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Chitosan: A Comprehensive Review of Structural Properties, Biological Activities, and Multidisciplinary Applications

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Abstract

Chitin deacetylation yields chitosan, a biopolymer gathered from different natural origins like animals and marine organisms. Chitosan quality is influenced by factors such as molecular weight, crystallinity, and degree of deacetylation, as well as purity parameters like ash content, protein content, and color. These inherent characteristics lead to biocompatibility, bio-adhesiveness, solubility, and its polycationic nature, making it suitable for a wide range of physical or chemical modifications. Despite its advantages, chitosan faces challenges such as seasonal and geographical availability, time-consuming extraction processes, and variability in quality due to different extraction methods. Technological advancements, such as genetic modification, hold promise for improving chitosan yield and expanding its applications. This review delves into the structure and properties of chitosan, exploring its extraction methods and emphasizing its diverse applications, including wound dressings, drug delivery systems, antimicrobial agents, wastewater treatment, and beyond. Finally, the discussion concludes with key challenges and future perspectives for chitosan research.

Keywords: Chitosan, Biological Properties, Applications.

Introduction

Chitosan is a biopolymer recovered from the exoskeletons of arthropods, cell walls of fungi, and other sources where chitin is abundantly present. It acts as a basis for many biological and industrial applications due to its unique characteristics, such as non-toxicity, antioxidative nature, biocompatibility, biodegradability, and renewability (1). Chitin, the precursor to chitosan, is the second most abundant biopolymer after cellulose, highlighting its wide occurrence in nature and potential use in various fields (2).

Chitosan which is a polysaccharide derived through deacetylation of chitin has various uses across several industries (3). Because of its non-toxicity, antioxidative nature, biocompatibility, biodegradability, and renewability (4), this substance finds use in several domains, including wound treatment (5), food science (6), agriculture (7), cosmetics (8), biotechnology (9), chelating agent (10), pharmaceutical and biomaterial purposes (11).

Chemical and biological methods can be used to extract chitosan from exoskeleton (12). Crabs (13), shrimp (14), desert locusts, honey bees (15, 16), beetles (17), crayfish, corals (18), fungi (19), and cockroaches (20, 21) could be exploited for the commercial production of chitosan. The importance of chitosan and its derivatives spans a broad spectrum, from environmental sustainability to potential health benefits, making a chitosan review not just relevant but essential for understanding its multifaceted role (22).

This review aims to provide a comprehensive overview of chitosan's chemical structure, sources, and benefits, focusing on its biodegradability, biocompatibility, and environmental impact. By understanding the biodegradability, biocompatibility, and environmental impact of chitosan, alongside its industrial and biomedical applications, readers will gain comprehensive insights into why natural chitosan's and chitosan products are increasingly becoming a focus of scientific and commercial interest.

Historical background

The discovery and development of chitosan can be traced back over two centuries, marked by significant milestones that have shaped its current applications. The journey began in 1799 when Hatchett used mineral acids to decalcify shells of crabs, crayfish, lobsters, and prawns, observing the formation of a soft, plastic material. This laid the groundwork for future research into chitin and subsequently chitosan (23).

Early discoveries and nomenclature

The early discoveries of chitosan date back to 1799 when Hatchett first observed the formation of a unique material through the decalcification of crab shells using mineral acids. This discovery laid the foundation for further research into chitin and chitosan. In 1811, Braconnot identified chitin in fungi and coined the term "chitin." Later, in 1823, Odier isolated a hornlike material from cockchafer elytra treated with potassium hydroxide, further solidifying the understanding of chitin's structure and properties (23). In 1859-1894, Rouget manipulated chitin through chemical and temperature treatments to become soluble, leading to the naming of "chitosan" by Hoppe-Seyler (24).

Developmental phases of chitin and chitosan

The evolution of chitin into chitosan encompasses five distinct phases, each contributing uniquely to its understanding and utility:

1799-1894: Discovery phase initiated by Hatchett and expanded by subsequent researchers (25).

1894-1930: A period of confusion and controversy, where the properties and structure of chitin were debated (25).

1930-1950: Exploration phase, where the potential applications of chitin and chitosan began to be realized (25).

1950-1970: Doubt phase, characterized by skepticism over the practical uses of chitosan (25).

Post-1970: Application phase, seeing a surge in commercial and biomedical uses of chitosan (25).

Advancements and Modern Applications

Chitosan's journey from a curious derivative to a widely used biopolymer is marked by significant research milestones:

1950s: The structure of chitosan was further understood through x-ray analysis (24).

1960s: Studies revealed chitosan's potential as a hemostatic agent due to its ability to bind with red blood cells (26).

Recent decades: Chitosan has been popularized as a dietary supplement in Japan and Europe, and its production involves a series of chemical reactions starting from chitin, highlighting its versatility and the expanding scope of its applications (26).

This historical perspective not only highlights the scientific milestones that have defined the development of chitosan but also underscores its evolving role across various sectors, driven by its unique properties and potential for innovation.

Major sources, chemical structure, and properties

Chitosan, a biopolymer derived from chitin, is primarily recovered from the exoskeletons of arthropods such as crabs and shrimp, as well as from fungal cell walls. Recent studies have highlighted its abundance in marine sources, with an estimated global production of chitin exceeding 10^{11} tons annually (22). Chitosan consists of copolymers of D-glucosamine and N-acetyl-D-glucosamine linked by β-(1-4) glycosidic bonds (27) (Figure 1). Its structure resembles cellulose, but the key distinction is the amino group at the C-2 position, giving chitosan a positive ionic charge (2). This positive charge enables chitosan to bind with negatively charged molecules, which is crucial for many of its applications (2).

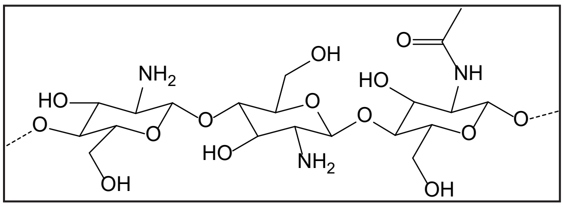

Figure 1. Structure of chitosan.

Key structural characteristics and modifications

Solubility and molecular weight

Chitosan's solubility is highly dependent on its degree of deacetylation (DD) and molecular weight (MW). Studies have shown that chitosan with a DD greater than 50% is soluble in acidic solutions (pH<6.5), while lower DD values result in reduced solubility (27). Additionally, chitosan oligomers with lower MW exhibit enhanced solubility across a broader pH range, making them suitable for various biomedical applications (28).

Degree of deacetylation (DD)

The DD significantly influences physicochemical properties of chitosan such as solubility and charge density. The degree of acetylation affects not only the solubility but also the biodegradability and biocompatibility of chitosan, making it suitable for various biomedical applications (2). Several techniques have been developed to measure the amount of DD found in insect chitosan and chitin. Infrared spectroscopy, UV spectroscopy, near-infrared spectroscopy, potentiometric titration, and magnetic resonance are a few of the analytical methods used to determine DD (29). Among them, the FT-IR, the conductometric, the acid-base, and the potentiometric titration methods are useful for completely soluble compounds.

Viscosity

Viscosity is a key factor in discovering the industrial usability of chitosan, with its dependency on the degree of deacetylation and the molecular weight of the compound. Viscosity increases with higher deacetylation levels and lower molecular weights. Additionally, it can vary based on the particle size and storage duration of chitosan (30). Temperature and concentration factors can affect the viscosity of chitosan solutions. The viscosity increases with decreasing temperature and increasing chitosan content. Due to depolymerization, the chitosan viscosity decreases with increasing demineralization time. The intrinsic viscosity of chitosan can be affected by physical factors (ultrasonic, milling, autoclaving, heating) and chemical (ozone) processes. Chitosan concentrated solutions with various levels of deacetylation differ in their viscosity and flow characteristics (31).

Crystallinity

One of the most important physical properties that determine the functionality of chitosan is its crystallinity. In the solid state, chitosan molecules often self-assemble into highly ordered crystallites within large amorphous domains. There are two primary crystal polymorphs of chitosan (32). The most prevalent polymorph is the hydrated "tendon chitosan" form, while the anhydrous crystal form is known as the "tempered polymorph". Both polymorphs consist of two antiparallel chitosan molecules in a double helix shape held together by hydrogen bonds to form the crystal cell. The inclusion of water molecules between these crystal cells stabilizes the structure via multiple hydrogen bonds, leading to distinctions between the polymorphs (33). X-ray diffraction (XRD) is used to measure the crystallinity of chitosan, which detects and analyzes the pattern created by X-ray diffraction through a dense atomic lattice in a crystal. One useful technique for visually verifying the shape and physical condition of the chitin surface is scanning electron microscopy. The surface shape of chitosan varies depending on the source species (20). Commercial chitosan not exhibited an apparent microfibrillar structure and has spherical in shape as indicated by the scanning electron micrograph (Figure 2).

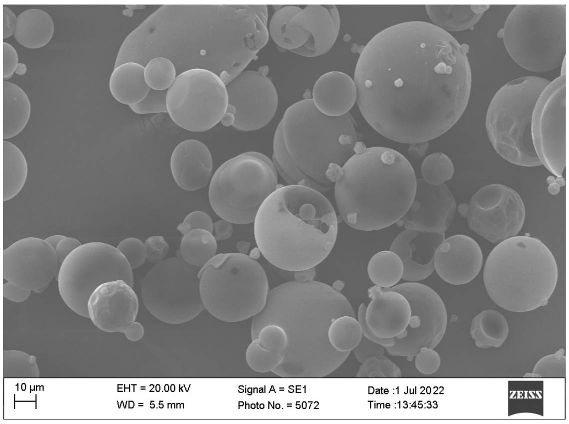

Figure 2. Scanning electron micrograph of commercial chitosan (20).

Chemical modifications

Chitosan, a versatile biopolymer, undergoes various chemical modifications to enhance its solubility, functionality, and application potential. These modifications include acylation, alkylation, carboxylation, and quaternization, each introducing specific functional groups that improve chitosan's water solubility and biological compatibility (28). For instance, acylation and carboxylation significantly enhance chitosan's solubility in water (34), while alkylation introduces properties beneficial for medical applications such as coagulation and antibacterial effects. Furthermore, quaternary ammonium chitosan exhibits superior antibacterial, biocompatibility, and biodegradability characteristics (35).

Unique properties and environmental benefits

Non-toxic nature

Chitosan is inherently non-toxic, making it safe for a wide range of applications, from pharmaceuticals to food packaging (2).

Biodegradability

As a biodegradable material, chitosan breaks down into natural substances, reducing environmental pollution and supporting sustainable material cycles (2).

Adsorption capabilities

Its excellent adsorption properties enable the removal of contaminants like heavy metals and dyes from wastewater, contributing to cleaner and safer water sources (2).

Chitosan's role extends beyond biocompatibility to its significant environmental impact. Chitosan is the second most abundant biopolymer after cellulose. This abundance ensures a sustainable supply of raw materials for producing chitosan, which is crucial for its widespread application in environmentally sensitive areas (22). The biopolymer's ability to degrade naturally complements its applications in reducing pollution, particularly in agricultural and food industries where its use can lead to less reliance on synthetic materials (22).

Major sources

Among the various sources available for chitosan production (Figure 3), shrimp is one of the most promising and much discussed, and many other species, such as beetles and insects, have also been used (36). Insects have emerged as a viable alternative supply of chitosan; nevertheless, this development has only occurred in recent times, and studies have only been conducted on a laboratory scale. Mollusks provide an additional source of chitosan. The use of species such as Sepia kobiensis, Sepia spp, Loligo lessoniana, and Loligo formosana has been seen in this regard. Compared to crustaceans, fungi are a source of chitosan and chitin that is not seasonal and not influenced by geographical factors. Chitin extraction from this source requires less use of chemicals, as there is usually no need for mineral removal and discoloration. In fungal chitin and chitosan, there are generally no heavy metal contaminants or allergenic proteins that can be found in marine sources (37).

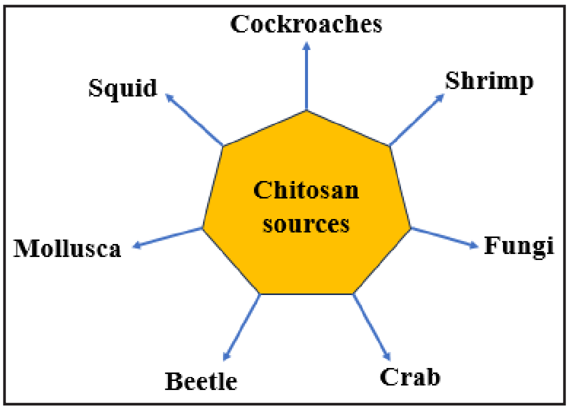

Figure 3. The most important sources of chitosan.

Industrial extraction and yield factors

The extraction of chitosan from chitin involves a deacetylation process using strong alkalis such as sodium hydroxide (NaOH), which is a critical step in determining the quality and yield of chitosan (2) (Figure 4). For instance, a study by Pacheco et al., demonstrated that treating chitin with 40% NaOH at 90°C for 4 hours resulted in chitosan with a DD of 85% (12). Alternative methods, such as enzymatic deacetylation using chitin deacetylase, have also been explored to achieve higher purity and controlled DD values (19). Factors such as temperature, alkali concentration, and reaction duration play significant roles in influencing the molecular weight and degree of deacetylation, thereby affecting the yield and purity of chitosan. The source of chitin, whether from animals, marine crustaceans or fungal biomass, along with the extraction method, impacts the final yield and quality of chitosan. Notably, solid-state fermentation of fungal biomass has been shown to produce higher yields of chitosan compared to submerged fermentation (2). Chemical and biological methods used to extract chitosan from exoskeleton of different sources are illustrated in Figure 3.

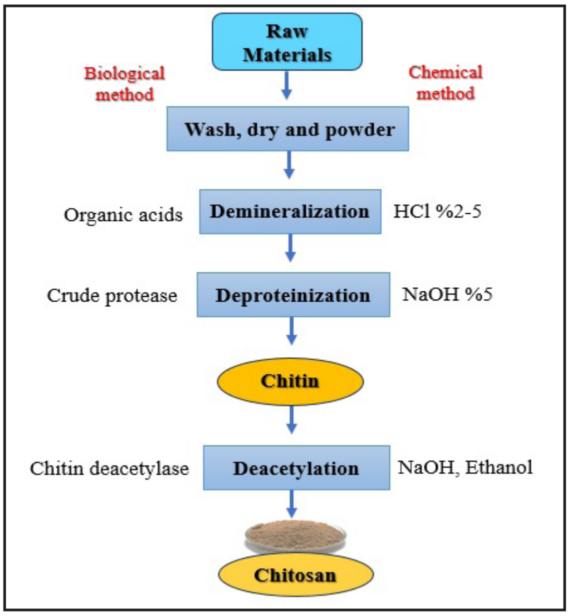

Figure 4. Scheme for the steps of chitosan preparation from raw materials (2) (Modified).

Applications of chitosan
Application in environmental fields

Chitosan's role in environmental management is particularly significant in water purification and waste treatment processes. It is employed in the development of water filtration membranes, where its ability to remove metal ions and heavy metals from industrial effluents is highly valued (38). Additionally, chitosan-based nanocomposites are increasingly favored for their efficacy in eliminating hazardous contaminants like dyes and other pollutants during the water purification process (38). These capabilities not only enhance water quality but also support sustainable industrial practices.

Water and wastewater treatment

Chitosan's excellent adsorption capabilities allow it to remove harmful contaminants such as heavy metals, dyes, and pharmaceuticals from water, making it an invaluable component in water purification systems (39).

Biodegradable packaging

Chitosan-based films offer a sustainable alternative to conventional plastic packaging. These films degrade more rapidly in soil environments compared to commercial starch-based films, thereby reducing environmental pollution and aiding in waste management (40).

Greenhouse gas absorption

Chitosan contributes to sustainable development by absorbing greenhouse gases. This capability, coupled with its potential to adsorb heavy ions and organic matter, positions chitosan as a beneficial material in efforts to combat environmental pollution and climate change (41).

Application in biomedical fields

Chitosan's utility in the biomedical field is vast and varied, driven by its unique properties that include biodegradability, biocompatibility, and antimicrobial activity. Its applications span across drug delivery, tissue engineering, wound healing, and more, making it a critical material in modern medicine (39, 42).

Drug delivery and tissue engineering

Chitosan is extensively used in drug delivery systems due to its ability to protect drug molecules from the acidic environment of the stomach, facilitating targeted drug release. This property is crucial for administering medications for gastrointestinal, neurological, and chronic systemic diseases. Chitosan-based materials are also used in developing scaffolds for tissue engineering, mimicking the natural extracellular matrix which supports the growth and regeneration of tissues (42).

The development of chitosan-based materials continues to push the boundaries in drug delivery and material science. Chitosan-coated nanoparticles, for example, are utilized as efficient bio-imaging agents and in delivering anti-tumor agents like Paclitaxel, demonstrating the polymer's versatility and efficacy in medical applications (1). Additionally, the design of chitosan-based biomimetic materials, which mimic natural structures like lotus flowers and honeycomb, highlights the innovative approaches in enhancing material properties for specific applications (43). These advancements underscore chitosan's role in driving technological and medical innovations, further solidifying its importance in scientific research and industry applications.

Wound healing

In the realm of wound care, chitosan's hemostatic and antibacterial properties expedite the healing process, making it an invaluable component in wound dressings and antimicrobial coatings. The biopolymer is also employed in dental and orthopedic implants due to its ability to promote bone regeneration and reduce infection rates (38, 44). Chitosan's ability to accelerate wound healing has made it a subject of significant research. This wound-healing property stems from chitosan-based materials' capacity to: mobilize polymorphonuclear cells and fibroblasts, cause cytokines, facilitate migration of giant cells, and stimulate the formation of type IV collagen. Additionally, chitosan's susceptibility to degradation by enzymes like lysozyme in the body results in chito-oligomers, which stimulate macrophages and further accelerate collagen deposition, ultimately speeding up wound healing (45). Commercially accessible wound dressings utilizing chitosan come in various forms, including non-wovens, hydrogels, films, and sponges (28, 46).

Biosensors and regenerative medicine

The development of chitosan-based biosensors illustrates the biopolymer's adaptability and effectiveness in medical diagnostics. These biosensors detect a wide array of substances, including glucose and cholesterol, essential for managing conditions like diabetes and cardiovascular diseases. Additionally, in regenerative medicine, chitosan is used to create innovative solutions such as bioimaging agents and cell encapsulation materials, which are fundamental in advanced therapeutic and diagnostic procedures (44).

Antimicrobial activity

Chitosan and its derivatives exhibit antibacterial activity against a wide range of microorganisms, such as bacteria, filamentous fungi, and yeast (47). The precise mechanism behind this antibacterial activity remains unclear. However, one offered mechanism suggests that chitosan disrupts cellular permeability, leading to leakage of intracellular components due to its interaction with the anionic components of the cell membrane, ultimately causing cell death. Another proposed mechanism involves chitosan penetrating the cell membrane and binding to DNA. This binding restrains DNA replication, ultimately leading to cell death (48). Several factors influence the antibacterial action of chitosan, including the degree of deacetylation, origin and level of polymerization, polymer viscosity, and particularly pH (49).

Chitosan has been suggested to operate on Gram-negative bacteria through two distinct mechanisms: chelation with divalent cations under acidic pH, diminishing membrane stability and nutrient uptake, and electrostatic interactions with lipopolysaccharides on the outer membrane, permitting chitosan to pass through the inner membrane and induce cell leakage (20, 50, 51). In contrast, the surface of Gram-positive bacteria is made up of peptidoglycans and teichoic acid, necessary for the function of various membrane-bound enzymes, ultimately leading to cell death (47, 52). The mechanism of chitosan's antifungal effect is similar to its antibacterial action and seems to be effective against fungi rich in polyunsaturated fatty acids (53).

Antioxidant activity

Chitosan and its derivatives exhibit potent antioxidant effects. They can reduce lipid oxidation by scavenging free radicals, due to their ability to bind metals. The antioxidant properties of chitosan and chitin are influenced by factors such as molecular weight, viscosity, and degree of deacetylation (DD). This free radical scavenging ability makes chitosan a potential therapeutic agent for oxidative stress and certain diseases (54).

Chitosan in nanomedicine

Chitosan nanoparticles hold significant promise in medical research as targeted delivery vehicles for drugs, adjuvants, and vaccines. They are particularly attractive as oral drug carriers for proteins because they can prevent enzymatic degradation in the gastrointestinal tract and facilitate muco-adhesion to the intestinal mucus layer (9, 55). This review highlights several applications of chitosan nanoparticles, including ocular-targeted drug delivery, delivery across the blood-brain barrier, targeted delivery of bioimaging markers, and vaccination by oral and intranasal application (56). Notably, a significant amount of research has been focused on chitosan nanoparticles in cancer medicine. These nanoparticles can encapsulate chemotherapeutic drugs, thereby reducing side effects, and can also increase the oral bioavailability of anti-cancer drugs (57).

Industrial and commercial applications

Chitosan's broad utility across various industries is underscored by its diverse applications ranging from agriculture to pharmaceuticals and environmental sustainability. Its role in enhancing agricultural practices is particularly noteworthy, where it is used in the pre- and post-harvest treatments such as coating seeds, fruits, and vegetables to preserve them and improve their resistance to diseases and pests. Additionally, chitosan-based coatings are instrumental in the slow and sustained release of encapsulated agrochemicals, optimizing their effectiveness and reducing environmental impact (39).

Chitosan contributes significantly to the agriculture and food sectors. It is used in creating biopolymeric films for food packaging, which are favored for their biodegradability and the reduction of pollution in comparison to conventional materials (26, 58). Additionally, chitosan's properties as a natural biocide make it effective as a preservative, enhancing the shelf life and safety of food products. In agriculture, chitosan is applied for its ability to enhance plant growth and yield, making it a valuable component in sustainable farming practices (26).

In the pharmaceutical sector, chitosan contributes significantly to the production of various forms such as tablets and capsules. Its unique properties also make it a preferred material for drug delivery systems, enhancing the efficacy of pharmaceutical products by protecting active ingredients and controlling their release within the body. Moreover, chitosan's biocompatibility and non-toxic nature have paved its way into the food industry, where it is utilized as a food additive, preservative, and packaging material, contributing to food safety and longevity (1).

The table below summarizes the key applications of chitosan across different industries:

Industry	Applications of Chitosan
Agriculture	Seed coating, plant growth regulation, controlled release fertilizers
Pharmaceuticals	Production of tablets and capsules, drug delivery systems
Food	Additives, preservatives, packaging materials
Cosmetics	Skincare and haircare products
Textile and Paper	Sizing, finishing, wastewater treatment
Energy	Dye-sensitized solar cells, wastewater treatment

These applications not only highlight chitosan's versatility but also its contribution to sustainable practices across various sectors (1, 27). The most significant properties and recent applications of chitosan are highlighted in Figure 5.

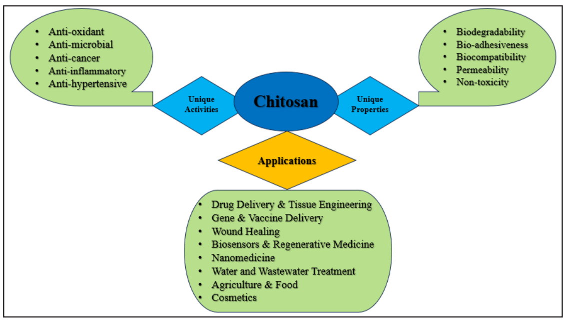

Figure 5. Unique Activities, Properties and Different applications of chitosan.

Recent advances in chitosan research

Technological enhancements and gene modification

Recent developments in chitosan research have focused on leveraging gene modification techniques to enhance the yield and functional properties of chitosan. This approach has opened new avenues for increasing the efficiency of chitosan production, which is crucial for its application across various industries. Technological advancements in genetic engineering provide a pathway to optimize the structural attributes of chitosan, thereby enhancing its solubility, biocompatibility, and overall effectiveness in industrial applications (2).

Breakthroughs in therapeutic applications and drug delivery

The potential of chitosan in therapeutic applications continues to grow with recent studies highlighting its efficacy in drug delivery systems. Research has shown that chitosan and its derivatives can be engineered to improve their therapeutic effects, offering targeted and controlled drug release mechanisms. These advancements are particularly significant in the development of non-invasive delivery systems for biologically active molecules, which can dramatically improve patient compliance and treatment outcomes (59).

Sustainable production and future directions

Combining traditional, biological, and alternative methods has proven to be the most effective strategy for the sustainable production of chitosan. This approach not only ensures high yields but also maintains the quality of chitosan, which is crucial for its application in various environmental and biomedical fields. The ongoing research and increasing number of publications related to chitosan highlight its growing importance and continuous development in sustainable practices (41).

Challenges and limitations

Chitosan, despite its widespread applications and benefits, faces several challenges and limitations that can impede its utility across various fields. These challenges stem primarily from its production process, physical and chemical properties, and the variability in its biological performance.

Production and standardization issues

Source and cost limitations: The primary raw materials for chitosan production are seasonal and localized, which can lead to supply inconsistencies and high production costs (60).

Extraction challenges: The extraction of chitosan is not only time-consuming but also costly, involving the use of harsh chemicals that can impact the environment (2).

Quality variability: Due to differences in the source and extraction methods, the quality of chitosan can vary significantly, which affects its reliability in various applications (60).

Lack of standardization: There is a notable lack of standardization in the production and quality control of chitosan, making it difficult to ensure consistent performance across different batches and products (60).

Physical and chemical property variability

Solubility Issues: Chitosan's solubility is highly pH-dependent and it shows poor solubility in neutral and basic media, limiting its use in various applications (27).

Property Variations: The physical and chemical properties of chitosan, such as molecular weight and degree of deacetylation, can vary greatly. These variations can significantly impact its performance, further complicating the standardization of chitosan products (61).

Biological performance and safety concerns

Mechanisms of action: There is a limited understanding of the mechanisms by which chitosan interacts with cells and tissues, which can hinder its application in biomedicine and other fields (61).

Immunogenicity and toxicity: Although chitosan is generally considered safe, there are concerns regarding its potential immunogenicity and toxicity in some applications, which necessitate further studies to clarify these aspects (61).

Disputed biological properties: Some of the claimed biological properties of chitosan, such as its antimicrobial and biodegradability characteristics, are disputed, indicating a need for more comprehensive research to validate these properties (22).

These challenges underscore the necessity for ongoing research and technological improvements to enhance the yield, standardization, and application of chitosan, ensuring its sustainable and effective use in the future (2). This comprehensive analysis not only highlights the innovative uses of chitosan in emerging fields but also sets the stage for addressing the key challenges that lie ahead in fully realizing the potential of chitosan in both environmental and biomedical sectors.

Conclusion and future perspectives

Having traversed the expansive landscape of chitosan from its historical roots to its modern applications, one can appreciate the significant strides made in understanding and utilizing this versatile biopolymer. Its unique chemical structure facilitates a myriad of applications across various fields, especially in biomedical and environmental sectors, underscoring its potential to address contemporary challenges in sustainability and healthcare. The exploration of chitosan's properties, modifications, and the breadth of its applications reinforces its status as a material of crucial interest, poised for further innovation and wider adoption in the pursuit of a greener and more sustainable future.

Yet, as we delve into the future prospects of chitosan, it's evident that overcoming existing challenges related to production, standardization, and biological performance is paramount to unlocking its full potential. The call for further research and technological advancements is clear, aimed at enhancing chitosan's yield, functionality, and application efficiency. In drawing together the threads of chitosan's story, from historical curiosity to a beacon of biopolymer innovation, we are reminded of the continual need for inquiry, adaptation, and application of science for the betterment of society and the environment.

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References

1. Thambiliyagodage C, Jayanetti M, Mendis A, Ekanayake G, Liyanaarachchi H, Vigneswaran S. (2023). Recent advances in chitosan-based applications—a review. Materials, 16(5):2073.

2. Alemu D, Getachew E, Mondal AK. (2023). Study on the Physicochemical Properties of Chitosan and their Applications in the Biomedical Sector. Int J Polym Sci, 2023(5):1-13.

3. Chauhan S, Das S, Baig FAH, Qadri SSH. (2022). APPLICATIONS OF CHITOSAN IN DENTISTRY-A REVIEW ARTICLE. J Pharm Negat Results, 13(10):1359-64.

4. Riaz Rajoka MS, Zhao L, Mehwish HM, Wu Y, Mahmood S. (2019). Chitosan and its derivatives: synthesis, biotechnological applications, and future challenges. Appl Microbiol Biotechnol 103:1557-71.

5. Madhumathi K, Sudheesh Kumar P, Abhilash S, Sreeja V, Tamura H, Manzoor K, Nair S, Jayakumar R. (2010). Development of novel chitin/nanosilver composite scaffolds for wound dressing applications. J Mater Sci: Mater Med, 21:807-13.

6. Zhang W, Zhang J, Jiang Q, Xia W. (2013). The hypolipidemic activity of chitosan nanopowder prepared by ultrafine milling. Carbohydr Polym, 95(1):487-91.

7. Minet EP, O'Carroll C, Rooney D, Breslin

C, McCarthy C, Gallagher L, Richards K. (2013). Slow delivery of a nitrification inhibitor (dicyandiamide) to soil using a biodegradable hydrogel of chitosan. Chemosphere, 93(11):2854-8.

8. Gomaa YA, El-Khordagui LK, Boraei NA, Darwish IA. (2010). Chitosan microparticles incorporating a hydrophilic sunscreen agent. Carbohydr Polym, 81(2):234-42.

9. Azmana M, Mahmood S, Hilles AR, Rahman A, Arifin MAB, Ahmed S. (2021). A review on chitosan and chitosan-based bionanocomposites: Promising material for combatting global issues and its applications. Int J Biol Macromol, 185:832-48.

10. Morin-Crini N, Lichtfouse E, Torri G, Crini G. Fundamentals and applications of chitosan. Sustainable agriculture reviews 35: chitin and chitosan: history, fundamentals and innovations2019. p. 49-123.

11. Yadollahi M, Farhoudian S, Namazi H. (2015). One-pot synthesis of antibacterial chitosan/silver bio-nanocomposite hydrogel beads as drug delivery systems. Int J Biol Macromol, 79:37-43.

12. Pacheco N, Garnica-Gonzalez M, Gimeno M, Bárzana E, Trombotto S, David L, Shirai K. (2011). Structural characterization of chitin and chitosan obtained by biological and chemical methods. Biomacromolecules, 12(9):3285-90.

13. Yen M-T, Yang J-H, Mau J-L. (2009). Physicochemical characterization of chitin and chitosan from crab shells. Carbohydr Polym, 75(1):15-21.

14. Badawy RM, Mohamed HI. (2015). Chitin extration, composition of different six insect species and their comparable characteristics with that of the shrimp. J Am Sci, 11(6):127-34.

15. Kaya M, Erdogan S, Mol A, Baran T. (2015). Comparison of chitin structures isolated from seven Orthoptera species. Int J Biol Macromol, 72:797-805.

16. Luo Q, Wang Y, Han Q, Ji L, Zhang H, Fei Z, Wang Y. (2019). Comparison of the physicochemical, rheological, and morphologic properties of chitosan from four insects. Carbohydr Polym, 209:266-75.

17. Shin C-S, Kim D-Y, Shin W-S. (2019). Characterization of chitosan extracted from Mealworm Beetle (Tenebrio molitor, Zophobas morio) and Rhinoceros Beetle (Allomyrina dichotoma) and their antibacterial activities. Int J Biol Macromol, 125:72-7.

18. Kaya M, Baran T, Mentes A, Asaroglu M, Sezen G, Tozak KO. (2014). Extraction and characterization of α-chitin and chitosan from six different aquatic invertebrates. Food Biophys, 9(2):145-57.

19. Chang AKT, Frias Jr RR, Alvarez LV, Bigol UG, Guzman JPMD. (2019). Comparative antibacterial activity of commercial chitosan and chitosan extracted from Auricularia sp. Biocatal Agric Biotechnol, 17:189-95.

20. Cheraghi E, Kababian M, Moradi-Asl E, Bafrouyi SMM, Saghafipour A. (2022). Structure and Antibacterial Activity of Chitosan from the American Cockroach, the German Cockroach and the Mealworm Beetle. Journal of Arthropod-Borne Diseases, 16(4):325-39.

21. Kaya M, Baran T. (2015). Description of a new surface morphology for chitin extracted from wings of cockroach (Periplaneta americana). Int J Biol Macromol, 75:7-12.

22. Aranaz I, Alcántara AR, Civera MC, Arias C, Elorza B, Heras Caballero A, Acosta N. (2021). Chitosan: An overview of its properties and applications. Polymers, 13(19):3256.

23. Crini G. (2019). Historical review on chitin and chitosan biopolymers. Environ Chem

Lett, 17(4):1623-43.

24. Qin Z, Zhao L. The history of chito/chitin oligosaccharides and its monomer. Oligosaccharides of Chitin and Chitosan: bio-manufacture and applications2019. p. 3-14.

25. Crini G. Historical landmarks in the discovery of chitin. Sustainable Agriculture Reviews 35: Chitin and Chitosan: History, Fundamentals and Innovations2019. p. 1-47.

26. Maliki S, Sharma G, Kumar A, Moral-Zamorano M, Moradi O, Baselga J, Stadler FJ, García-Peñas A. (2022). Chitosan as a tool for sustainable development: A mini review. Polymers, 14(7):1475.

27. Yadav M, Kaushik B, Rao GK, Srivastava CM, Vaya D. (2023). Advances and challenges in the use of chitosan and its derivatives in biomedical fields: A Review. Carbohydr Polym Technol Appl:100323.

28. Zhao D, Yu S, Sun B, Gao S, Guo S, Zhao K. (2018). Biomedical applications of chitosan and its derivative nanoparticles. Polymers, 10(4):462.

29. Fatima B. Quantitative Analysis by IR: Determination of Chitin/Chitosan DD. Modern spectroscopic techniques and applications. 1072020.

30. Chattopadhyay D, Inamdar MS. (2010). Aqueous behaviour of chitosan. Int J Polym Sci, 2010:939536.

31. Fenice M, Gorrasi S. (2021). Advances in chitin and chitosan science. Molecules, 26(6):1805.

32. Ogawa K. (2000). Crystalline behavior of chitosan. Molecules: Advances in Chitin Science, 4:324-9.

33. Kawada J, Yui T, Okuyama K, Ogawa K. (2001). Crystalline behavior of chitosan organic acid salts. Biosci Biotechnol Biochem, 65(11):2542-7.

34. Wang W, Meng Q, Li Q, Liu J, Zhou M, Jin Z, Zhao K. (2020). Chitosan derivatives and their application in biomedicine. Int J Mol Sci, 21(2):487.

35. Chen Q, Qi Y, Jiang Y, Quan W, Luo H, Wu K, Li S, Ouyang Q. (2022). Progress in research of chitosan chemical modification technologies and their applications. Mar Drugs, 20(8):536.

36. Iber BT, Kasan NA, Torsabo D, Omuwa JW. (2022). A review of various sources of chitin and chitosan in nature. J Renew Mater, 10(4):1097.

37. Hahn T, Roth A, Ji R, Schmitt E, Zibek S. (2020). Chitosan production with larval exoskeletons derived from the insect protein production. J Biotech, 310:62-7.

38. Hameed AZ, Raj SA, Kandasamy J, Baghdadi MA, Shahzad MA. (2022). Chitosan: a sustainable material for multifarious applications. Polymers, 14(12):2335.

39. Merzendorfer H, Cohen E. Chitin/chitosan: versatile ecological, industrial, and biomedical applications. Extracellular Sugar-Based Biopolymers Matrices2019. p. 541-624.

40. Matica A, Menghiu G, Ostafe V. (2017). Biodegradability of chitosan based products. New Front Chem, 26(1).

41. Lam WS, Lam WH, Lee PF. (2023). The Studies on Chitosan for Sustainable Development: A Bibliometric Analysis. Materials, 16(7):2857.

42. Ojeda-Hernández DD, Canales-Aguirre AA, Matias-Guiu J, Gomez-Pinedo U, Mateos-Díaz JC. (2020). Potential of chitosan and its derivatives for biomedical applications in the central nervous system. Front Bioeng Biotechnol, 8:389.

43. Piekarska K, Sikora M, Owczarek M,

Jóźwik-Pruska J, Wiśniewska-Wrona M. (2023). Chitin and chitosan as polymers of the future—obtaining, modification, life cycle assessment and main directions of application. Polymers, 15(4):793.

44. Budiarso IJ, Rini ND, Tsalsabila A, Birowosuto MD, Wibowo A. (2023). Chitosan-based smart biomaterials for biomedical applications: Progress and perspectives. ACS Biomater Sci Eng, 9(6):3084-115.

45. Araújo D, Ferreira IC, Torres CA, Neves L, Freitas F. (2020). Chitinous polymers: extraction from fungal sources, characterization and processing towards value□added applications. J Chem Technol Biotechnol, 95(5):1277-89.

46. Sharma S, Bhende M, Goel A. (2024). A review: polysaccharide-based hydrogels and their biomedical applications. Polym Bull:1-22.

47. Mondal A, Dhar AK, Banerjee S, Hasnain MS, Nayak AK. Antimicrobial uses of chitosan. Chitosan in Biomedical Applications: Elsevier; 2022. p. 13-36.

48. Kravanja G, Primožič M, Knez Ž, Leitgeb M. (2019). Chitosan-based (Nano) materials for novel biomedical applications. Molecules, 24(10):1960.

49. Gahruie HH, Niakousari M. (2017). Antioxidant, antimicrobial, cell viability and enzymatic inhibitory of antioxidant polymers as biological macromolecules. Int J Biol Macromol, 104:606-17.

50. Basseri H, Bakhtiyari R, Hashemi SJ, Baniardelani M, Shahraki H, Hosainpour L. (2019). Antibacterial/antifungal activity of extracted chitosan from American cockroach (Dictyoptera: Blattidae) and German cockroach (Blattodea: Blattellidae). J Med Entomol, 56(5):1208-14.

51. Kababian M, Cheraghi E, Asl EM, Saghafipour A, Nabizadeh Z. (2024). COMPARATIVE STUDY OF PHYSIOCHEMICAL AND ANTIMICROBIAL PROPERTIES OF ADULT COCKROACHES-EXTRACTED CHITOSAN. J Appl Biol Sci, 18(1):94-105.

52. Omura Y, Shigemoto M, Akiyama T, Saimoto H, Shigemasa Y, Nakamura I, Tsuchido T. (2003). Antimicrobial activity of chitosan with different degrees of acetylation and molecular weights. Biocontrol Sci, 8(1):25-30.

53. Kabanov VL, Novinyuk LV. (2020). Chitosan application in food technology: A review of rescent advances. Food Syst, 3(1):10-5.

54. Ivanova DG, Yaneva ZL. (2020). Antioxidant properties and redox-modulating activity of chitosan and its derivatives: Biomaterials with application in cancer therapy. BioResearch open access, 9(1):64-72.

55. Reshad RAI, Jishan TA, Chowdhury NN. (2021). Chitosan and its broad applications: A brief review. Available at SSRN 3842055.

56. Frigaard J, Jensen JL, Galtung HK, Hiorth M. (2022). The potential of chitosan in nanomedicine: An overview of the cytotoxicity of chitosan based nanoparticles. Front Pharmacol, 13:880377.

57. Khan MM, Madni A, Torchilin V, Filipczak N, Pan J, Tahir N, Shah H. (2019). Lipid-chitosan hybrid nanoparticles for controlled delivery of cisplatin. Drug Deliv, 26(1):765-72.

58. Shahbaz U, Basharat S, Javed U, Bibi A, Yu XB. (2023). Chitosan: A multipurpose polymer in food industry. Polym Bull, 80(4):3547-69.

59. Xia Y, Wang D, Liu D, Su J, Jin Y, Wang D, Han B, Jiang Z, Liu B. (2022). Applications of chitosan and its derivatives in skin and soft tissue diseases. Front Bioeng Biotechnol, 10:894667.

60. Mujeeb A, Miller AF. Peptide Bionanomaterials Global Market: The Future of Emerging Industry. Peptide Bionanomaterials: From Design to Application: Springer; 2023. p. 539-55.

61. Yu J, Wang D, Geetha N, Khawar KM, Jogaiah S, Mujtaba M. (2021). Current trends and challenges in the synthesis and applications of chitosan-based nanocomposites for plants: A review. Carbohydr Polym, 261:117904.