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Research Paper

Preparation and Performance Study of Drug-Loaded Film Materials Enhanced by Modified Cellulose Nanocrystals and Keratin

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Abstract. Aldehyde-functionalized cellulose nanocrystals (DCNC) were prepared using the sodium periodate oxidation method. The aldehyde groups on DCNC can react with amino groups on keratin molecular chains, providing both crosslinking and enhancing effects on keratin film materials. Enhanced keratin drug-loaded film materials were prepared, and their drug release performance was studied. Research showed that modified cellulose nanocrystals provide crosslinking and enhancing effects. Compared to pure keratin film, the mechanical properties and water resistance stability of the DCNC/keratin composite film were significantly improved. The enhancement and crosslinking by DCNC effectively addressed the burst release phenomenon of pure keratin drug carrier films. The DCNC/keratin composite drug carrier film exhibited sustained release of the encapsulated drug. The research results not only contribute to the application of keratin natural polymer film materials but also provide a good reference for preparing other composite materials.

Keywords: *Modified cellulose nanocrystals; Keratin; Drug-loaded film*

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1 Introduction

The development of biodegradable and biocompatible polymer films for drug delivery applications has garnered significant attention in recent years, particularly in the fields of wound dressings and tissue engineering [1]. Keratin, a natural protein derived from sources such as animal feathers and human hair, exhibits excellent biological properties, including biocompatibility, biodegradability, and the ability to promote cell adhesion and proliferation [2]. These characteristics make keratin-based films promising candidates for use as drug carriers in medical applications [3]. However, the practical utilization of keratin films is often limited by their inherent weaknesses, such as low mechanical strength, poor water resistance, and tendency toward burst drug release. These limitations can compromise the material's performance during application, leading to uncontrolled drug release and reduced efficacy. To address these challenges, researchers have explored various strategies to enhance the properties of keratin-based materials, with one promising approach being the incorporation of nanoscale reinforcements [4]. Among these, cellulose nanocrystals (CNCs) have emerged as attractive reinforcing agents due to their high strength, biodegradability, and abundance in nature [5]. This literature review aims to provide a comprehensive overview of the recent advances in the development of modified cellulose nanocrystal-reinforced keratin drug-loaded film materials, focusing on the preparation methods, enhancement mechanisms, and drug release performance, as well as identifying future research directions [6].

Keratin-based materials have been extensively studied for their potential in biomedical applications. Reichl (2009) demonstrated that films based on human hair keratin could serve as effective substrates for cell culture and tissue engineering, highlighting their excellent biocompatibility [7]. The smart design of biomaterials for tissue engineering, as discussed by Furth et al. (2007), emphasizes the importance of materials that can respond to

physiological conditions, which keratin films can potentially achieve due to their natural origin [8]. Katoh et al. (2004) developed keratin sponge scaffolds with controlled pore size and porosity, further showcasing the versatility of keratin in forming various structures suitable for drug delivery [9]. However, pure keratin films often suffer from inadequate mechanical properties. For instance, Kim et al. (2004) noted that the mechanical strength of polymer composites [10], including keratin-based systems, could be enhanced through the incorporation of reinforcing phases, but this must be balanced with maintaining the material's flexibility and drug release characteristics [11]. The burst release phenomenon in pure keratin films, as observed in drug release studies, is a significant drawback. Yang et al. (2007) and Uhrich et al. (1999) both highlighted that controlled drug release is crucial for effective therapy [12], and materials that exhibit sudden release can lead to suboptimal outcomes. Thus, improving the mechanical and release properties of keratin films is essential for their practical application.

Cellulose nanocrystals, derived from the acid hydrolysis of cellulose, offer a sustainable and effective means of reinforcing polymer matrices [13]. CNCs possess high tensile strength, large surface area, and the ability to form percolating networks within composites, leading to significant enhancements in mechanical properties. Habibi et al. (2010) provided a comprehensive review of the chemistry, self-assembly, and applications of CNCs, underscoring their potential in nanocomposites [14]. However, a critical issue in CNC-reinforced composites is the weak interfacial adhesion between the hydrophilic CNCs and hydrophobic or protein-based matrices like keratin [15]. This weak interface can lead to poor stress transfer and reduced composite performance. Karatrantos et al. (2016) discussed the importance of modeling polymer structures and interfaces in nanocomposites, pointing out that the interfacial region plays a key role in determining mechanical properties [16]. To improve interfacial bonding, surface modification of CNCs has been widely explored. Kim et al. (2009) used nonionic surfactants to alter the polarity of CNCs, enhancing their dispersion and compatibility with hydrophobic polymers. Yu et al. (2014) employed chemical grafting to functionalize CNCs, improving their interfacial interaction with matrices and resulting in better mechanical performance. These studies illustrate that modifying CNC surfaces can significantly enhance the interface quality in composites [17].

A particularly effective modification method is the oxidation of CNCs to introduce aldehyde groups, creating dialdehyde cellulose nanocrystals (DCNCs). The aldehyde groups can react with amino groups present in keratin chains, forming Schiff base linkages that act as chemical crosslinks. This reaction not only improves interfacial adhesion but also introduces crosslinking within the keratin matrix, leading to synergistic enhancements in mechanical and barrier properties. Tang (2013) investigated the design and application of functionalized CNCs in controlled drug delivery, noting that aldehyde-functionalized CNCs could provide reactive sites for covalent bonding with biopolymers. Similarly, Zhou (2014) studied the interface and mechanical properties of ramie fiber-reinforced composites, highlighting that chemical bonding between reinforcement and matrix is crucial for stress transfer [18]. The oxidation process, typically using sodium periodate, selectively targets the hydroxyl groups on CNC surfaces. Petersson et al. (2007) found that the incorporation of CNCs into polylactic acid matrices improved thermal and mechanical properties, but emphasized that interface optimization is key. In the context of keratin, the reaction between aldehyde groups on DCNCs and amino groups on keratin can create a robust network [10]. Lim et al. (2006) demonstrated that strong interfacial bonding, even in carbon nanotube composites, could dramatically enhance mechanical performance [20]. Therefore, the use of DCNCs in keratin films represents a promising strategy to overcome the limitations of pure keratin materials.

The preparation of DCNC-reinforced keratin composites involves several steps, including the extraction of CNCs, their oxidation to introduce aldehyde groups, and the subsequent composite formation. The oxidation conditions, such as the mass ratio of oxidant to CNC, reaction temperature, and time, critically influence the aldehyde content and yield of DCNCs. Optimal conditions ensure sufficient functionalization without excessive degradation of the cellulose crystals. The composite films are typically prepared using solution casting, where keratin and DCNCs are dispersed in a suitable solvent, followed by evaporation. The enhanced interfacial interaction due to chemical crosslinking leads to improved mechanical properties. For instance, studies have shown that the tensile strength and elongation at break of keratin films can be significantly increased with the addition of DCNCs. Moreover, the crosslinked network can reduce water sensitivity, enhancing the material's stability in aqueous environments, which is crucial for wound dressing applications where exposure to bodily fluids is common.

In terms of drug release performance, the incorporation of DCNCs can mitigate the burst release effect commonly seen in pure keratin films. The crosslinked structure slows down the diffusion of drug molecules, resulting in a more sustained release profile. This is particularly important for antibiotics like gentamicin, where maintaining therapeutic levels over time is essential for preventing infections. The release behavior can be influenced by factors such as pH, as the swelling and degradation of keratin-based materials may vary under different conditions. For example, at physiological pH, the release might be modulated by the ionization state of functional groups. The ability to tailor the release profile through material design makes DCNC-reinforced keratin films attractive for controlled drug delivery.

Despite the progress, several challenges remain. The long-term stability of the chemical bonds between DCNCs and keratin, the potential cytotoxicity of modified CNCs, and the scalability of the preparation methods require further investigation [21]. Future research should focus on optimizing the modification protocols, exploring in vivo performance, and expanding the application of these composites to other therapeutic areas. In conclusion, the integration of modified cellulose nanocrystals into keratin matrices offers a viable pathway to develop advanced drug delivery systems with enhanced properties, paving the way for their practical use in biomedical applications.

The schematic diagram illustrates the preparation process of dialdehyde cellulose nanocrystals (DCNCs) through periodate oxidation, highlighting the introduction of aldehyde groups on the cellulose surface [22]. This modification is crucial for enabling subsequent reactions with keratin's amino groups, facilitating strong interfacial bonding in the composite.

It shows that the effects of key parameters—oxidant dosage, reaction temperature, and time—on the aldehyde content and yield of DCNCs, providing insights into the optimization of the modification process for maximum functionalization efficiency.

The characterization of DCNCs and their composites with keratin involves various techniques. Fourier transform infrared spectroscopy (FT-IR) confirms the successful introduction of aldehyde groups, while electron microscopy reveals the morphology and dispersion of nanocrystals within the matrix. Mechanical testing demonstrates the enhancements in strength and flexibility, and drug release studies evaluate the controlled release capabilities. Overall, the literature supports the potential of DCNC-reinforced keratin films as effective drug carriers, with ongoing research aimed at further improving their performance and expanding their applications.

In this study, we used sodium periodate oxidation to introduce reactive aldehyde groups onto the surface of cellulose nanocrystals, obtaining aldehyde-functionalized cellulose nanocrystals (DCNC). The oxidation modification of cellulose nanocrystals was systematically studied. Aldehyde-functionalized cellulose nanocrystals were used as reinforcing agents to prepare keratin composite films, and the properties of the composite films were studied in detail. The enhancement and toughening mechanisms of modified cellulose nanocrystals on composite films were discussed. The best-performing keratin composite film material was used as a drug carrier to study its release behavior of encapsulated drugs.

2 Materials and Methods

2.1 Materials and Reagents

Cellulose powder: analytical pure, Shanghai Macklin Biochemical Technology Co., Ltd.; Sulfuric acid: analytical pure, Hangzhou Gaojing Fine Chemical Co., Ltd.; Glacial acetic acid: analytical pure, Hangzhou Gaojing Fine Chemical Co., Ltd.; Urea: analytical pure, Shanghai Macklin Biochemical Technology Co., Ltd.; L-cysteine: analytical pure, Shanghai Aladdin Biochemical Technology Co., Ltd.

2.2 Preparation of Aldehyde-Functionalized Cellulose Nanocrystals

Extraction of CNC by sulfuric acid hydrolysis: Weigh 1 g cellulose powder, slowly add to 50 mL of 64% (mass fraction) sulfuric acid solution, hydrolyze at 45°C water bath for 55 min. After reaction, centrifuge the mixture, collect the solid product, wash with water 4-5 times. Finally, dialyze the CNC suspension in a dialysis bag with a

molecular weight cutoff of 5000 for 2 days. Using sodium periodate as oxidant, oxidatively modify cellulose nanocrystals under certain mass ratio, temperature, and time conditions. Then dialyze to remove unreacted oxidant.

2.3 Preparation of Keratin

Weigh 10 g animal feathers, dissolve in 8 mol/L urea solution, add 5% (mass fraction) L-cysteine reducing agent relative to feather mass, bath ratio 1:100, react in 85°C water bath for 7 h, obtain keratin suspension. Centrifuge the suspension, collect supernatant, dialyze in dialysis bag with large amount of deionized water for 2 days. Precipitate keratin by isoelectric point precipitation, centrifuge to collect solid, freeze-dry to obtain keratin solid powder.

2.4 Preparation of Aldehyde-Functionalized Cellulose Nanocrystal Enhanced Keratin Drug-Loaded Films

Weigh 6 g keratin, dissolve in 94 g acetic acid/water solution (volume ratio 4:1), ultrasonicate to remove bubbles. Add 5.0% glycerol plasticizer relative to keratin mass to the keratin film-forming solution, prepare pure keratin film by solution casting method. Preparation of modified cellulose nanocrystal/keratin composite film: Mix keratin solution and modified cellulose nanocrystal solution in ratios of m(CNC):m(Keratin) as 1%, 2.5%, 5%, 10%, stir evenly, pour into polytetrafluoroethylene film-forming plate to make films.

Gentamicin is a broad-spectrum aminoglycoside antibiotic with strong inhibitory and bactericidal effects on various Gram-negative and Gram-positive bacteria, suitable for small wound treatment to prevent infection. This experiment uses gentamicin as drug model to test drug sustained-release performance of keratin composite films. Select 5.0% DCNC/keratin composite film as drug carrier matrix material. Drug loading process: Add 60 mg gentamicin solid to 20 mL 5.0% (mass fraction) DCNC/keratin film-forming solution, stir to dissolve, pour into film-forming plate, evaporate solvent to obtain drug-loaded keratin composite film.

2.5 Characterization of Aldehyde-Functionalized Cellulose Nanocrystals

2.5.1 Determination of Aldehyde Group Content in DCNC

Principle of aldehyde group determination: Use hydroxylamine hydrochloride solution to react with aldehyde groups in DCNC to form oxime, simultaneously generating hydrochloric acid, titrate generated hydrochloric acid with standard sodium hydroxide solution, calculate aldehyde group content on cellulose nanocrystals from consumed sodium hydroxide volume [18]. Reaction equation as (1):

$$-CHO + NH_2OH \cdot HCl \rightarrow CH = NOH + HCl + H_2O$$

$$HCl + NaOH \rightarrow NaCl + H_2O$$

Before titration, adjust pH of 0.05 mol/L hydroxylamine hydrochloride solution to 5 using standard NaOH solution (0.1 mol/L) to remove free HCl. Accurately weigh 1 g freeze-dried aldehyde-functionalized cellulose nanocrystals, place in 100 mL beaker, add 50 mL deionized water, adjust pH of suspension to 5 with NaOH solution, then add precise volume of 40 mL hydroxylamine hydrochloride solution (pH=5), react at 40°C for 4 h, then titrate reaction solution to pH=5 with standard NaOH solution, repeat 3 times, record volume of standard NaOH used each time, simultaneously run 3 blank controls (using same mass of cellulose nanocrystals as blank group).

2.5.2 Morphology Characterization of DCNC

Use SEM and TEM to characterize morphology of modified cellulose nanocrystals.

2.6 Testing and Characterization of Aldehyde-Functionalized Cellulose Nanocrystal/Keratin Films

2.6.1 Mechanical Properties Testing of DCNC/Keratin Nanocomposite Films

Condition composite films at 25°C, 65% humidity for 24 h. Then test tensile properties of composite films using Instron 3367 universal material testing machine, set parameters: gauge length 20 mm, tensile speed 20 mm/min.

2.6.2 Water Resistance Testing of DCNC/Keratin Nanocomposite Films

DOI:

Dry CNC/keratin composite films in oven, weigh as m1. Immerse in ultrapure water at room temperature for 3 days, remove and dry in oven, weigh as m2, calculate mass loss rate by formula (2):

$$\text{Mass loss} = \frac{m_1 - m_2}{m_1} \times 100\% \quad (2)$$

2.6.3 Drug Release Performance Testing of DCNC/Keratin Nanocomposite Films

Place prepared keratin drug-loaded film materials in conical flasks containing 50 mL buffer solutions of different pH values, place in constant temperature oscillating incubator at 37°C, oscillate at 30 r/min, take 3 mL solution at intervals, simultaneously add 3 mL fresh buffer solution (use pH 3 and 5 citrate buffer solutions, pH 7.4 PBS phosphate buffer solution). Use UV-Vis spectrophotometer to determine gentamicin content in solution. Gentamicin can derivatize with o-phthalaldehyde reagent, derivative has characteristic absorption at 332 nm, thus determine gentamicin content by UV-Vis spectrophotometry and standard curve.

3 Results and Discussion

3.1 Preparation and Characterization of DCNC

Sodium periodate oxidation of cellulose is a selective reaction with few side reactions. Hydrogen atoms on C6 hydroxyl groups of cellulose molecules easily form hydrogen bonds with oxygen atoms of adjacent glucose units, while sodium periodate mainly attacks secondary hydroxyl groups on C2-C3 positions of glucose units, oxidizing them to aldehyde groups. Schematic diagram of reaction process shown in Figure 1.

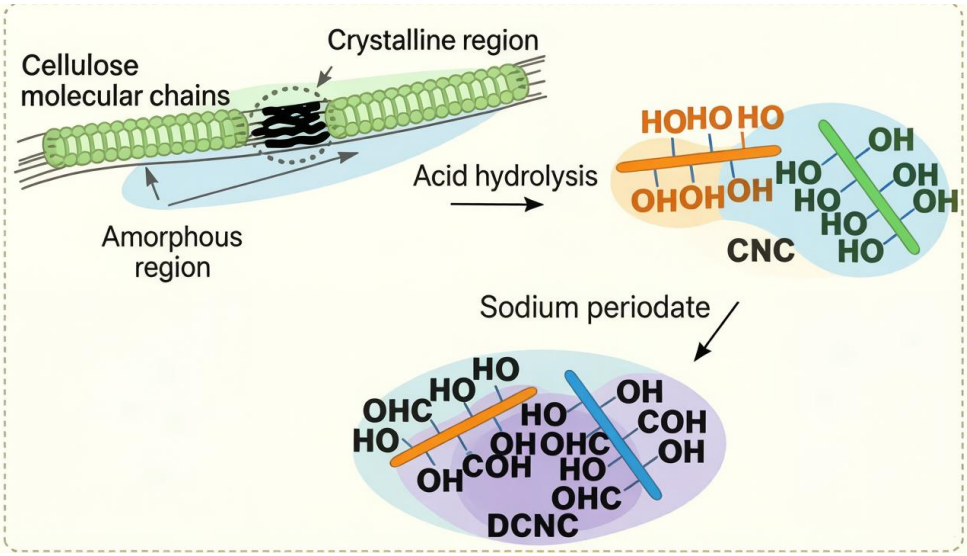

Figure 1 Schematic illustrate the preparation of dialdehyde cellulose nanocrystal

Oxidation conditions mainly affect aldehyde group content and yield of DCNC. 2 shows effect of different reaction conditions on aldehyde group content and yield of aldehyde-functionalized cellulose nanocrystals. 2(a) shows effect of mass ratio of sodium periodate to cellulose nanocrystals on aldehyde group content and yield of resulting DCNC. As oxidant amount increases, aldehyde group content on DCNC gradually increases, reaching maximum when oxidant amount is 1.5 times nanocrystal mass. Yield of aldehyde-functionalized nanocrystals gradually decreases with increasing oxidant amount, due to oxidative degradation of cellulose by sodium periodate, reducing yield. 2(b) shows effect of reaction temperature on aldehyde content and yield. As temperature increases from 30°C to 50°C, aldehyde content increases from 1.6 mmol/g to 2.7 mmol/g. From 2(c), under conditions of oxidant to nanocrystal mass ratio 1:1, temperature 40°C, time 2 h, resulting product has aldehyde content 2.1 mmol/g, yield 78%.

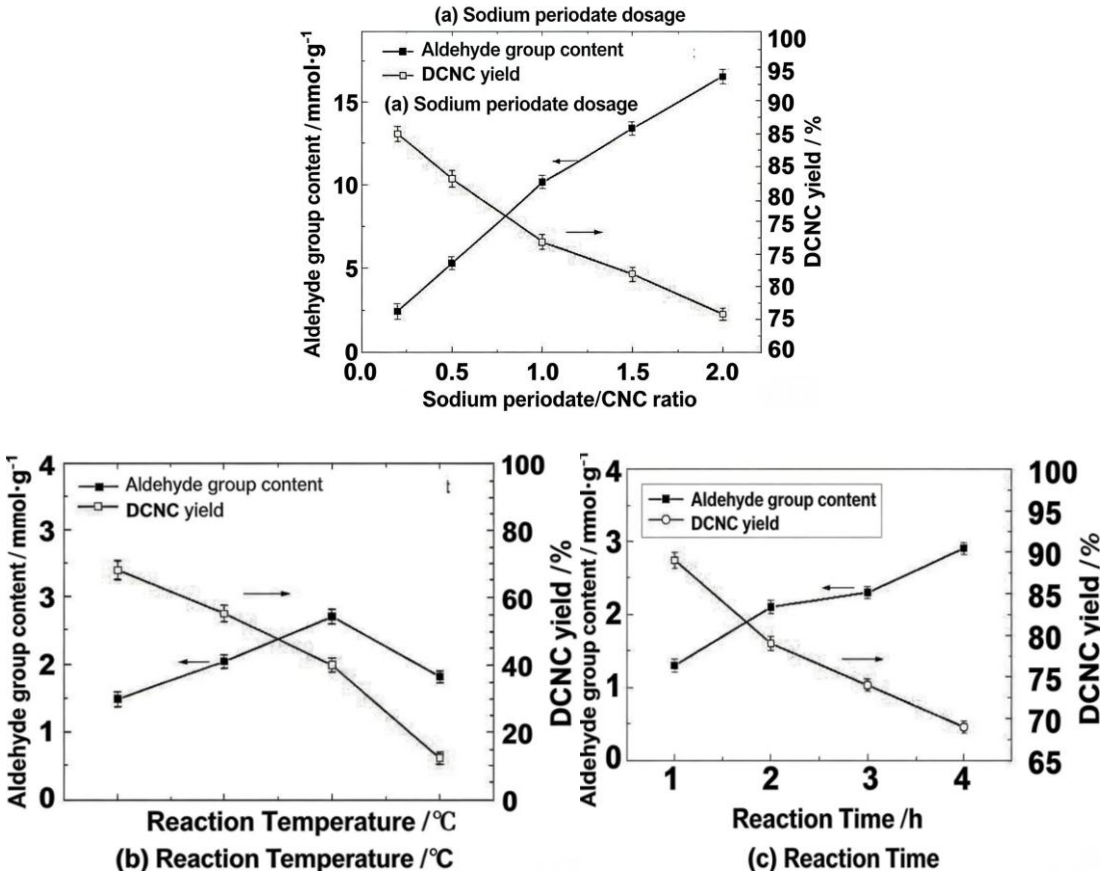

Figure 2 Effect of NaIO4 dosage, temperature and reaction time on aldehyde content and yield of dialdehyde cellulose nanocrystal

Use FT-IR to characterize structure of aldehyde-functionalized cellulose nanocrystals, results shown in 3. Unmodified cellulose nanocrystals show typical cellulose IR spectrum. Comparing IR spectrum of aldehyde-functionalized cellulose nanocrystals, peak positions and intensities basically unchanged, but new peak appears at 1732 cm^{-1}, characteristic absorption peak of aldehyde group, indicating successful introduction of aldehyde groups after sodium periodate oxidation [23].

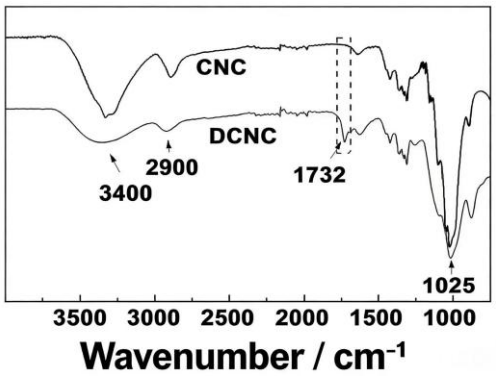

Figure 3 FT-IR spectra of dialdehyde cellulose nanocrystal

Figure 4 shows morphology and particle size distribution of resulting aldehyde-functionalized cellulose nanocrystals. From 4(a), DCNC morphology shows typical rod-like shape, but due to severe agglomeration after freeze-drying, single fiber morphology not clear, thus use TEM to characterize morphology of aldehyde-

functionalized cellulose nanocrystals, as shown in 4(b). Aldehyde-functionalized cellulose nanocrystals have rod-like or needle-like morphology. As shown in 4(c), average particle size of aldehyde-functionalized cellulose nanocrystals is about 187 nm, suspension appears milky white as shown in inset [24].

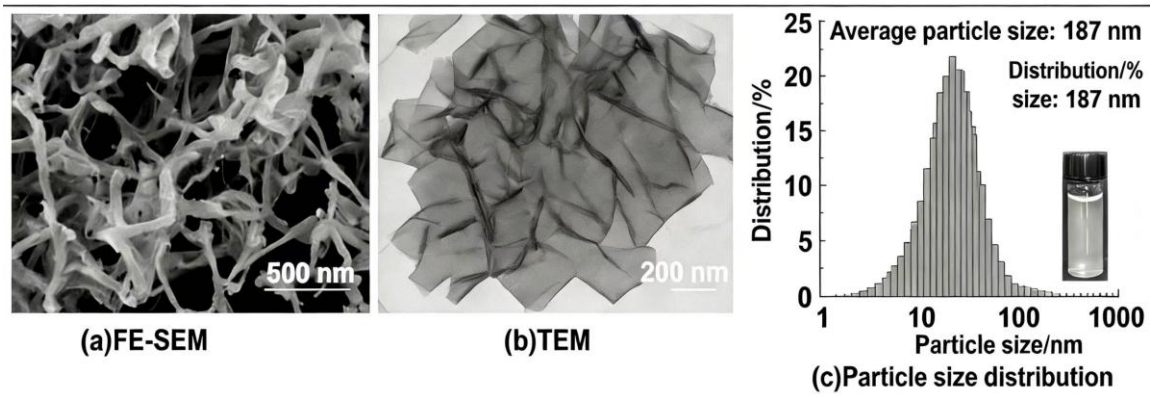

Figure 4 FE-SEM micrograph, TEM micrograph and particle size distribution of DCNC determined by dynamic light scattering (inset: digital graph of DCNCs suspension)

2.2 Preparation and Performance of DCNC/Keratin Composite Films

Preparation of aldehyde-functionalized cellulose nanocrystal enhanced keratin-based composites shown in 5. Add aldehyde-functionalized cellulose nanocrystals at 1.0%, 2.5%, 5.0%, and 10.0% relative to keratin mass to keratin film-forming solution, ultrasonicate to disperse evenly, cast films on polytetrafluoroethylene plates, after solvent evaporation, heat in oven at 80°C for 1.5 h to promote reaction between aldehyde groups and amino groups on keratin, establishing chemical bonds between aldehyde-functionalized cellulose nanocrystals and keratin.

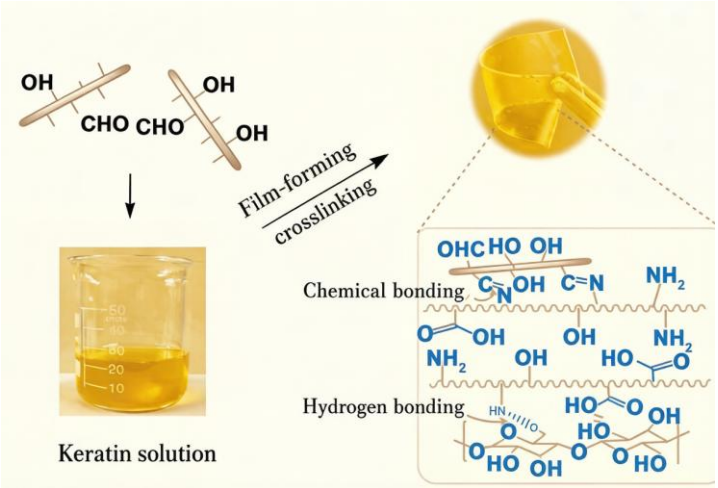

Figure 5 Schematic plot of the preparation process of dialdehyde cellulose nanocrystal reinforced keratin nanocomposites

Improve mechanical properties by adding aldehyde-functionalized cellulose nanocrystals, thus test fracture strength and elongation of composites, results shown in 6. Pure keratin film without DCNC has poor mechanical properties, low fracture strength and elongation, fracture strength only 2.7 MPa, elongation 11.0%. Compared to pure keratin film, after adding DCNC, fracture strength of composite films significantly increases. When DCNC addition is 1.0%, fracture strength increases to 8.5 MPa, and as DCNC addition increases, fracture strength greatly increases, reaching maximum 23.5 MPa at 5.0% addition. Further increasing DCNC amount leads to decrease in

fracture strength. DCNC addition well improves fracture strength of keratin composite films. Compared to CNC, DCNC addition shows better improvement in mechanical properties [25].

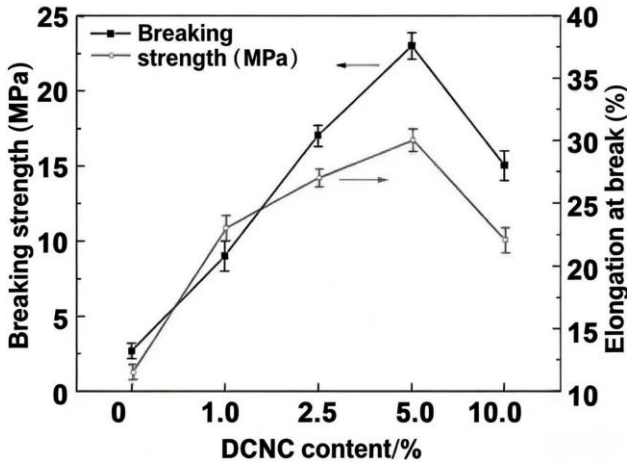

Figure 6 Mechanical properties of dialdehyde cellulose nanocrystal reinforced keratin nanocomposites

Figure 7 shows dynamic mechanical properties test results of DCNC/keratin composite films. 7(a) shows storage modulus of DCNC/keratin composites versus temperature. As temperature increases, storage modulus decreases around 100°C, this temperature range is glass transition region, storage modulus reaches maximum. Below glass transition temperature, material in rubbery state, storage modulus small. After adding different amounts of DCNC, storage modulus increases, similar to fracture strength trend. Increase in storage modulus may due to: (1) Cellulose nanocrystals themselves have high modulus, as reinforcing phase can greatly improve mechanical properties, increasing storage modulus; (2) Aldehyde-functionalized cellulose nanocrystals crosslink with keratin, establishing chemical bonds between nanocrystals and keratin, enhancing interfacial bonding, improving interface strength. Under combined effect of DCNC reinforcement and strong interface, mechanical properties well improved, thus storage modulus increases.

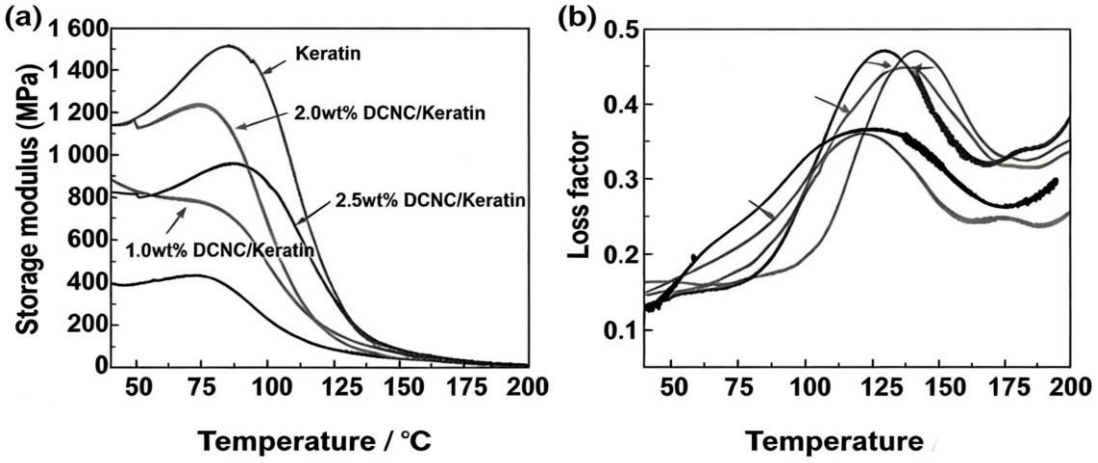

Figure 7 Dynamic mechanical thermal analysis of dialdehyde cellulose nanocrystal reinforced keratin nanocomposites

7(b) shows loss factor versus temperature for DCNC/keratin composites. After adding DCNC, tan δ peak shifts to higher temperature. Tan δ peak indicates glass transition temperature Tg. Adding DCNC can entangle with keratin molecular chains, increasing movement resistance, making free movement difficult; on the other hand chemical crosslinks between DCNC and keratin also increase resistance to free movement of keratin chains, both reasons leading to increase in Tg.

2.3 Drug Sustained-Release Performance of DCNC/Keratin Composite Films

From above studies, DCNC enhancement can well improve properties of keratin film materials. Use 5.0% DCNC enhanced keratin composite film as drug carrier material, compare with pure keratin film, use gentamicin sulfate as drug model, study application performance of keratin-based film materials as drug sustained-release carriers, results shown in 8. Figs. 8(a)-(c) show cumulative drug release rate of keratin-based film materials versus time in pH 3, 5, and 7.4 buffer solutions, respectively. Pure keratin film shows burst release for all pH conditions, indicating no sustained release effect. This is because keratin film materials have poor properties, easily damaged during use causing drug burst release. Such release behavior not suitable for wound dressing materials requiring sustained drug release. DCNC/keratin composite film still releases drug after 60 h, indicating sustained release, potential for wound dressing applications.

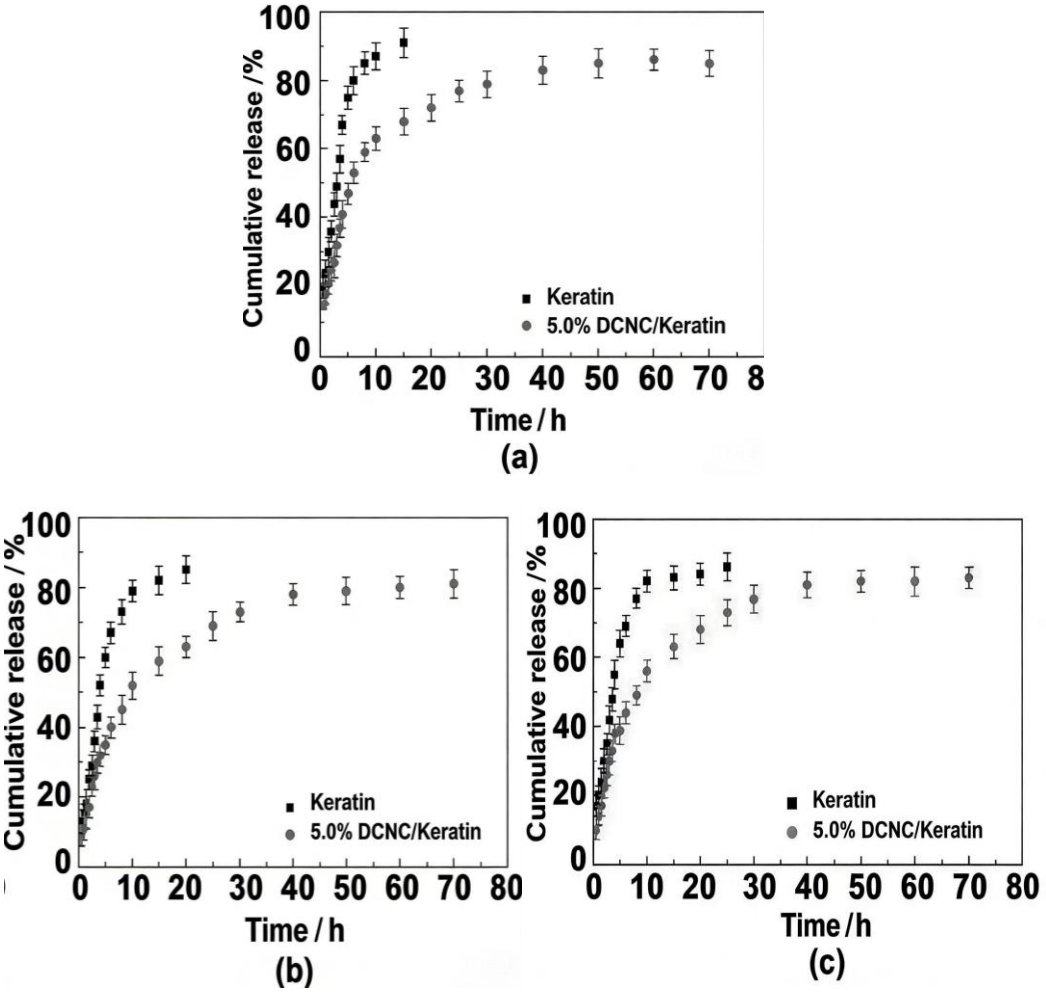

Figure 8 Drug release profile of keratin films at different pH solution

Based on the comprehensive experimental data presented in the document, the mechanism underpinning the enhanced performance of the dialdehyde cellulose nanocrystal (DCNC)/keratin drug-loaded composite films is fundamentally a synergistic combination of nanoscale reinforcement and covalent interfacial crosslinking, which collectively transforms the microstructure and material properties. The process initiates with the selective periodate oxidation of cellulose nanocrystals (CNCs), which introduces reactive aldehyde groups onto their surface, as unequivocally confirmed by the appearance of the characteristic FT-IR absorption peak at 1732 cm^{-1}. These aldehyde-functionalized DCNCs, possessing a rod-like morphology with an average length of about 187 nm, are then integrated into the keratin matrix. The core enhancement mechanism lies in the chemical reaction between the aldehyde groups on the DCNCs and the primary amino groups (-NH_2) present on the side chains of keratin protein molecules. During the film formation and subsequent heat treatment at 80°C, these groups react

to form covalent Schiff base linkages (-C=N-), creating a robust, crosslinked network. This chemical bonding serves a dual purpose: firstly, it dramatically improves the interfacial adhesion between the hydrophilic nanocellulose reinforcement and the protein matrix, facilitating efficient stress transfer from the relatively weak keratin to the high-strength DCNCs; and secondly, it introduces additional crosslinking points within the keratin matrix itself, restricting the mobility of the protein chains. This combined effect is the primary reason for the remarkable mechanical enhancement, where the fracture strength of the composite film increases from 2.7 MPa for pure keratin to a maximum of 23.5 MPa at an optimal 5.0% DCNC loading, while elongation also improves from 11.0% to 30.0%. The formation of this crosslinked network is further supported by dynamic mechanical analysis (DMA), which shows an increase in storage modulus and a shift of the tan δ peak to a higher temperature, indicating a raised glass transition temperature (Tg) due to the restricted chain mobility imposed by the DCNC crosslinks. Beyond mechanical reinforcement, this covalently bonded, denser network significantly alters the film's interaction with water. The crosslinked structure reduces the availability of hydrophilic sites and creates a more tortuous path for water molecules, thereby improving the material's water resistance stability, a critical factor for biomedical applications like wound dressings that are exposed to aqueous environments. Most importantly, this tailored microstructure is directly responsible for transforming the drug release profile from a burst release to a sustained, controlled release. In pure keratin films, the weak, porous structure allows for rapid diffusion and dissolution of the encapsulated drug (gentamicin sulfate), leading to complete release within a short timeframe. In the DCNC/keratin composite, the crosslinked network acts as a physical barrier, slowing down the diffusion of drug molecules out of the matrix. Furthermore, the improved hydration stability reduces excessive swelling and structural disintegration in buffer solutions (pH 3, 5, and 7.4), which helps maintain the integrity of the film and provides a more gradual, sustained release over extended periods (beyond 60 hours). The optimization of the oxidation conditions (mass ratio, temperature, time) to achieve a DCNC with an aldehyde content of 2.1 mmol/g is crucial, as it determines the density of available crosslinking sites; insufficient aldehyde groups would lead to weak interfacial bonding, while excessive oxidation could degrade the CNC structure, compromising its reinforcing capability. Therefore, the superior performance of the composite film emerges from an interconnected mechanism where chemical crosslinking enhances interfacial adhesion for mechanical reinforcement, creates a denser matrix for improved water resistance, and establishes a diffusive barrier network that effectively modulates the kinetic release of therapeutic agents.

Building upon the clearly illustrated multi-stage flame-retardant mechanism involving endothermic decomposition, gas-phase dilution, and protective barrier formation, the future application prospects for magnesium hydroxide/regenerated cellulose composites are expansive and strategically aligned with global demands for sustainable, non-toxic fire safety solutions across diverse industries. The inherent synergy between the bio-based, biodegradable cellulose matrix and the endothermically active, residue-forming $Mg(OH)_2$ filler, as depicted in the mechanism diagram, positions these composites as ideal candidates for next-generation, environmentally benign flame-retardant materials. In the construction and building sector, these composites could be engineered into interior panels, insulation foams, or decorative surface laminates, where the $Mg(OH)_2$'s heat absorption and water vapor release would effectively delay flashover and suppress smoke, while the regenerated cellulose offers a low-environmental-impact alternative to synthetic polymers. For the transportation industry, particularly in automotive and aerospace interiors for seat backings, headliners, or cable insulation, the material's ability to form a stable MgO char layer provides a critical protective barrier, preventing flame spread and meeting stringent safety standards without relying on halogenated compounds that produce toxic smoke. The packaging industry for sensitive electronics or high-value goods represents another promising avenue, where the composite films could serve as protective, flame-resistant layers that are also compostable or easily recyclable, addressing both fire safety and end-of-life environmental concerns. Furthermore, advancements in processing could lead to their integration into technical textiles and nonwovens for protective workwear, curtains in public spaces like hotels and hospitals, or upholstery fabrics, leveraging the comfort of cellulose with added fire safety. Future research will likely focus on enhancing this core mechanism through the development of synergistic systems, such as combining nano-sized or surface-modified $Mg(OH)_2$ with other eco-friendly additives like phytic acid or layered double hydroxides (LDHs) to further reduce loading requirements, improve mechanical properties, and possibly introduce additional functionalities like antimicrobial activity. The scalability of the in-situ precipitation or blending process with regenerated cellulose will be key to commercial viability, potentially enabling the production of these multifunctional, fire-safe biocomposites on an industrial scale to replace conventional, less sustainable options.

Conclusion

This study introduced reactive aldehyde functional groups onto cellulose nanocrystals, using aldehyde groups to form chemical bonds with amino groups on keratin, improving interfacial bonding between cellulose nanocrystals and keratin. A keratin composite film material with good mechanical properties was prepared, and its performance as drug carrier was studied. Studies show that under conditions of sodium periodate to nanocrystal mass ratio 1:1, temperature 40°C, time 2 h, resulting aldehyde-functionalized cellulose nanocrystals have aldehyde content 2.1 mmol/g, yield 78%. TEM confirms needle-like morphology of modified cellulose nanocrystals, FT-IR confirms oxidation modification does not destroy chemical structure of cellulose nanocrystals. When DCNC addition is 5.0%, fracture strength of composite film increases from 2.3 MPa to 23.5 MPa, elongation increases from 11.0% to 30.0%. DCNC enhanced keratin composite film shows sustained drug release, still releasing drug after 50 h, indicating good sustained-release properties. Such drug release behavior suitable for wound dressing materials.

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