against deterioration and enables precise control of their release. This can be achieved using micro- or nanotechnology, such as liposomes, cyclodextrins, polymers and lipid nanoparticles (16). For example, the antibacterial activity of oregano and thyme essential oils is increased against *Staphylococcus aureus, Escherichia coli, Listeria monocytogenes* when they are encapsulated in chitosan nanoparticles (17). In pharmaceutical and cosmetic formulations, eucalyptus essential oil encapsulated in gelatin or alginate microparticles exhibits enhanced antifungal efficacy and a prolonged release rate. Thus, by improving the bioavailability, stability and safety of natural essential oils, this method offers great potential in the pharmaceutical, agri-food and cosmetics industries.

6. Essential oil encapsulation in nanocellulose

There is growing interest in using nanocellulose as a matrix for encapsulating essential oils. Nanocrystalline or nanofibrillar nanocellulose provides a three-dimensional structure that stabilizes and traps volatile substances (figure 2). This matrix prevents essential oils from oxidizing or evaporating, while enhancing their dispersion in aqueous media. For instance, it has been demonstrated that encapsulation of lemongrass essential oil in cellulose nanofibrils enhances its antifungal activity (18). Likewise, nanocellulose films containing thyme, cinnamon and oregano essential oils exhibit potent antibacterial properties and are being explored for use in active food packaging to prolong the shelf life of goods (19). These findings support the use of nanocellulose as an efficient, sustainable carrier that increases the value of essential oils in a variety of industrial settings.

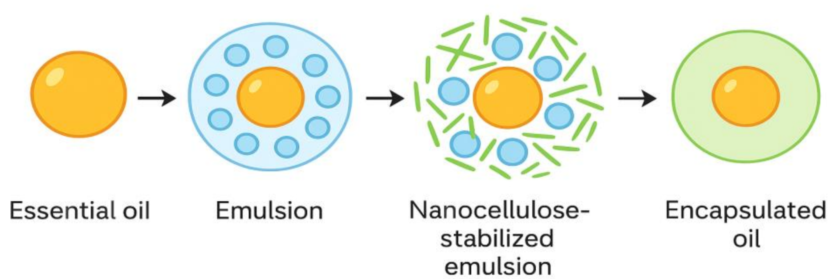

Figure 3. Essential oil encapsulated in nanocellulose

7. In-silico studies on essential oil encapsulation and nanocellulose-based carriers

In addition to experimental approaches, computational (*in silico*) studies play a key role in understanding the interactions between essential oils and nanocellulose. Molecular docking helps to predict how bioactive compounds bind to the cellulose surface (20), while DFT provides insights into electronic stability and reactivity (21). Moreover, molecular dynamics (MD) simulations allow the monitoring of capsule behavior in aqueous or biological environments, predicting the long-term stability of the encapsulated oil (22). These combined approaches contribute to the rational design of efficient and stable delivery systems.

Table 2. Recapitulative summary of In-Silico studies on essential oils and nanocellulose-based carriers

Recent studies		Ref
Cellulose Nanocrystal-Based Emulsion of Thyme Essential Oil		
Objective	This study examined the stabilization of thyme essential oil using cellulose nanocrystals (CNC), motivated by the inherent instability and volatility of essential oils that limit their bioactive potential. The general objective of this work was to develop a sustainable emulsion system that maintains the stability and enhances the antimicrobial properties of thyme oil. To support this aim, the in-silico perspective was introduced to explain how CNC particles interact at the oil–water interface.	(23)
Results	While the study itself did not present new docking or molecular dynamics simulations, the authors relied on prior computational evidence to strengthen their interpretation, particularly regarding the adsorption behavior of CNC and its ability to form steric and electrostatic barriers around oil droplets. The inclusion of in-silico reasoning was important because it provided molecular-level support to the experimental results, highlighting the role of CNC in creating a hydrophilic protective shell.	
Conclusion	The conclusion of the computational aspect was that modelling confirms and rationalizes the enhanced stability observed experimentally, showing that CNC effectively reduces droplet coalescence and preserves oil bioactivity.	
Nanoencapsulation of Oregano Essential Oil with CNC from Agricultural Waste		
Objective	This investigation explored the encapsulation of oregano essential oil using cellulose nanocrystals extracted from agricultural waste, driven by the dual motivation of valorizing agro-residues and improving the stability of bioactive essential oils. The general objective was to produce eco-friendly CNC with high encapsulation efficiency and to evaluate their ability to retain and protect oregano oil.	(24)
Results	The in-silico focus of the work was directed toward understanding the molecular interactions that explain the high retention of oil molecules on the CNC surface. Although the authors did not perform original large-scale simulations, they integrated computational insights from docking and molecular dynamics studies in the literature to rationalize their results, particularly emphasizing the roles of surface charge and hydrogen-bonding capacity of CNC. They incorporated these in-silico concepts because experiments alone could not explain the exact nature of oil–CNC interactions.	

Conclusion	The conclusion of the computational discussion was that favorable adsorption energetics and surface interactions justify the high encapsulation efficiency observed experimentally, confirming that CNC derived from agro-waste can be effective carriers for essential oils.	
Molecular Dynamics Simulation of CNC-Stabilized Pickering Emulsions		
Objective	A more computation-intensive contribution was presented in simulation studies on CNC-stabilized Pickering emulsions, where researchers used molecular dynamics (MD) approaches to directly observe how nanocellulose interacts with oil–water interfaces. The motivation stemmed from the experimental observation that CNC can stabilize emulsions, but the molecular mechanisms of adsorption, conformational adjustment, and interfacial energy reduction remained unclear. The general objective was therefore to provide atomic-scale visualization of CNC adsorption and its effects on emulsion stability. The in-silico objective specifically aimed at quantifying the interfacial free energy changes and identifying how CNC conformation and concentration influence droplet stabilization.	(25)
Results	Using atomistic and coarse-grained MD simulations, supported by interfacial energy and density profile analyses, the researchers were able to explain the process in great detail. The reason to use in-silico methods here was to access phenomena that cannot be visualized experimentally, such as adsorption kinetics and molecular layering at interfaces.	
Conclusion	The conclusion of the simulations was that CNC strongly adsorb to oil–water interfaces, form dense interfacial barriers, and their stabilizing effect depends on both particle orientation and concentration-results that closely matched experimental data and highlighted the predictive value of MD.	
Docking and Molecular Dynamics on Cellulose–Ligand Systems		
Objective	In a representative work on molecular interactions involving cellulose, docking and molecular dynamics simulations to explore how ligands and enzymes interact with cellulose fragments are combined. The motivation was to clarify binding specificity and stability of cellulose–ligand complexes, which are crucial for understanding recognition and reactivity in biological and material systems. The general objective was to identify binding modes and validate their stability under dynamic conditions. The in-silico aim was thus to predict possible binding sites using docking and then refine these predictions using MD simulations.	(26)
Results	The authors employed AutoDock for docking to propose initial binding poses and then ran all-atom MD simulations in explicit solvent to assess stability and monitor hydrogen bonds, RMSD, and contact persistence. They turned to in-silico approaches because experimental structural resolution of such complexes is difficult and computational methods can efficiently screen and validate interactions.	
Conclusion	The conclusion of this in-silico analysis was that docking suggested plausible binding modes, while MD confirmed their stability and provided atomistic details consistent with experimental patterns, thereby strengthening the reliability of the predictions.	
Computational and Experimental Studies on EO-Loaded Biopolymer Composites		
Objective	This study presented a combined computational and experimental study on essential oil-loaded biopolymer composites, motivated by the need to design materials that enhance the retention, release, and antimicrobial properties of essential oils. The general objective was to formulate composite carriers and assess their performance in controlled release and bioactivity. Within this work, the in-silico objective was to predict compatibility between essential oil molecules and polymer matrices, ensuring that chosen components would lead to effective formulations.	(27)

Results	The authors first used molecular docking to estimate binding affinities between major essential oil constituents and the polymer surface, followed by MD simulations to evaluate stability, hydrogen-bond persistence, and diffusion behavior in water. The rationale for applying in-silico methods was to reduce experimental trial-and-error and to obtain mechanistic explanations of the sustained release observed in vitro.	
Conclusion	The computational conclusions confirmed that selected oil molecules had strong and stable interactions with the biopolymer, explaining the improved antimicrobial activity and demonstrating how docking and MD can guide successful formulation development.	

8. Conclusion

Nanocellulose is positioned as a novel and adaptable biomaterial in pharmaceutical industry and essential oil encapsulation. Its distinct qualities, along with its biological compatibility and natural abundance, make it a suitable platform for the creation of novel therapeutic approaches. However, before extensive integration is feasible, more research must be conducted to address production and regulatory limitations. Otherwise, *in silico* approaches, particularly docking and molecular dynamics are essential to understand molecular interactions and guide the design of stable and efficient essential oil–cellulose encapsulation systems.

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