

# A Review of the Current Status of Research on Chitosan-Modified Polymer

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**Abstract:** As the only naturally occurring alkaline polymeric polysaccharide, chitosan has good biological properties such as good biocompatibility, biodegradability, low immunogenicity and low bioactivity, making it a promising application in the field of medicine, especially as a drug carrier, which can modify the drug release mode while ensuring safety, but its extremely poor in water and organic solvents. However, its extremely poor solubility in water and organic solvents has limited its application scope. In recent years, reports on the modification of chitosan by physical and chemical methods have emerged, and many scholars have physically and chemically modified chitosan to give new properties and structures to chitosan materials, and the modified chitosan materials have been widely used in the fields of medicine, chemical industry and environmental protection, etc. This paper reviews the structure, properties and their applications of recent chitosan-modified polymers.

**Keywords:** Chitosan, Polymer, Bioavailability, Modification.

## 1. Introduction

Chitosan (CS) is a natural straight-chain polysaccharide composed of a structure of alkali glucose units, also known as deacetylated chitin because it is mainly prepared by deacetylation of natural chitin (Chitin), and is the most abundant polysaccharide in nature after cellulose [1], as well as the only known natural alkaline polysaccharide [2,3]. The structural monomers are shown in Figure 1.1. Chitosan has good biocompatibility [4], hemostatic [5] and bacteriostatic properties [6], and is widely used in medicine because of its abundant and biodegradable source. Due to the presence of a large number of hydroxyl and amino groups in the molecule, chitosan has a large number of intramolecular and intermolecular hydrogen bonds, resulting in very poor water solubility of chitosan. In addition, the good film-forming properties [7], adsorption [8] and antibacterial properties [9] of chitosan make chitosan-based materials widely used in the field of cyclic materials. Chitosan has a polysaccharide-like long-chain structure and contains a large number of amino and hydroxyl groups on the molecule, which gives chitosan great room for modification. The modified chitosan materials have been widely used in pharmaceutical, chemical, environmental protection and other fields.

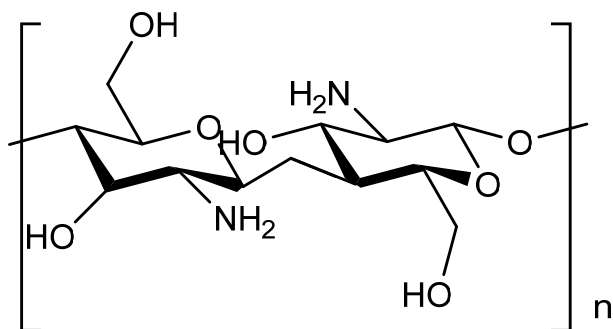


Figure 1. The chemical structure of chitosan

## 2. Modification Method of Chitosan

### 2.1. Quaternized Chitosan

Chitosan has a broad-spectrum antibacterial effect and has a certain inhibitory effect on a variety of bacteria and fungi, the main principle is the presence of NH<sub>3</sub><sup>+</sup> in chitosan, which interacts with the negative charge on the surface of microorganisms and damages the cell wall, leading to the outflow of intracellular material and thus cell death, and the quaternization of chitosan, which increases the positive charge of chitosan, is an effective way to strengthen the antibacterial properties of chitosan, while the introduction of quaternary ammonium group also confers better water solubility to chitosan, and this feature also extends the use of quaternary ammonium salts. Wang Fei [10] et al. used 90% deacetylated chitosan, prepared chitosan tertiary amine under formaldehyde formic acid, and further oxidized tertiary amine to quaternary ammonium using iodomethane to obtain N,N,N-trimethyl chitosan, and showed by solubility and antibacterial experiments that compared to chitosan, quaternized chitosan The water solubility at any pH was improved and showed higher inhibitory activity against *Escherichia coli* and *Staphylococcus aureus* compared to chitosan. Yi Zhang [11] et al. prepared etherifying agents from triethylamine and epichlorohydrin, and synthesized quaternary ammonium chitosan by etherification reaction one method using chitosan as raw material, and obtained quaternary ammonium chitosan by deacetylation reaction, and the antibacterial effect of its fabric reached more than 99.9% against *E. coli*, which was significantly higher than the antibacterial performance of natural chitosan. In addition, the adsorption of metal ions by chitosan quaternary ammonium salts has been widely used in environmental and chemical fields. Viviane A. Spinelli [12] et al. synthesized chitosan quaternary ammonium salts using glycidyltrimethylammonium chloride containing quaternary ammonium salt substituents as catalysts, and through adsorption experiments, it was demonstrated that chitosan quaternary ammonium salts have better adsorption effect on

chromium (VI) ions.

## 2.2. Amidated Chitosan

The amidation modification of chitosan is mainly based on the reaction of amino or hydroxyl groups on chitosan with a variety of organic acid derivatives, which can obtain N-amidated and O-amidated derivatives, respectively, and it is generally difficult to obtain a single reaction product due to the comparable activity of the two groups on the chitosan group. molecular crystallinity becomes smaller, which increases the solubility of chitosan in organic solvents. Meanwhile, the water solubility of chitosan molecules can also be improved if the introduced groups contain a large number of hydrophilic groups. Yang [13] et al. used transglutaminase as a catalyst to amidate chitosan and grafted serine peptide (SFP) onto hydroxypropyl chitosan molecule chains under aqueous phase conditions, prepared chitosan amidated derivatives with different degrees of substitution under different conditions, and tested the properties of different substitutions Ana [14] et al. prepared chitosan derivatives with 3%-15% substitution by grafting oligomeric chitosan with lactic acid through amide bonding, and compared with natural chitosan, the water and lipid solubility of the derivatives with different substitutions were improved, with the highest substitution degree having the best water solubility. Li [15] et al. grafted oxidized chitosan onto cashmere fibers by amide covalent modification to produce chitosan-cashmere fibers rich in C-N amide bonds, and the chitosan-cashmere fibers showed good moisture retention and better antibacterial effects against *S. aureus* and *E. coli* than the original cashmere fibers. The chitosan-cashmere fiber has good moisture retention and better antibacterial effect on *S. aureus* and *E. coli* than the original cashmere fiber.

## 2.3. Carboxylation of Chitosan

Carboxylation modification of chitosan is a common modification method to give chitosan water solubility, mainly by using the reactivity of amino and hydroxyl groups on the chitosan molecule to carry out carboxylation reaction on the molecular chain to form N/O-carboxylated chitosan. The water solubility of carboxylated chitosan is significantly improved compared with chitosan, partly because carboxylated chitosan can be soluble in water as sodium salt of carboxylic acid, and partly because the introduction of carboxyl group destroys the secondary structure of chitosan, weakens the hydrogen bond within the molecule, makes the product much less crystalline, becomes amorphous molecule and increases its water solubility. Carboxymethylation is the most commonly used and most studied reaction in carboxylation modification, and Wang [16] et al. first used chloroacetic acid as an etherifying agent and prepared carboxymethyl chitosan with different degrees of substitution by controlling the temperature and reaction time under alkaline environment, and found by characterization that the degree of substitution increased gradually with the rise of temperature and reaction time. Only then, Ji [17] et al. used chitosan with acrylic acid and succinate glucoside as raw materials and prepared a variety of carboxymethyl chitosan with different degrees of substitution by controlling the reactant feeding, reaction time and temperature, and proved that the derivatives with different degrees of substitution had different absorption of ammonia by ammonia adsorption test.

## 2.4. Alkylation of Chitosan

The alkylation reaction of chitosan is mainly through chemical reactions N alkylation reaction on chitosan molecules, generally used is Schiff base reaction and halohydrocarbon substitution reaction, the introduction of alkanes can weaken the hydrogen bonds within the chitosan molecule and increase the solubility of chitosan materials, Lee [18] experimentally found that lower alkylation can destroy the crystalline structure of chitosan into, but too long alkyl chains will reduce the derivatives water solubility [19], and this property was also used to control the hydrophilic properties of chitosan materials by controlling different degrees of alkylation. Guo [20] et al. attached chitosan amino groups to dodecanal by Schiff base reaction and then made N-alkylated chitosan by reduction reaction, and then prepared a composite lyophilized powder from the modified alkylated material, which showed by water absorption experiments and characterization that the material can absorb 2-3 times its own weight of water and has the potential to be used as a hemostatic material

## 3. Main Applications of Chitosan and Its Derivatives

### 3.1. Antibacterial Effect

As a recognized broad-spectrum antibacterial agent, the antibacterial mechanism of chitosan is still subject to some controversy. Xy Wu [21] compared the minimum inhibitory concentrations of *S. aureus*, *E. coli* and *B. subtilis* under the same conditions with different degrees of deacetylation and different molecular weights. The results showed that chitosan with the same degree of deacetylation had stronger antibacterial activity with increasing molecular weight between 400-800 kDa, while chitosan of similar molecular weight with different degrees of deacetylation had comparable antibacterial activity, while the maximum inhibitory activity was found at pH about 5.5-6. Xiao [22] et al. used the optical density method to study the effect of chitosan with different molecular weights and several carboxymethyl chitosan on the activity of *E. coli*, and the results showed that different molecular weights, degrees of deacetylation, solution concentrations and medium pH had different degrees of inhibition on *E. coli*, and the mechanism of inhibition was found by fluorescent probes, which might be the inhibition of DNA transcription in *E. coli*.

### 3.2. Medical Dressings

Medical dressing is an important medical device, idealized wound dressing needs to provide a moist environment with good biocompatibility, better permeability and protection, due to the antimicrobial properties, good biocompatibility and degradability of chitosan, and wide sources of low price, making chitosan an ideal raw material for wound dressing, recent scholars have found that chitosan and its derivatives under certain conditions Chen [23] used oxidized microcrystalline cellulose grafted chitosan to prepare a new and chitosan film dressing, and the characterization proved that the grafting rate of the chitosan film was the largest at 50 °C, reaching 42.4%, and the oxidized microcrystalline cellulose - chitosan film had better performance when the concentration of the casting solution was 40 g/L. -The performance of the chitosan film was relatively excellent, with light transmission rate of 75.7%, swelling rate of

169.09%, dissolution loss rate of 10.91%, porosity of 95.2%, tensile strength of 80.06 MPa, and elongation at break of 35.5%, which is expected to be a new type of wound dressing material. Zhang [24] et al. used carboxymethyl chitosan (CMCS) to co-polymerize into a novel hydrogel membrane by aqueous emulsion before using this membrane loaded with aqueous polyurethane-gelatin hydrolysis products. Through mechanical strength tests and characterization, the results showed that the hydrogel membrane has good thermal stability, swelling properties and controlled biodegradability, especially when loaded with CMCS content at 6% concentration, the maximum strength and elongation at break of the hydrogel membrane reached 31.69 MPa and 447.187%, respectively. The hydrogel film was shown to have significant antibacterial activity against *E. coli* and *S. aureus* by paper diffusion tests. These results indicate that this hydrogel film has high mechanical strength and high antimicrobial activity as a hydrogel film for wound dressing applications.

### 3.3. Drug Carrier Materials

The polymeric structure of chitosan and the rich active groups in the molecule provide the possibility of chitosan-modified materials for drug loading, and because chitosan has good biocompatibility and biodegradability and the amino and hydroxyl groups on its molecular chain give chitosan a variety of biological properties, it has a broad prospect in the field of drug carriers. Ida Genta [25] et al. used chitosan of different molecular weights to prepare chitosan microspheres and used ketoprofen as an encapsulated model drug and found that chitosan microspheres had a good encapsulation effect on the model drug, and the best encapsulation effect was achieved at a polymer:drug ratio of 1:2. Sun [26] et al. prepared a degradable chitosan-based multilayer membrane using chitosan with hyaluronic acid, alginate acid and tannic acid to encapsulate drug models such as adriamycin hydrochloride (DOX), fluorescein isothiocyanate (FITC) and ovalbumin (Ova) into the multilayer membrane and analyzed the drug loading and release profiles in phosphate-buffered saline (PBS) buffer with the same molar osmolar concentration and temperature. The drug loading and release profiles in phosphate-buffered saline (PBS) buffer with the same molar osmolar concentration and temperature were analyzed, and it was found that the multilayer membrane increased the drug loading of the model drug on the one hand, and significantly reduced the release rate of the drug on the other hand, acting as a slow release and continuous drug delivery.

Thanoo [27] et al. prepared a chitosan microsphere with good spherical geometry and smooth surface by using dioctyl sulfosuccinate as a stabilizer and cross-linking chitosan with glutaraldehyde in aqueous acetic acid solution, and prepared chitosan microspheres with different degrees of swelling by varying the cross-linking density. The drug-loaded microspheres were prepared with theophylline, aspirin or ashwagandha as model drugs, and it was found that the drug encapsulation rate of the microspheres for these drugs could reach more than 80%.

### 3.4. Environmental Protection Materials

In addition to the application of chitosan in the field of medicine, its film-forming properties, degradability and good adsorption properties to metal ions make chitosan derivative materials widely used in the field of industrial pollution control and environmental protection. Chitosan modified

composites can have good adsorption of dyes and heavy metal ions. jin [28] et al. studied the adsorption of lead by chitosan/polyvinyl alcohol hydrogel beads in aqueous solution by batch adsorption experiments and found that the maximum adsorption capacity at pH 4 and the minimum adsorption capacity at pH 6.4, and Fourier transform infrared spectroscopy and X-ray photoelectron spectroscopy showed that its adsorption capacity of lead. The adsorption capacity was mainly achieved through the interaction of lead ions with N atoms in chitosan. Zhao [29] et al. used in situ coprecipitation method to synthesize a composite adsorbent from chitosan and hydroxyapatite, and demonstrated its good adsorption of fluoride ions by adsorption-desorption experiments. Wsw Ngah [32] et al. systematically investigated the adsorption of Fe<sup>2+</sup> and Fe<sup>3+</sup> ions by chitosan and cross-linked chitosan microbeads in aqueous solution using batch adsorption experiments to evaluate the adsorption capacity and rate of Fe<sup>2+</sup> and Fe<sup>3+</sup> ions by chitosan and cross-linked chitosan microbeads. And the chitosan beads were cross-linked with glutaraldehyde (GLA), epichlorohydrin (ECH) and ethylene glycol diglycidyl ether (EGDE) to enhance the chemical resistance and mechanical strength of chitosan beads. Experiments based on pH, stirring time, stirring rate and concentration of Fe(II) and Fe(III) ions showed that chitosan and cross-linked chitosan beads were favorable adsorbents for ferrous ions..

## 4. Future Works and Perspectives

In this paper, the modification of chitosan and its main uses are reviewed. From the literature, it can be seen that through the modification of chitosan, a variety of new physicochemical properties can be given to chitosan, and these make chitosan have a wide range of applications in many fields. In addition to the modification of groups mentioned in Chinese, grafting other small molecules or polymeric compounds can be considered in the future to improve the properties of chitosan, and in addition to the chemical modification methods mentioned in the paper, physical modification also has a wide application prospect in the field of chitosan.

## 5. Conclusion

At present, many scholars modify chitosan by various chemical modification methods, and then prepare a new, green and safe material, these materials are widely used in the pharmaceutical and chemical fields, which is one of the important directions for the development of chitosan. chitosan is only soluble in acidic media, and this property limits the wide application of chitosan, and by modifying the chemical groups of chitosan, a new property is given to chitosan So that it can be used in medicine, chemical industry and environmental protection with its advantages of wide source and natural green, and there is hope to create better drug carriers, medical excipients or chemical products.

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