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Medical, Pharmaceutical, and Biomedical Applications of Chitosan: A Review

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Abstract

Chitosan is a biopolymer chitin derivative discovered in 1811 by Henri Braconnot, and it was first used in 1985 by Charles Rouget. It is produced via the deacetylation of chitin (the natural component of the arthropods exoskeletons and the fungal cell wall). The unique solubility and the chemical and biological characterization of chitosan attracted more scientific and industrial attention, specifically in the past 20 years. Its properties depend on the degree of deacetylation and its molecular weight. Therefore, recently, different forms of chitosan (solutions, suspension, gels/hydrogels, sponges, microparticles/nanoparticles, membranes and films, fibers/nanofibers) and its derivatives have been used in many fields. It has a wide range of applications in various fields, such as medicine, industry, agriculture, and commercial research. Medicinally, because of its biocompatibility, biodegradability, nontoxicity, natural origin, and similarity with human macromolecules, chitosan is widely used in pharmaceutical applications, antimicrobial applications, gene delivery, gene therapy, wound healing and burns, regenerative medicine, tissue engineering, cancer applications, dermatology, ophthalmology, dentistry, biosensors, as well as bioimaging, support for immobilized enzymes, and veterinary medicine. In this review, some medicinal applications of chitosan will be highlighted.

Keywords: Application of chitosan, benefit of chitosan, biomedical, chitosan, pharmaceutical

Introduction

Over the past 30 years, in the vital material field, great scientific attention has been directed toward natural functional polymers, and these have been used as an alternative to the synthetic polymers that are unsafe to the environment. Structurally, vital polymers are similar to the biological macromolecules; this facilitates them to be recognizable and decomposed to the nontoxic remnants by the bioenvironment. Chitosan and its derivatives are bioactive polymers that received big attention not only in the biomedical field but also in numerous fields such as agriculture, biotechnology, cosmetics, medicine, pharmacy, and food industry.[1-6] Chitosan is a functional polysaccharide polymer that originated from a natural source (chitin), a component of the cell wall and the exoskeleton of fungi and crustaceans. It is characterized by a random distribution of deacetylated and acetylated units (β-[1–4]-linked D-glucosamine and N-acetyl-D-glucosamine).[7] Its commercial production involves the deacetylation of chitin, which can vary from 70% to 95%, and its properties are influenced by the degree of deacetylation and molecular weight.[8] Chitin and chitosan are similar to the cellulose structure; however, commercially, they have received more attention than synthetic cellulose because of a high content of nitrogen percentage (nearly 6.89%) compared with synthetic cellulose[9] [Figure 1]. Moreover, chitosan's physical and chemical properties, biodegradability, biocompatibility, and functional group properties facilitate it to be used in different forms; also, its nontoxicity is another reason for it to attract more researchers' attention in various fields.[1,7,10-12]

There are several advantages of using biopolymer chitosan as an alternative natural polymer to synthetic polymers. First of all, chitosan extraction from a crustacean's

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exoskeleton is useful in recycling food waste, which is considered convenient economically because it is not an expensive resource.[1,7] Second, its commercial production benefits in promoting human health because it allows the regaining of different nutritional material such as proteins, pigments, and nutraceuticals.[6,7,13] The third advantage of using chitosan as an alternative polymer is that it provides a good source of nitrogen and therefore it is effectively used as a chelating and complexing factor.[7]

In conclusion, chitosan is a good alternative biopolymer to synthetic polymers such as cellulose. It has unique properties that facilitate it to be used in different fields. This review will summarize and highlight some medicinal applications of this important biopolymer.

Medical Chitosan's Applications

Generally, the usage of chitosan in medical and biomedical fields can be summarized in pharmaceutical applications, as described later, and in biomedical applications.

Pharmaceutical usage

The usage of chitosan and its derivatives in the pharmaceutical applications was started in the late 1980s.[7,14-16] These compounds were mainly used as excipients in drug formulations and in drug delivery systems.[17] The advantages and important properties of using chitosan were thoroughly reviewed.[18] The main characteristics of chitosan facilitate and expand its usage in the pharmaceutical industry, for example, (a) it is able to control drug and protein release such as anti-inflammatory naproxen; therefore, it is used in drug delivery as well as in vaccines and genes; (b) it shows mucoadhesive activity and enhancing absorbant ability, which facilitate it to be used in buccal delivery; (c) it is able to enhance transfection; (d) it can increase the permeation ability; (e) it works as a gelling agent; and (f) it is able to inhibit an efflux pump.[7,18] Moreover, the possibility of chitosan being available in different forms and derivatives, and the variability of their taken route contributed to the expansion of application and the decrease of toxicity. For example, solutions or tablets or capsules form can be taken orally, vaginally, ocularly, and nasally.[19] Over the past 20 years, chitosan has been used orally as a safe excipient.[15,16,20] Also, compared with commercial products, tablets represent the sustainable release of the drug. Tablets form is the most favorable because of several reasons, such as the accuracy of their dose, facility of their manufacturing and handling, and their favorability by patients.[18] Moreover, lately, considerable attention has been directed toward the preparation of chitosan as an injected form. Further, chitosan properties contribute to the development of vaccine delivery.[18] Chitosan also plays an important role in delivering polar drugs orally and nasally, the administration of peptide proteins, and vaccine delivery because of its transmucosal absorption.[7,21] Also, chitosan is used as a film form in tissue engineering and wound care dressing because of its adhesion property.[21,22] In fact, the applications of chitosan and its derivatives in different forms were expanded to involve biomedical applications also.

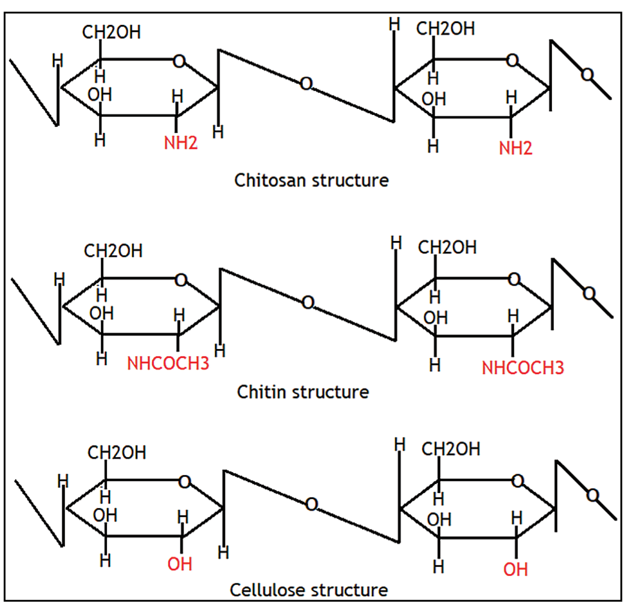

Figure 1: Differences between chitosan, chitin, and cellulose structure

Biomedical applications

The biomedical application of chitosan involves the engineering of tissue and the healing of wound and gene therapy. In wound healing, chitosan helps in preventing the infection as it has antibacterial and antifungal properties. The positive charge of chitosan's molecule enables it to bind with the microbial cell wall, which brings a negative charge and disrupts the cell membrane function. Therefore, intracellular components leak and the nutrients' transport into the cell is inhibited.[9,23-25] This ability explains chitosan's antimicrobial activity against a wide range of bacteria and fungi. Another suggestion for the antimicrobial activity of chitosan is its ability to penetrate the nuclei and interfere with DNA, mRNA, and protein synthesis, eventually suppressing microbial growth. Further, chitosan's biocompatible properties and its ability to aid in pharmaceutical delivery help in the prevention of inflammation and irritation.[7,26] Therefore, chitosan is widely used in preparing various wound dressings and it exhibits long antibacterial activity.[9] Moreover, chitosan helps in accelerating the healing of wounds and the regeneration of the dermis because of its stimulation activity to the cells.[7] In addition, chitosan's structure facilitates the transporting of oxygen and nutrients as well as its adhesion properties, thereby reducing scaring. Therefore, it is used in tissue engineering.[7,27,28] Many chitosan derivatives are used as emerging products in tissue engineering of the bone .[28,29]

In addition to antimicrobial activity and biocompatibility, chitosan has the ability to protonate and form a complex with DNA in acidic medium.[30] Therefore, it is used widely in gene therapy to treat a variety of diseases.[27,30-33] Compared with the commonly used system, chitosan–DNA complex is prepared easily and more effectively; also, it can be transfected in a variety of cells, such as embryonic cells of the human kidney, cancer cervical cells, and fibroblast cells.[31]

Finally, there are several extensive medical applications of chitosan. One of them is using chitosan as an anticoagulant. The interference of the chitosan derivative (sulfated chitosan) with blood clots and the lack of antiplatelet activity facilitate the use of chitosan as an anticoagulant agent. Consequently, no more bleeding occurs in patients as with heparin usage.[31] Another application involves treating chronic vaginal diseases through the preparation of vaginal tablets.[18] However, this application could have a negative impact because of the antimicrobial activity of chitosan, which could affect the normal flora in the vagina.[34] An additional application involves using modified particles of chitosan in bioimaging.[20,27]

In conclusion, polysaccharide biopolymer chitosan has a unique chemical structure and properties that subject it and its derivatives to several pharmaceutical and biomedical applications, such as pharmaceutical formulations, drug delivery, wound healing, engineering of tissue, antimicrobial agents, gene therapy, and bioimaging.

Conclusion

The first biopolymer polysaccharide that was identified by humans is chitin, and it was found about thirty years before cellulose. The product of chitin's deacetylation is called chitosan, and it is the most attractive biopolymer that is of scientific interest in different fields. There are major reasons behind the interest and attraction of scientists. One of them is the big similarity between chitosan molecules and biological macromolecules. In addition, the uniqueness of its biological properties as well as the availability of different forms of chitosan and it modification possibility open new scientific horizons in various fields. This review focused on the usage of chitosan in medical science, particularly pharmaceutical and biomedical applications, because they have direct contact with human health. Therefore, mention is made of the various pharmaceutical and biomedical benefits of chitosan based on its different biological properties.

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Conflicts of interest
There are no conflicts of interest.

References

1. Crini G, Badot PM, Guibal E, editors. Chitine et chitosane—du biopolymère à l'application. Besançon: PUFC; 2009. p. 303.
2. Kim SK, editor. Chitin, Chitosan, Oligosaccharides and Their Derivatives: Biological Activities and Applications. Boca Raton: CRC Press/Taylor & Francis Group LLC; 2011. p. 666.
3. Miranda Castro SP, Lizárraga Paulín EG. Chapter 1: Is chitosan a new panacea? Areas of application. In: Karunaratne DN, editor. The Complex World of Polysaccharides. Rijeka, Croatia: InTech; 2012. p. 3-45.
4. Kim SK, editor. Chitin and Chitosan Derivatives. Advances in Drug Discovery and Developments. Boca Raton: CRC Press/Taylor & Francis Group LLC; 2014. p. 511.
5. Dima JB, Sequeiros C, Zaritzky N. Chapter 3: Chitosan from marine crustaceans: Production, characterization and applications. In: Shalaby EA, editor. Biological Activities and Application of Marine Polysaccharides. Rijeka, Croatia: InTech; 2017. p. 39-56.
6. Philibert T, Lee BH, Fabien N. Current status and new perspectives on chitin and chitosan as functional biopolymers. Appl Biochem Biotechnol 2017;181:1314-37.
7. Morin-Crini N, Lichtfouse E, Torri G, Crini G. Fundamentals and applications of chitosan. In: Crini G, Lichtfouse E, editors. Sustainable Agriculture Reviews 35. Chitin and Chitosan: History, Fundamentals and Innovations, vol. 35. Cham: Springer International Publishing AG; 2019, pp. 338.
8. Ruel-Gariépy E, Leroux J. Chitosan: A Natural Polycation with Multiple Applications. Washington, DC: American Chemical Society; 2006. p. 243-59.
9. Ramya R, Venkatesan J, Kim SK, Sudha PN. Biomedical applications of chitosan: An overview. J Biomater Tissue Eng 2012;2:100-11.
10. Rinaudo M. Chitin and chitosan: Properties and applications. Prog Polym Sci 2006;31:603-32.
11. Kurita K. Chitin and chitosan: Functional biopolymers from marine crustaceans. Mar Biotechnol 2006;8:203-26.
12. Crini G. Recent developments in polysaccharide-based materials used as adsorbents in wastewater treatment. Prog Polym Sci 2005;30:38-70.
13. Dave D, Routray W. Current scenario of Canadian fishery and corresponding underutilized species and fisheries byproducts: A potential source of omega-3 fatty acids. J Cleaner Product 2018;180:617-41.
14. Nagai T, Sawayanagi Y, Nambu N. Application of chitin and chitosan pharmaceutical preparations. In: Zikakis JP, editor. Chitin, Chitosan, and Related Enzymes, Part I. Orlando: Academic; 1984. p. 21-40.
15. Felt O, Buri P, Gurny R. Chitosan: A unique polysaccharide for drug delivery. Drug Dev Ind Pharm 1998;24:979-93.
16. Kumar MN, Muzzarelli RA, Muzzarelli C, Sashiwa H, Domb AJ. Chitosan chemistry and pharmaceutical perspectives. Chem Rev 2004;104:6017-84.
17. Badwan AA, Rashid I, Omari MM, Darras FH. Chitin and chitosan as direct compression excipients in pharmaceutical applications. Mar Drugs 2015;13:1519-47.
18. Bernkop-Schnürch A, Dünnhaupt S. Chitosan-based drug delivery. Eur J Pharm Biopharm 2012;81:463-9.
19. Ali A, Ahmed S. A review on chitosan and its nanocomposites in drug delivery. Int J Biol Macromol 2018;109:273-86.
20. Ravi Kumar MNV. A review of chitin and chitosan applications. React Funct Polym 2000;46:1-27.
21. Illum L, Davis SBS. Chapter 27: Chitosan as delivery system for the transmucosal administration of drugs. In: Dumitriu S, editor. Polysaccharides. Structural Diversity and Functional Versatility. New York: Marcel Dekker; 2004. p. 643-65.
22. Kato Y, Onishi H, Machida Y. Application of chitin and chitosan derivatives in the pharmaceutical field. Curr Pharm Biotechnol 2003;4:303-9.
23. Chen Y, Chou C. Factors affecting the susceptibility of *Staphylococcus aureus* CCRC 12657 to water soluble lactose chitosan derivative. Food Microbiol 2005;22:29.
24. Roller S, Covill N. The antimicrobial properties of chitosan in mayonnaise and mayonnaise-based shrimp salads. J Food Prot 2000;63:202-9.
25. Sudarshan N, Hoover D, Knorr D. Antibacterial action of chitosan. Food Biotechnol 1992;6:257.

26. Lorenzo-Lamosa ML, Remuñán-López C, Vila-Jato JL, Alonso MJ. Design of microencapsulated chitosan microspheres for colonic drug delivery. J Control Release 1998;52:109-18.
27. Dash M, Chiellini F, Ottenbrite RM, Chiellini E. Chitosan—A versatile semi-synthetic polymer in biomedical applications. Prog Polym Sci 2011;36:981-1014.
28. Ahmed S, Annu, Ali A, Sheikh J. A review on chitosan centred scaffolds and their applications in tissue engineering. Int J Biol Macromol 2018;116:849-62.
29. Logith Kumar R, Keshav Narayan A, Dhivya S, Chawla A, Saravanan S, Selvamurugan N. A review of chitosan and its derivatives in bone tissue engineering. Carbohydr Polym 2016;151:172-88.
30. Choi C, Nam JP, Nah JW. Application of chitosan and chitosan derivatives as biomaterials. J Ind Eng Chem 2016;33:1-10.
31. Badawy MEI, Rabea EI. Chapter 1: Chitosan and its modifications as biologically active compounds in different applications. In: Masuell M, Renard D, editors. Advances in Physicochemical Properties of Biopolymers. Sharjah: Bentham e-Books. Bentham Science Publishers; 2017. p. 1-108.
32. Kedjarune-Leggat U, Leggat PA. Chapter 18: Chitosan and its modification: Are they possible vehicles for gene therapy? In: Xubo Y, editor. Non-viral Gene Therapy. Rijeka, Croatia: InTech Publisher; 2011. p. 439-54.
33. Lee KY. Chitosan and its derivatives for gene delivery. Macromol Res 2007;15:195-201.
34. Raafat D, Sahl HG. Chitosan and its antimicrobial potential—A critical literature survey. Microbiol Biotechnol 2009;2: 186-201.