



## A Review of the Uses of Chitosan and Chitin

Falah Mahmood Hameed<sup>1</sup>, Abeer Fadeel kadeer<sup>2</sup>, Naseer A. Al-Arubaye<sup>3</sup>

<sup>1,2,3</sup> College of Veterinary Medicine, Kerbala University  
Email: [falah.m@uokerbala.edu.iq](mailto:falah.m@uokerbala.edu.iq)

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### Abstract

The process of chitin's alkaline deacetylation, the main ingredient in many crustaceans' protective cuticles, including those of crabs, shrimp, prawns, lobsters, and so forth, yields chitosan. Extensive research has been conducted on the potential uses of chitosan in horticulture, agriculture, medicine, and therapeutic settings. Because chitosan is known as non-toxic, biodegradable, bacteriostatic, and fungistatic, it finds extensive use in the pharmaceutical industry. The present review provides comprehensive details regarding the properties, uses, and potential applications of chitosan in the pharmaceutical industry.

**Keywords:** - Chitosan, Chitin, Applications, Deacetylation, Polymers

### Introduction

Over the past 20 years, chitosan and its derivatives have shown to be good and safe options for promoting medication transport to the mucosa and transmucosal; this is primarily because of their mucoadhesive and absorption-enhancing qualities, which are strongly linked to the cationic nature of the polymer [1,2]. Polymers now play a significant part in all biological applications. Utilizing the qualities of novel polymeric materials, such as blends and composites, has resulted in numerous noteworthy technological advancements [3]. It has been documented that biopolymer contain polymers derived from animal proteins (such as collagen, gelatin, chitosan, wool, and silk) and polysaccharides (cellulose and starch). In particular, polymers based on carbohydrates have demonstrated a highly promising industrial application in a range of forms [4].

Chitosan's many vital benefits are its ability to interact with tissue, which results in minimal or no toxicity when broken down, and its antibacterial and anti-inflammatory properties [5,6]. Furthermore, chitosan promotes tissue regeneration and functions as an active hemostatic agent, aiding wound healing [7,8].

### 1. Chitosan's Applications in Biomedicine

#### 1.1. Antimicrobial Activity

Chitosan exhibits a wide range of antibacterial action directed against molds, yeasts, and bacteria. It works well against foodborne bacteria that are both Gram-positive and negative. Many reasons lead to the incomplete understanding of chitosan's precise mechanism of antibacterial activity [9]. Three models have been put forth to describe how chitosan works as an antibacterial. The most plausible theory contends that chitosan's polycationic composition gives it antibacterial properties. The NH<sub>2</sub> groups in chitosan's C2 position protonate to produce NH<sub>3</sub><sup>+</sup> in an acidic environment. This NH<sub>3</sub><sup>+</sup> binds to the

negatively charged carboxylic acid groups ( $-\text{COO}^-$ ) on the surface of bacterial and fungal cells, thereby impairing the outer membrane (barrier properties) of the microbial and allowing leakage of cellular components (10). Studies using electron microscopy have shown that chitosan adheres to the outer membrane of bacteria, supporting this theory (11). The relative concentration (ratio) of protonated and non-protonated amino groups depends on the pH of the chitosan microenvironment. 50% of the amino groups are protonated at pH values below the pKa. Positively charged amino groups provide 90% of the concentration at pH 5.5 and 99% at pH 4.5. Chitosan is the most soluble, and its protonated form predominates below pH 6.0, which is also the pH at which it appears to be most effective against microorganisms [12].

### **1.2. Antioxidant Activity**

There have been reports of high antioxidant action for chitosan and its derivatives. Their capacity to chelate metals allows them to scavenge free radicals, which controls lipid oxidation. Chitin and chitosan's viscosity, molecular weight, and deacetylation degree all affect their antioxidant activity [10].

### **1.3 Chitosan in biotechnology**

Importantly, both Chitin and chitosan are helpful as a matrix for the immobilization of different enzymes for the production of organic compounds, sugar, and wine, as well as the development of advanced biosensors that are used in measurements of environmental pollutants and metabolite control in artificial organisms [13].

### **1.4. Chitosan as a matrix for medication delivery**

Chitosan is believed to be the twenty-first century's medicine delivery system. Drugs are delivered effectively in the shape of films, granules, microspheres, microparticles, or nanoparticles. According to [14], under regulated conditions, chitosan microspheres can be used to release proteins and peptide medications, vaccines, anticancer medicines, antihypertensive pharmaceuticals, antibodies, and nutraceutical chemicals.

### **1.5. Chitosan as a wound healing agent**

Skin ointments contain chitosan as a wound healing agent because it has bacteriostatic and fungistatic properties. Animal tissues implanted with chitosan promote hemostatic and wound-healing properties. Hydrogels, xerogels, powders, composites, and films are among the biocompatible wound dressings made from chitin [15].

### **1.6. Drug-Loaded Scaffolds Based on Chitosan for Wound Healing**

Additionally, the researchers tested with chitosan scaffolds filled with drugs. It was discovered that thiolated chitosan loaded with poly (N-isopropyl acrylamide) was cytocompatible and modified the integrated ciprofloxacin's release sustainably, suggesting that it was appropriate for long-term wound protection. When thiolated chitosan, poly (N-isopropyl acrylamide), and ciprofloxacin were combined, the deadly bacterium *Escherichia coli* exhibited antimicrobial properties, indicating that the combination has potential as a wound dressing [16].

### **1.7. Anticancer Activity**

The use of chitosan derivatives in nano drug delivery systems is an innovative delivery technique used in the biomedical field. With its highest cytotoxicity to cancer cells and tumors and minor systemic damage, this approach is a necessary targeted treatment for cancer [17]. Chitosan can directly inhibit tumor cell development, induce necrosis and cell death, and increase immunity to achieve anticancer effects. The chitosan-containing nanoparticles can operate on cancer cells by accurately delivering the loaded drugs and maintaining drug stability [18].

## **1.8. Nanoparticles**

The discipline of biomedicine has recently shown a growing interest in nanomaterials. The essential functions of Chitosan nanoparticles are to improve the loaded pharmaceuticals' stability and control the drug release rate while preserving chitosan's biological properties. Anticancer medications incorporated into chitosan nanoparticles to target malignant tumors have been supported by data that increases the medication's anticancer efficacy, lowers its toxicity, and extends its duration of action [19]. Chitosan nanoparticles are a promising technique for gene delivery because they are non-toxic, biodegradable, and simple to build DNA or protein complexes with [20]

## **1.9. Regeneration of Nerves**

The nerves not connected to the brain or spinal cord are known as peripheral nerves. Injuries in these nerves may develop problems with motor and sensory abilities. Nerve injury can be treated with biomaterials that contain chitosan as the primary polymer. The pertinent mechanism is displayed. [20] Talk about how chitosan may be used as a gene transfer tool. It has been proposed that the nanofibrous hydrogels in a mouse sciatic nerve defect model, electrospinning, and mechanical stretching can be used to prepare the sciatic nerve for healing; this can induce the production of neurotrophic silver secretion, Schwann cell proliferation, and brain-derived neurotrophic factor. [21]. Furthermore, anomalies of the sciatic nerve in rats were treated using chitosan nerve guides longitudinally reinforced with chitosan membranes. An autologous nerve graft anastomosis was the outcome [22].

## **1.10. Regeneration of Tendons**

The tendon is among the crucial elements in charge of preserving the range of motion in the body's many joints. Permanent limitation of movement can result from a traumatic tendon rupture. Furthermore, in addition to alginate gel, a unique naturally occurring biological scaffold suitable for tendon restoration in the outer layer, with poly (L-lactic acid) nanofibers modeling the tendon structure may both encourage the regeneration of the damaged flexor tendons and inhibit tendon adhesion. Rat tendon stem/progenitor cells have been encased in asymmetric chitosan scaffolds to stimulate tendon regeneration [23]. The electrostatic spinning procedure produces a polycaprolactone/chitosan nanofiber biocomposite that can assist in the repair of tendons and ligaments and encourage human osteoblast adhesion and proliferation [24]. Patients suffering from torn tendons may benefit from using biomaterials that promote tendon healing and reduce adhesion around tendons by utilizing chitosan and its derivatives.

## **Conclusion**

Based on the data presented in the review above, it is simple to determine that chitosan is a readily available, affordable, and naturally occurring supply. Chitosan has several uses in the pharmaceutical, food, biological, and clinical domains. Therefore, proper preparation techniques and conjugates will produce the required results. The best topic to explore is chitosan, a popular subject for many scholars. When chitosan and traditional excipients are evaluated for a particular purpose, it is observed that the chitosan has better qualities than the traditional one. Moreover, chitosan is extensively employed in various delivery methods, such as controlled medication delivery systems that produce an extended hormone release effect. Additionally, it is utilized in nasal and oral drug delivery systems.

## **References**

1. Peppas NA, Thomas JB, McGinty J. Molecular aspects of mucoadhesive carrier development for drug delivery and improved absorption. *Journal of Biomaterials Science, Polymer Edition*. 2009 Jan 1;20(1):1-20.
2. Grenha A, Al-Qadi S, Seijo B, Remuñán-López C. The potential of chitosan for pulmonary drug delivery. *Journal of Drug Delivery Science and Technology*. 2010 Jan 1;20(1):33-43.

3. Qin Y, Xing R, Liu S, Li K, Meng X, Li R, Cui J, Li B, Li P. Novel thiosemicarbazone chitosan derivatives: Preparation, characterization, and antifungal activity. *Carbohydrate Polymers*. 2012 Mar 1;87(4):2664-70.
4. Singh AV. Biopolymers in drug delivery: a review. *Pharmacologyonline*. 2011;1:666-74.
5. Moradi S, Hamed H, Tonelli AE, King MW. Chitosan/graphene oxide composite films and their biomedical and drug delivery applications: A review. *Applied Sciences*. 2021 Aug 24;11(17):7776.
6. Hassan MA, Tamer TM, Valachová K, Omer AM, El-Shafeey M, Eldin MS, Šoltés L. Antioxidant and antibacterial polyelectrolyte wound dressing based on chitosan/hyaluronan/phosphatidylcholine dihydroquercetin. *International Journal of Biological Macromolecules*. 2021 Jan 1;166:18-31.
7. Feng P, Luo Y, Ke C, Qiu H, Wang W, Zhu Y, Hou R, Xu L, Wu S. Chitosan-based functional materials for skin wound repair: Mechanisms and applications. *Frontiers in Bioengineering and Biotechnology*. 2021 Feb 18;9:650598.
8. Vivcharenko V, Benko A, Palka K, Wojcik M, Przekora A. Elastic and biodegradable chitosan/agarose film revealing slightly acidic pH for potential applications in regenerative medicine as artificial skin graft. *International Journal of Biological Macromolecules*. 2020 Dec 1;164:172-83.
9. Vishu Kumar AB, Varadaraj MC, Gowda LR, Tharanathan RN. Characterization of chito-oligosaccharides prepared by chitosan analysis with the aid of papain and Pronase, and their bactericidal action against *Bacillus cereus* and *Escherichia coli*. *Biochemical Journal*. 2005 Oct 15;391(2):167-75.
10. Venugopal V. *Marine polysaccharides: Food applications*. CRC press; 2016 Apr 19.
11. Tsai GJ, Su WH. Antibacterial activity of shrimp chitosan against *Escherichia coli*. *Journal of food protection*. 1999 Mar 1;62(3):239-43.
12. Raafat D, Von Bargen K, Haas A, Sahl HG. Insights into the mode of action of chitosan as an antibacterial compound. *Applied and environmental microbiology*. 2008 Jun 15;74(12):3764-73.
13. Kumar MN. A review of chitin and chitosan applications. *Reactive and functional polymers*. 2000 Nov 1;46(1):1-27.
14. Dash M, Chiellini F, Ottenbrite RM, Chiellini E. Chitosan—A versatile semi-synthetic polymer in biomedical applications. *Progress in polymer science*. 2011 Aug 1;36(8):981-1014.
15. Gavhane YN, Gurav AS, Yadav AV. Chitosan and its applications: a review of literature. *Int. J. Res. Pharm. Biomed. Sci*. 2013;4(1):312-31.
16. Radhakumary C, Antonty M, Sreenivasan K. Drug loaded thermoresponsive and cytocompatible chitosan based hydrogel as a potential wound dressing. *Carbohydrate polymers*. 2011 Jan 10;83(2):705-13.
17. Verlee A, Mincke S, Stevens CV. Recent developments in antibacterial and antifungal chitosan and its derivatives. *Carbohydrate polymers*. 2017 May 15;164:268-83.
18. R Kamath P, Sunil D. Nano-chitosan particles in anticancer drug delivery: an up-to-date review. *Mini reviews in medicinal chemistry*. 2017 Oct 1;17(15):1457-87.
19. Rizeq BR, Younes NN, Rasool K, Nasrallah GK. Synthesis, bioapplications, and toxicity evaluation of chitosan-based nanoparticles. *International journal of molecular sciences*. 2019 Nov 16;20(22):5776.
20. Bowman K, Leong KW. Chitosan nanoparticles for oral drug and gene delivery. *International journal of nanomedicine*. 2006 Dec 1;1(2):117-28.
21. Rao F, Wang Y, Zhang D, Lu C, Cao Z, Sui J, Wu M, Zhang Y, Pi W, Wang B, Kou Y. Aligned chitosan nanofiber hydrogel grafted with peptides mimicking bioactive brain-derived neurotrophic factor and vascular endothelial growth factor repair long-distance sciatic nerve defects in rats. *Theranostics*. 2020;10(4):1590.

22. Meyer C, Stenberg L, Gonzalez-Perez F, Wrobel S, Ronchi G, Udina E, Suganuma S, Geuna S, Navarro X, Dahlin LB, Grothe C. Chitosan-film enhanced chitosan nerve guides for long-distance regeneration of peripheral nerves. *Biomaterials*. 2016 Jan 1;76:33-51.
23. Chen TY, Wen TK, Dai NT, Hsu SH. Cryogel/hydrogel biomaterials and acupuncture combined to promote diabetic skin wound healing through immunomodulation. *Biomaterials*. 2021 Feb 1;269:120608.
24. Wu X, Farooq MA, Li T, Geng T, Kutoka PT, Wang B. Cationic chitosan-modified silica nanoparticles for oral delivery of protein vaccine. *Journal of Biomedical Materials Research Part A*. 2021 Nov;109(11):2111-9.