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Core Properties of Chitosan and Its Research Progress in Applications to the Medical and Food Industries

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Abstract. This paper explores the advancements and applications of chitosan, a naturally sourced, non-toxic, biocompatible and biodegradable polymer primarily derived from chitin extracted from crustacean exoskeletons and fungal cell walls, in both the medical and food industries. In the medical field, chitosan exhibits significant potentials such as broad-spectrum antimicrobial activity against pathogenic bacteria and fungi, and high utility as a biocompatible, biodegradable carrier in drug delivery systems. In the food industry, owing to its excellent properties like biodegradability, non-toxicity, and film-forming ability alongside antimicrobial activity, chitosan has been widely applied in food and fruits preservation, often formulated as a coating to block oxygen and inhibit microbial growth, thereby effectively prolonging the shelf life of food and fruits. Moreover, chitosan can be chemically modified or physically combined with other substances like nanoparticles to tailor its properties, such as solubility, mechanical strength and antimicrobial efficiency, for specific applications in both sectors. Overall, chitosan holds great promise for revolutionizing applications in the medicine and food industries, and with further research and development to address current limitations like poor water solubility in neutral environments, its practical value will be further unlocked.

Keywords: Chitosan; biocompatibility; antibacterial activity; medical applications; food Industry.

1. Introduction

In recent years, natural polymeric materials have gradually ascended to the forefront of research endeavors within the realms of medicine and the food industry due to their properties, such as renewability and excellent biocompatibility. Among them, the structure of chitosan, a natural alkaline polysaccharide [1,2], endows this biopolymer with a suite of functional properties that are highly sought after in applied science: good biocompatibility, biodegradability, antibacterial activity, and film-forming ability. These properties make it naturally meet the demands of the medical and food industries, rendering them a focus of interdisciplinary research. In the medical field, the polycationic nature of chitosan allows it to encapsulate drugs for protection, and its biodegradability, biocompatibility, and non-toxicity enable its application in drug delivery [3,4,5]. Meanwhile, these excellent properties also make it an ideal material for bone tissue engineering scaffolds [6,7]. Its antibacterial activity is applied in the antibacterial treatment of oral diseases and the prevention of bacterial infections in surgeries [1,8]. In the food industry, due to its excellent properties, chitosan has been widely applied and recognized in the field of coating preservation. In the food industry, the preservation of fruits and vegetables after harvest is a challenging issue due to bacterial proliferation. Leveraging the antibacterial activity of chitosan, films and packaging materials can be fabricated by combining it with other materials for application in the storage and preservation of fruits and vegetables, making it one of the technologies to ensure quality and extend the shelf life of post-harvest fruits and vegetables [9,10,11]. Based on this, this paper reviews the properties of chitosan and summarizes its application progress in the medical field and food industry.

2. Basic Properties of Chitosan

2.1. Structure of Chitosan

Chitosan is obtained by the deacetylation of chitin, which is widely distributed in nature. The main sources of chitin include the exoskeletons of crustaceans and the cell walls of fungi [1,2,3]. The chemical structures of chitin and chitosan are shown in **Fig. 1**. Chitosan is a linear amino polysaccharide composed of D-glucosamine and N-acetyl-D-glucosamine linked by β-1,4-glycosidic bonds. Its molecular chain contains a large number of hydroxyl and amino groups. These functional groups grant chitosan excellent chemical reactivity, rendering it susceptible to chemical modification and thus altering characteristics like solubility and antibacterial activity. For example, quaternization can improve the solubility of chitosan under neutral or alkaline pH conditions.

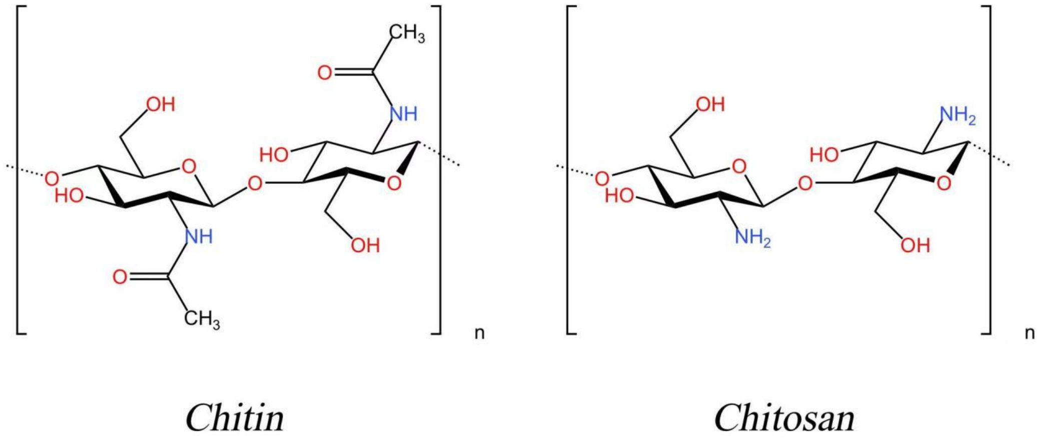

Fig 1. Structure of Chitin and Chitosan.

2.2. Properties of Chitosan

2.2.1. Solubility

In general, the solubility of a molecule is closely related to its molecular configuration. As a polymer with a large number of amino and hydroxyl groups on its molecular chain, chitosan has extremely strong intermolecular forces—with hydrogen bonds and van der Waals forces as the main ones—due to this configuration. This significantly limits its solubility in alkaline solutions, neutral solutions, and most organic solvents. When charges are uniformly distributed on the chitosan molecular chains, the strong electrostatic repulsion generated between adjacent chains overcomes the intermolecular forces, preventing the aggregation of chitosan molecular chains. Additionally, the ammonium groups can form strong hydrogen bonds with water, endowing chitosan with hydrophilicity and thus enabling it to bind more effectively with the solvent

2.2.2. Biocompatibility

Due to its structural similarity to certain polysaccharides in the human body, chitosan is more readily accepted by organisms, which reduces the risk of immune rejection. Therefore, Chitosan possesses excellent biocompatibility, enabling its widespread application in the biomedical field.

2.2.3. Biodegradability

Chitosan molecules are mainly composed of carbon, hydrogen, oxygen, and nitrogen elements, and their functional groups (hydroxyl and amino groups) are all common and harmless groups in organisms. Therefore, it does not contain any toxic chemical groups or heavy metal ions. In organisms, chitosan can be gradually degraded by enzymes into small-molecule oligosaccharides or monosaccharides. These degradation products are inherent metabolites in organisms; thus, chitosan does not release toxic, carcinogenic, or mutagenic substances during its in vivo degradation process and exhibits non-toxicity and biodegradability.

2.2.4. Film-forming ability

Chitosan molecular chains contain both amino and hydroxyl groups, which can form hydrogen bonds and electrostatic interactions either intermolecularly or intramolecularly. Through these interactions, a large number of chitosan molecules cross-link and aggregate. With the evaporation of water, they gradually transform from a dispersed state into a solid film.

2.2.5. Oxygen-barrier and CO_2-selective permeability

The structure of chitosan allows carbon dioxide to permeate more easily than oxygen. The core reason lies in that carbon dioxide is a polar molecule, which can form directional weak interactions with a large number of polar groups on the chitosan molecular chain. Although these interactions are far weaker than chemical bonds, they are sufficient to trap carbon dioxide molecules and enable their rapid diffusion in the material. However, oxygen is a non-polar molecule and cannot form such interactions with polar groups, thus diffusing much more difficultly compared to carbon dioxide.

2.2.6. Hygroscopicity with water retention

Its hygroscopicity with water retention is mainly achieved through the hydrogen bonds formed between the hydroxyl and amino groups on its molecular chain and the moisture in the air. Meanwhile, the porous structure of the chitosan film can trap moisture through capillary adsorption. When moisture forms hydrogen bonds with the intra-molecular amino and hydroxyl groups, the force of the hydrogen bonds is much stronger than the evaporation force of water molecules at room temperature, making it difficult for moisture to escape through evaporation. Additionally, the linear molecular chains of chitosan entangle with each other to form a network structure, which can physically hinder the free diffusion of water molecules adsorbed inside, further reducing moisture loss.

3. The antibacterial mechanism of chitosan

The antibacterial activity of chitosan is widely believed to be mediated by positive charge adsorption: due to the presence of a large number of amino groups in its molecules, chitosan is a cationic polymer that can bind to the anionic components on the surfaces of bacterial cell membranes and cell walls through electrostatic interactions. Upon contact with the bacterial cell membrane, the integrity of the membrane is disrupted, its permeability increases, and intracellular substances leak out, ultimately leading to bacterial death [2]. Studies have shown that chitosan kills *Escherichia coli* by disrupting the cell membrane. Additionally, chitosan can interfere with the synthesis of bacterial cell walls and destroy their structure, rendering bacteria unable to maintain normal morphology and function.

4. Applications of Chitosan

4.1. Medicine

4.1.1. Biomedicine

As a drug carrier, chitosan primarily leverages its biocompatibility, biodegradability, low toxicity, and polycationic nature to achieve drug encapsulation, protection, targeted delivery, and controlled release[3, 4]. Chitosan has been extensively utilized in the field of drug delivery, including the delivery of analgesic compounds, antibiotics (e.g., vancomycin), and other pharmaceutical ingredients. Through diverse techniques such as ionic gelation, chitosan is capable of encapsulating drugs within its internal structure to form a drug carrier, and this carrier can exert a protective effect on drugs to prevent their degradation. Through research, carboxymethyl chitosan (CMCS) nanoparticles with pH-sensitive properties have been fabricated, enabling pH-triggered drug release under weakly acidic conditions. Nanoparticles subjected to surface fluorination treatment exhibit enhanced cellular uptake efficiency, higher accumulation at tumor sites, and improved killing efficacy against different tumor cells. These nanoparticles significantly boost the bioavailability of anticancer drugs and in vivo antitumor efficacy [5].

4.1.2. Tissue Engineering

In the domain of materials science and biomedical engineering, bone tissue engineering is defined by its core objective: the targeted repair or functional replacement of bone tissue that has been impaired by trauma, disease, or congenital defects. Chitosan has emerged as an ideal candidate for bone tissue engineering scaffolds due to its excellent biocompatibility, biodegradability, and non-toxicity. Chitosan-magnesium composite scaffolds can simulate the physical and chemical properties of the natural extracellular matrix of tissues, and cytotoxicity studies have shown that they are non-toxic and can support cell growth [6]. In addition, chitosan plays an important role in cartilage tissue engineering due to its flexibility and good interaction with other materials. Combined with other materials like collagen, it can form composites for application in cartilage tissue engineering [7].

4.1.3. Antibacterial Applications

Chitosan nanomaterials, benefiting from its antibacterial activity, have also attracted significant attention in the antibacterial treatment of oral diseases. Studies have shown that chitosan exhibits a synergistic antibacterial effect. Chitosan-based coatings exhibit a distinct performance in inhibiting microbial adhesion of *Escherichia coli* and *Staphylococcus aureus* and are expected to find broader applications in dentistry in the future. [8]. In the context of orthopedic surgical procedures, infections associated with biomaterials continue to pose a severe complication that cannot be overlooked. Consequently, within both experimental research and clinical practice, antibacterial prophylactic measures are recognized as an indispensable component for the prevention of such infections. Bone cement, as a carrier for antibiotics, can load antibiotics without causing systemic toxicity. Studies have found that incorporating CS nanoparticles and quaternized CS derivatives into bone cement can provide effective antibacterial effects against *Staphylococcus aureus* and *Streptococcus epidermidis*.

4.2. Food Industry

4.2.1. Food Packaging

Chitosan has been increasingly widely applied in the field of food packaging, mainly benefiting from its excellent biodegradability, antibacterial activity, biocompatibility, and good film-forming properties.

Food spoilage is generally considered to stem from the following main causes: spoilage caused by the proliferation of microorganisms; oxidative spoilage induced by oxygen; and decomposition reactions of nutrients (e.g., starch, protein, fat, and carbohydrates) in food catalyzed by endogenous enzymes. Enzymes can directly or indirectly lead to food spoilage, and spoilage can be divided into three types according to enzyme categories: oxidases and peroxidases catalyze oxidation reactions, causing food to discolor, develop off-flavors, and generate heat; amylases catalyze starch decomposition, resulting in food softening, souring, heat generation, and gas production; proteases catalyze protein decomposition, leading to food putrefaction (foul odor), sliminess, and heat generation.

Benefiting from its antibacterial activity, chitosan can undergo electrostatic interactions with the cell membranes of negatively charged microorganisms (such as bacteria and molds), disrupting membrane integrity. This leads to the leakage of intracellular contents and the loss of metabolic capacity in microorganisms, thereby delaying food spoilage. In addition, the dense film structure formed by chitosan can effectively block oxygen from the outside of the package from entering the interior of food, reducing the contact between oxygen and components such as fats and vitamins in food, and delaying oxidative rancidity. A novel composite film (CS/TCNF/AgNPs) for fruit and vegetable preservation has been developed by combining chitosan (CS) with TEMPO-oxidized nanocellulose (TCNF) immobilized with silver nanoparticles (AgNPs)[9]. It exhibits antibacterial activity against Escherichia coli and Staphylococcus aureus, is safe and non-toxic, and can extend the shelf life of strawberries (**Fig. 2**).

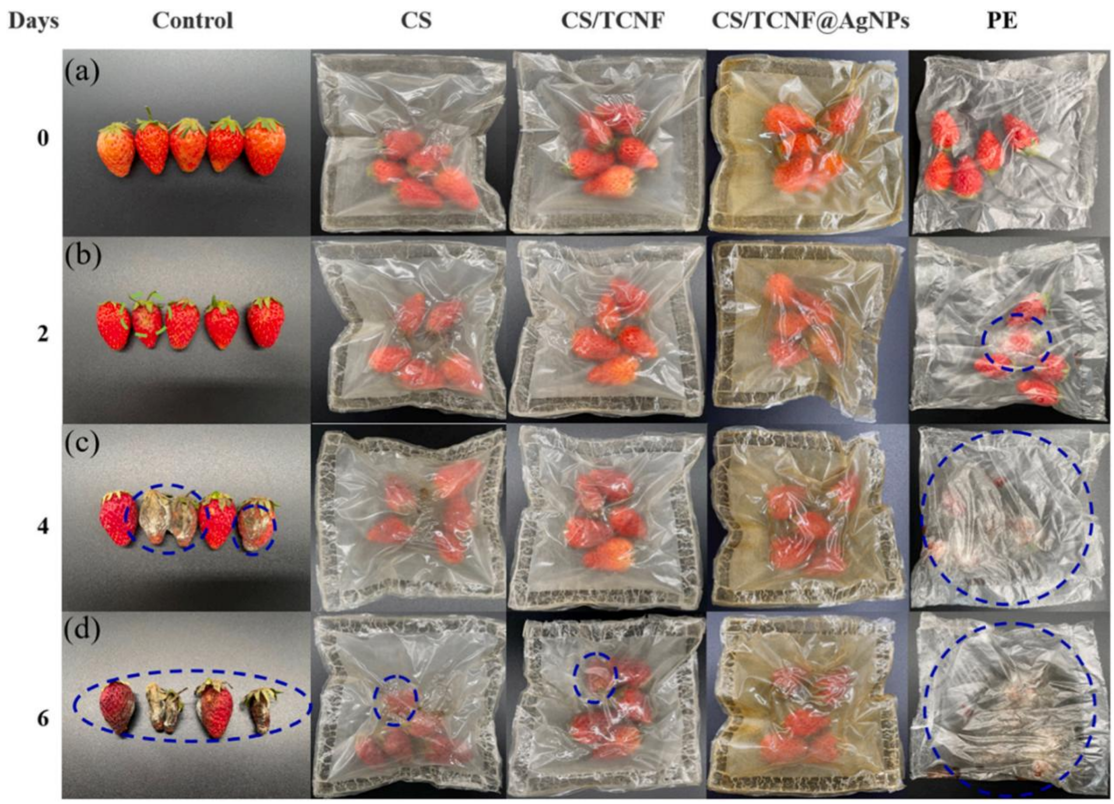

Fig 2. The preservation effect of strawberries under different packaging conditions. On the 4th and 6th days, the strawberries in the control group showed obvious signs of spoilage, while the strawberries in the CS/TCNF@AgNPs group (chitosan/TEMPO-oxidized nanocellulose@silver nanoparticles) maintained good freshness [9].

4.2.2. Food Preservation

Chitosan films can be applied in food preservation, with the core mechanism based on its oxygen-barrier and CO_2-selective permeability as well as hygroscopicity with water retention of the films formed by chitosan.

Based on these properties, chitosan has been widely used in food preservation. Fruits and vegetables continue to undergo respiration after harvesting. If the package is too tightly sealed or the storage space is narrow, it may lead to excessive carbon dioxide accumulation, which inhibits the aerobic respiration of fruits and vegetables and forces them to switch to anaerobic respiration. The products of anaerobic respiration directly damage the structure and quality of fruits and vegetables, manifesting as physiological spoilage. Owing to oxygen-barrier and CO_2-selective permeability, composite packaging incorporating chitosan can appropriately allow carbon dioxide to permeate out while blocking external oxygen from entering. This reduces the carbon dioxide concentration around fruits and vegetables, thereby weakening the respiration intensity and extending the ripening period. In addition, chitosan itself has certain antibacterial activity, and its coating can also directly inhibit molds adhering to the surface, further reducing decay.

Experiments have shown that a multifunctional composite film for food packaging was prepared by modifying chitosan derivatives (HA-CS-NP) with quaternary ammonium salts and quaternary phosphates and then combining them with polyvinyl alcohol (PVA); the preservation effect of this film on mangoes and papayas was evaluated [10]. The results indicated that the composite film could effectively inhibit the respiration of fruits and exhibited excellent performance in delaying fruit spoilage and suppressing fungal growth. Another study involved embedding copper nanoparticles and thyme essential oil in liposomes, then combining them with chitosan to prepare a coating film for litchi preservation. This composite coating significantly extended the shelf life of litchis and inhibited their spoilage [11].

5. Conclusion

As a natural alkaline polysaccharide from chitin, chitosan's value in medicine and food industry is fully verified, becoming a core cross-field natural polymer research direction. Its applications in both fields depend on core properties: biocompatibility, biodegradability, antibacterial activity, and film-forming properties.

In medicine, it excels in drug delivery, enabling efficient delivery via low toxicity and polycationic nature, bone tissue engineering, combining with other materials for ideal scaffolds, and antibacterial uses. In food industry, its antibacterial and film-forming properties aid food and vegetable preservation: chitosan-based films inhibit respiration and spoilage microbes, extending shelf life; composite modification with nanoparticles enhances adaptability.

Poor water solubility, weak mechanical properties, and limited antibacterial activity restrict it. Future research will improve these via modification and optimization to expand its complex biomedical and food applications.

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