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Kitin Deasetilasyonu ile Elde Edilen Kitosanın Biyolojik ve Farmakolojik Özellikleri ile Kullanım Alanları

Mehmet Alperen ARIK[1], Emine YALÇIN[2], Kültigin ÇAVUŞOĞLU[3], Tuğçe KALEFETOĞLU MACAR[4], Oksal MACAR[5]

Özet

Kitosan, doğada bol bulunan bir polisakkarit olan kitinden elde edilen bir biyopolimerdir. Günümüzde pek çok sektörde sentetik kimyasalların kullanılması ve bu kullanıma bağlı olarak gün geçtikçe çevre kirliliğinin artması, doğal ürünlerin kullanımını zorunlu hale getirmektedir. Kitosan sergilediği pek çok biyolojik aktivite sayesinde medikal uygulamalarda güvenilir bir şekilde kullanılmaktadır. Biyouyumlu, biyoparçalanabilir olması ve toksisite sergilememesi bu güvenilirliği arttırmaktadır. Medikal uygulamalar kadar tarımsal alanlarda da çeşitli amaçlarla kullanılan kitosanın, özellikle gübre olarak kullanımı hem verimi arttırmakta hem çevre dostu bir sonuç ortaya çıkarmaktadır. Bu derleme makalede kitosanın kitinden elde edilmesi, deasetilasyon derecesinin önemi, biyolojik ve farmakolojik özellikleri ile kullanım alanları hakkında kapsamlı bir bilgi sunulmuştur.

Anahtar Kelimeler: Biyolojik aktivite, İlaç salımı, Kitin, Kitosan, Farmakolojik özellik

Biological and Pharmacological Properties and Uses of Chitosan Obtained by Deacetylation of Chitin

Abstract

Chitosan is a biopolymer derived from chitin, a polysaccharide abundant in nature. Currently, the widespread use of synthetic chemicals across various sectors and the resulting environmental pollution necessitates the adoption of natural products.

Due to its diverse biological activities, chitosan is safely utilized in the field of medicine. Its biocompatibility, biodegradability, and lack of toxicity further enhance this reliability. Beyond medical applications, chitosan is also employed for various purposes in agriculture; specifically, as a fertilizer, it enhances productivity while yielding environmentally friendly results. In this review article, a comprehensive overview is presented regarding the extraction of chitosan from chitin, the importance of the degree of deacetylation, its biological and pharmacological properties, and its diverse areas of use.

Keywords: Biological activity, Drug release, Chitin, Chitosan, Pharmacological property

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Biologist (Master's Student)) Mehmet Alperen ARIK, Giresun University/Faculty of Science and Art/Department of Biology/Giresun-Türkiye, alperenarik018@gmail.com, https://orcid.org/0009-0004-7833-0015
Prof. Dr. Emine YALÇIN, Giresun University/Faculty of Science and Art/Department of Biology/Giresun-Türkiye, kultigin.cavusoglu@giresun.edu.tr, https://orcid.org/0000-0002-5280-5375.
Prof. Dr. Kültiğin ÇAVUŞOĞLU, Giresun University/Faculty of Science and Art/Department of Biology/Giresun-Türkiye, emine.yalcin@giresun.edu.tr, https://orcid.org/0000-0002-4767-9132.
Assoc. Prof., Tuğçe KALEFETOĞLU MACAR, Giresun University/Faculty of Science and Art/Department of Biology/Giresun-Türkiye, tugce.macar@giresun.edu.tr, https://orcid.org/0000-0002-9946-8054.
Assoc. Prof., Oksal MACAR, Giresun University/Faculty of Science and Art/Department of Biology/Giresun-Türkiye, oksal.macar@giresun.edu.tr, https://orcid.org/0000-0002-5067-8712.

Introduction

Chitosan, a polysaccharide derived from chitin, is a natural compound of significant interest due to its diverse applications. Its repeating units consist of N-acetyl-D-glucosamine and D-glucosamine. The increasing environmental pollution and health concerns associated with synthetic compound use have led to a resurgence of interest in natural products. Chitosan possesses a wide range of applications across various sectors and functions. This review article provides a comprehensive overview of the utilization of chitosan. It is therefore essential to first understand the structure and sources of chitin in order to fully grasp the structure and applications of chitosan (Castro et al., 2012).

1. Chitin

Chitin, a structural component of many organisms, is particularly prevalent in their skeletal structures (Tsurkan et al., 2021). Chitin demonstrates a high level of resistance to alkaline treatment and is capable of maintaining its structure even under conditions where many biopolymers undergo denaturation. However, it undergoes deacetylation to form chitosan in highly basic (>1 M NaOH) environments. It has been demonstrated that partial deacetylation can be achieved through the application of enzymes. The study of Chitin has a long history, and with technological advancements, especially in the fields of medicine, biomimetics, molecular biology, and biotechnology applications, it remains a subject of ongoing research. The determination of the applications and functions of chitin thus necessitated the elucidation of its structure, a task that required the development of sensitive and advanced analytical methods (Tsurkan et al., 2021). Chitin characterization studies have yielded novel developments in the diagnosis of parasitic and various immunological diseases. Sendid et al. (2008) found that Candida albicans infection is a factor in the pathogenesis of Crohn's disease. The finding that both the disease itself and the Candida infections exhibited a common increase in chitin antibodies served to strengthen this diagnosis. The possible presence of chitin in Alzheimer's disease, a topic that has gained increasing attention in recent years, has raised various questions and hypotheses, although definitive evidence is still lacking. The presence of chitin was detected in central nervous system tissue samples taken from patients with Alzheimer's disease. This finding suggests a potential link between dementia and Alzheimer's disease and fungal infections (Tsurkan et al., 2021).

1.1. Sources of Chitin

As stated by Muzzarelli (1977), chitin is present in various parts of many organisms, including algae, Aschelminthes (roundworms), Bryozoa, Phoronida, Echinodermata, Mollusca, and Arthropods. Chitin is found in different parts of these organisms, especially in the exoskeletal tendons of arthropods and in the linings of respiratory and digestive systems. In addition, chitin has been detected in the exoskeletons of insects and in the cell walls of certain fungi (Herring, 1979). In the case of *Ascomycetes, Basidiomycetes,* and *Phycomycetes,* chitin is found in the structure of mycelium and spores as well as the cell wall (Peter, 2005).

The primary commercial sources of chitin are lobster, shrimp, and crab. Chitin is a polysaccharide, and there are three forms of this substance according to the state of the polysaccharide chains: α, β, and γ. The α-form, which consists of antiparallel polysaccharide chains, is predominantly obtained from crustaceans such as lobster and shrimp. This form of chitin is most found in fungal and yeast cell walls, as well as in the tendons and shells of lobster and crab, and in the exoskeletons of shrimp. The β-chitin, which is rarer than the α-form, consists of parallel polysaccharide chains and is found in proteins in cuttlefish cuttlebones and in tubes synthesized by *Pogonophoran* and *Vestimetiferan* worms. It has also been detected in *Aphrodite chaetae*, as well as in certain species of marine algae and protozoa, and contains two parallel chains alternating with an antiparallel chain (Herth et al., 1986).

1.2. Preparation of Chitosan and its Biological Properties

Chitosan is obtained via the deacetylation of chitin whereby N-acetyl-D-glucosamine is converted to D-glucosamine. As complete conversion is rarely achieved during his process, the resultant chitosan contains a mixture of D-glucosamine and N-acetyl-D-glucosamine in varying proportions. The ratio of these two compounds is defined as the degree of deacetylation (DD). It is notable that neither fully acetylated nor fully deacetylated forms of chitin occur in nature. Chitin with a DD of 50% and above is generally classified as chitosan. (No and Meyers, 1995; Kozma et al., 2022).

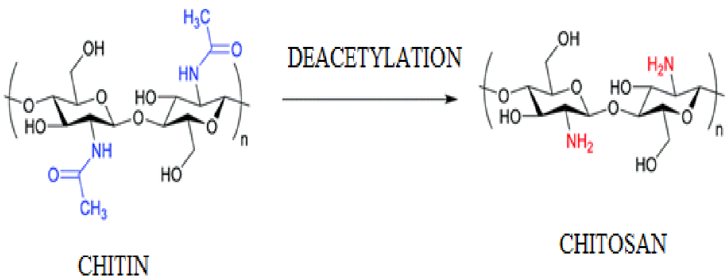

Figure 1: Preparation of Chitosan by Chitin Deacetylation

Deacetylation of chitin yields chitosan, a derivative possessing diverse biological characteristics. These attributes include minimal environmental toxicity, antibacterial qualities, biocompatibility, and biodegradability. Chitosan's potential for biomedical use is further highlighted by its demonstrated analgesic and wound-healing properties. Due to its multifaceted applications across various industries, such as medicine, agriculture, and the production of biodegradable plastics, chitosan is regarded as the most valuable derivative of chitin (Ji et al., 2014).

1.3. Biocompatibility and Biodegradability

The biocompatibility of biomaterials is contingent upon the capacity to avoid inducing toxic or on biological systems (Keong and Halim, 2009). The most intensive applications in biomedical research are carried out with materials derived from nature because natural materials exhibit high biocompatibility in both in vitro and in vivo settings. Chitosan, for instance, has been shown to exhibit significant biocompatibility, attributable to the presence of the monomeric unit N-acetylglucosamine in its structure. Chitosan shares structural similarities with glycosaminoglycans (GAGs) found in all mammals, including heparin, chondroitin sulphate, and hyaluronic acid. The presence of this monomeric unit in the structure of hyaluronic acid, an important extracellular macromolecule in wound repair, makes chitosan an important wound healing agent. Furthermore, its capacity to interact with various growth factors, receptors, and adhesion proteins has been demonstrated to enhance its bioavailability (Suh and Matthew, 2000).

The term 'biodegradability' is frequently linked to the concept of environmentally friendly products and is defined as the ability to break down into simpler components through natural processes. The biodegradation of products is typically facilitated by the actions of bacteria, fungi, or other microorganisms. In the case of chitosan, it is hypothesized that the process of degradation is predominantly catalyzed by lysozyme and bacterial enzymes within the colon of vertebrates (Kean and Thanou, 2010). The assessment of the biodegradability of chitosan is typically undertaken by the utilization of a viscometer and/or gel permeation chromatography techniques to ascertain the decline in molecular weight. It has been demonstrated that lysozyme effectively degrades chitosan, and that 50% acetylated chitosan lost 66% of its viscosity after 4 hours of lysozyme incubation at pH 5.5. Furthermore, it has been reported that this degradation depends on the degree of acetylation (Castro et al., 2012).

1.4. Antimicrobial Activity

Chitosan is a broad-spectrum antibacterial compound that works well against a variety of filamentous fungi, yeasts, and bacteria. Chitosan is highly potent and has a wide range of activity against both Gram-positive and Gram-negative bacteria, while being less harmful to mammalian cells. Although the exact mechanism by which chitosan exerts its antibacterial effect is still unclear, it is thought that a major contribution from its polycationic structure is responsible. According to one theory, the negatively charged elements of microbial cell membranes interact with the positively charged amino groups of the glucosamine units in the chitosan structure, changing the barrier's characteristics and either obstructing nutrient intake or allowing intracellular contents to leak out. As an alternative, it has been documented that low-molecular-weight chitosan can enter cells, bind to DNA, and then suppress the synthesis of RNA and proteins (Fernandez-Saiz et al., 2010). Furthermore, it has been shown that chitosan can initiate a variety of defense mechanisms in plant tissues, which restrict the growth of microorganisms and the production of toxins (Castro et al., 2012). This result is explained by chitosan's ability to chelate metal ions, which alters biological processes and makes it harder for pathogenic microbes to survive. According to EI-Ghaouth et al. (1992), chitosan's contact with the cell surface alters cell permeability, which prevents metabolites from entering the cell or causes intracellular to leak out (Figure 2). However, no proof has been offered to show a connection between the bacterial cell wall's surface characteristics and chitosan's antibacterial action. Many factors contribute to the difference in chitosan's antibacterial activity, including: (1) microbial factors such as the species of microorganisms and cell age; (2) chitosan's positive charge density, molecular weight, concentration, hydrophilic/hydrophobic property, and chelation capacity; and (3) environmental factors, such as the medium's ionic strength, pH, temperature, and reaction time (Kong et al. 2010). It has been shown that chitosan has a variety of distinct biological properties, such as the capacity to prevent phage infection in infected microbial cultures, block viral infection in animal cells, and develop resistance to viral infections in plants (Castro et al., 2012). There are some clear benefits that it offers over other disinfectants. For example, its broad-spectrum antiviral, antifungal, and antibacterial qualities are important benefits. Chitosan also has the advantage of having a higher rate of antibacterial activity and efficacy while being relatively less harmful to healthy mammalian cells. However, in certain situations, chitosan's antibacterial potency is still less than that of certain antibiotics and antifungal medications, even with its broad-spectrum antimicrobial activity (Kou et al., 2022). Although chitin and chitosan derivatives are therapeutic polymers exhibiting antioxidant, antimicrobial, antitumor, and anti-inflammatory properties, it is noteworthy that they have not yet been accepted as drugs for the treatment of diseases and are only used as regulatory agents (Aranaz et al., 2021). The antioxidant activity of chitosan has been demonstrated using various test systems such as ABTS, DPPH, FRAP, and ORAC. The most important factor that provides this compound with its unique property is that it possesses several hydroxyls and one amino group that react with free radicals and eliminate these substances (Zhou et al., 2021).

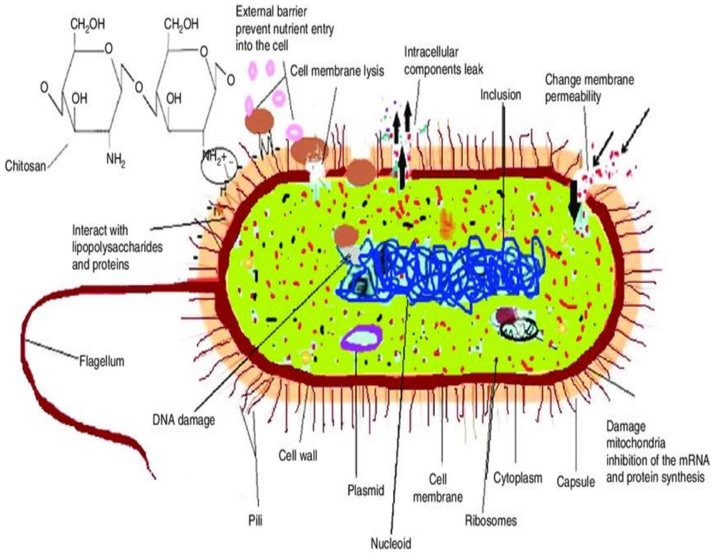

Figure 2: Potential Antibacterial Action Mechanisms of Chitosan (Gafri et al., 2019)

1.5. Analgesic Activity

Numerous studies in the relevant literature have documented the analgesic properties of chitin and chitosan. According to Allan (1984), applying chitosan to open wounds provides a cooling and soothing effect. Similarly, Ohshima et al. (1987) found that when applied topically to a variety of open wounds, such as burns, skin abrasions, skin ulcers, and skin graft areas, chitin was an effective pain reliever in 83 out of 91 cases. Furthermore, Minami (1993) and Okamoto (1993) observed that when chitin and chitosan were applied to animal wounds, the animals did not experience pain. One of the most important phases in wound healing is hemostasis, or blood coagulation. Platelets are the main biological constituents involved in this process. It has been shown that chitosan possesses hemostatic properties. By aggregating platelets, Chitin is an efficient agent in maintaining hemostasis, according to Okamoto et al. (2003). They proposed that the physical and chemical characteristics of these biopolymers—particularly their amino groups—are responsible for this action (Castro et al., 2012).

1.6. Immunological Activity

Products made from chitin derivatives have been shown to exert immunomodulatory effects in a variety of biomedical applications. The underlying mechanisms of these effects have been investigated. In the presence of interferon-γ (IFN-γ), chitin has been found to enhance nitric oxide production from macro through NF-κB signaling (Jeong et al., 2000). Furthermore, Minami et al. (1998) discovered that chitin and chitosan influence the complement system's C3 and C5 components, leading them to conclude that chitin and chitosan activate the complement system in a distinct manner. Polymorphonuclear cells migrate to the damaged tissue after complement activation. Even though this is a typical inflammatory response, it has been found that chitin and chitosan do not induce systemic inflammatory symptoms such as fever and abscess formation (Castro et al., 2012). To clarify the immunomodulatory effects of chitin and chitosan, further research is required.

1.7. Activity against Hypercholesterolemia

Among the crucial substances used to address obesity and hypercholesterolemia are chitin and chitosan (Razdan & Pettersson, 1994). Numerous theories have been proposed to explain the mechanism of action of chitosan, which has been thoroughly studied and found to be helpful in lowering cholesterol levels in rats. The electrostatic interaction between aminopolysaccharides and lipids is one example of this (Muzzarelli & Muzzarelli, 2006). Chitin slows absorption by binding to lipid (cholesterol) micelles. The rise in bile acid excretion is another theory suggested. Humans (Gallaher et al., 2000). Humans have also been shown to benefit from chitosan's hypocholesterolemic effects. Chitosan is thought to cholesterol by sequestering bile acids in the digestive tract and excreting them in the feces. This reduces bile acid reabsorption, lowers the body's cholesterol pool, and ultimately lowers serum cholesterol levels (Castro et al., 2012).

1.8. Applications of Chitosan in Agriculture

Recent years have seen the beneficial application of chitosan in agriculture due to its antiviral, antifungal, and antibacterial qualities. It is favored as a defensive mechanism activator, a growth promoter for plant protection, and an enhancer of secondary metabolite production for soil improvement (Castro et al., 2012). Because of its high nitrogen concentration, chitosan has been found to act as a potent fertilizer when added to soil, preventing plant wilting (Utsunomiya et al., 1998). In certain crops, including broad beans, radish, passion fruit, potatoes, gerbera, cabbage, and soybeans, chitosan added to irrigation has been shown to stimulate plant development, boost crop yields, and shield plants against disease. According to El Hadrami et al. (2010), chitosan also significantly affects the growth rates, abundance, and development of roots, shoots, and flowers. Furthermore, it promotes vigorous plant growth by preventing fungal diseases caused by pathogens such as *Aspergillus flavus*, *Cylindrocladium floridanum, Fusarium acuminatum*, and *Fusarium sp*. (Lizárraga-Paulín et al., 2011). Bio-based pesticides are becoming more popular due to the danger that synthetic pesticides pose to the environment and non-target organisms. In agriculture, chitosan is employed as a bionematicide and bioinsecticide. Although there is some research on the use of chitosan as a bioinsecticide, its primary applications are in the control of bacterial and fungal pathogens. One of the initial conclusions is that chitosan has an 80% mortality rate against certain insects, including homoptera and lepidoptera, and that this rate rises as the concentration of oligo-chitosan increases (Zhang et al., 2003). The inclusion of chitin derivatives in formulations containing these microorganisms has been regarded as a way to improve biopesticide efficacy, offer a favorable growing environment, and increase resistance against adverse conditions. Because they are non-toxic to humans and animals and possess a biodegradable matrix, new chitosan derivatives with insecticidal or fungicidal capabilities could be ideal substitutes for broad-spectrum and highly persistent insecticides (Ramírez et al., 2010). It is possible to inhibit nematode multiplication by applying chitosan to the soil. Chitinolytic microbes multiply in the presence of chitosan, neutralizing nematode eggs and breaking down the chitin-containing cuticle of juvenile nematodes. The high nitrogen content of chitosan and chitin molecules causes ammonia emissions to rise, which is toxic to nematodes, mostly affecting plant roots and shoots (Ramírez et al., 2010). Although further research is required fully exploit chitosan in agriculture, it is now recognized that this polymer offers an inexpensive and simple solution to crop issues in the pre-, mid-, and after-harvest phases (Rabea et al., 2005; Castro et al., 2012).

1.9. The Use of Chitosan in Medicine

Chitosan possesses a diverse range of medical applications. Its utilization has increased recently, particularly in the orthopedic domain. In the treatment of bone and cartilage healing, chitosan-based products have shown remarkable success. It has been found that injecting chitosan solution (0.1%) into the rat knee joint cavity boosted chondrocyte and induced intra-articular fibrous development. A chitosan-glycerol phosphate gel was discovered to promote chondrocyte production in rabbit cartilage defects. These findings demonstrate that chitosan promotes cartilage formation and wound healing. Another practical application for chitosan is in mucosal drug delivery. Because of its physicochemical characteristics, chitosan can be utilized in drug delivery systems as a functional biomaterial and a matrix with controlled release (Kean & Thanou, 2011). Chitosan polymers have been utilized to deliver medications for the treatment of various cancers in diverse forms, including hydrogels, nanoparticles, and nanofibers. Due to their versatility, chitosan polymers are excellent candidates for targeted chemotherapy. Enhanced functionality and targeted delivery can be achieved by altering their surface moieties—such as by adding a membrane-penetrating peptide, monoclonal antibodies, or surface receptors that target particular cancer cells (Figure 3) (Baharlouei & Rahman, 2022). Additionally, chitosan applications exhibit anti-cancer properties by boosting the immune system. According to recent reports, chitosan's tumor-inhibitory action is most likely connected to the activation of lymphocyte cytokines and an increase in T cell proliferation (Park & Kim, 2010). Chitosan is used as a carrier for drug or gene therapies due to its biocompatible and biodegradable structure. The most significant advantages of this application are targeted distribution, controlled release, and reduced toxicity, which are facilitated due to the modifiable nature of the chitosan surface (Mohammed et al., 2017).

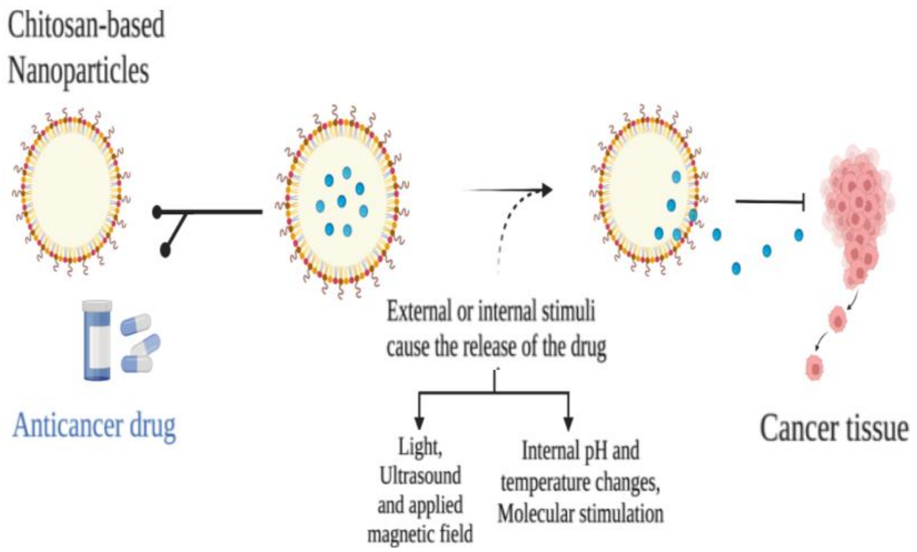

Figure 3: Applications of Chitosan-Based Nanoparticles in Tumor-Targeted Drug Delivery (Baharlouei & Rahman, 2022)

1.10. Advantages of Chitosan in Food Packaging

Glass and metals, along with plastic-based materials such as polyethylene and polypropylene, contribute to the long-term preservation of food by forming a barrier against factors like oxygen, moisture, contaminants, and light (Bopp, 2019). However, the lack of natural antimicrobial properties in plastics, the fragility and transportation costs of glass, and the high cost and difficulty of recycling and disposing of metals have made it necessary to find alternatives to these packaging materials. Research conducted to date has shown that chitosan stands out as a sustainable and functional biopolymer film in food packaging (Figure 4).

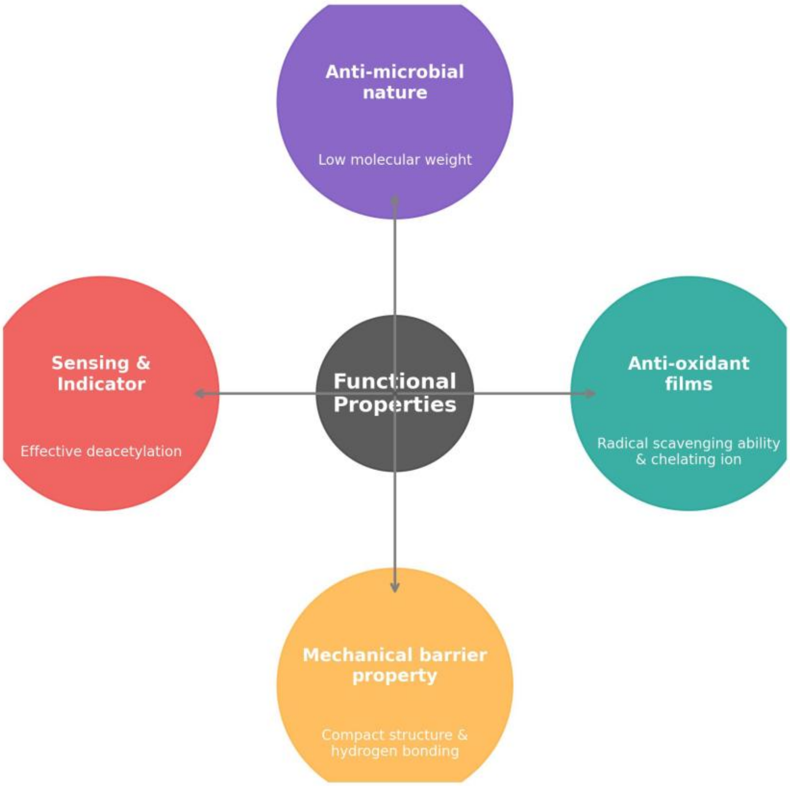

Figure 4: Advantages of Chitosan Film Utilization in Food Packaging (Prasannamedha et al., 2024).

Due to its environmental qualities and natural antimicrobial properties, chitosan prevents food spoilage and extends shelf life (Prasannamedha et al., 2024). It has been reported that chitosan is particularly effective in preserving meat, dairy products, fruits, vegetables, and fish products (Qu et al., 2025). The mechanical and barrier properties of chitosan have been enhanced through nanotechnology and composite film developments. Furthermore, modifications using cross-linking agents such as glycerol, chitosan oligosaccharide, and gallic acid have reduced water vapor permeability and increased mechanical strength (Flórez et al., 2022). In smart and active packaging designs, chitosan has become a fundamental component for materials that can indicate spoilage or enable controlled release. By incorporating natural bioactive compounds such as flavonoids, both active packaging (e.g., inhibiting microbial growth) and smart packaging (e.g., indicating spoilage) functions are achieved (Liu et al., 2025). Moreover, chitosan-based electrospun nanofiber films demonstrate effectiveness in protecting fresh foods such as fruits, vegetables, and salads. These films exhibit antimicrobial activity and modify gas permeability while preserving the firmness and weight of food products (Yang et al., 2025).

Conclusion

Chitin is a natural and biological polymer that can be converted into chitosan, and its natural source guarantees its biodegradability and biocompatibility. It is crucial to employ biocompatible materials, particularly in medical applications. Apart from its biocompatibility, chitosan's non-toxicity facilitates a multitude of applications. The demand for natural active ingredients has become increasingly critical, particularly considering the rise in illnesses and the adverse effects or secondary disorders that arise from the use of synthetic drugs. Because of its broad-spectrum antibacterial qualities, chitosan is safe to use, particularly in wound healing and other clinical applications. Currently, it is critical to develop solutions that mitigate environmental degradation, and controlled drug release devices are used with a specific goal in mind. Chitosan's biodegradable qualities make it an excellent choice for drug delivery systems. In addition to its medical uses, chitosan has been effectively employed in agriculture as a biofertilizer and biopesticide. Currently, it is critical to develop solutions that mitigate environmental degradation. The quality of agricultural lands and the resulting crops will also improve when natural agents are used for applications like fertilization, which is a major contributor to the development of soil pollution. The success of Chitosan in medicinal applications, as well as its ability to increase agricultural productivity, is highlighted in this review study.

Future Perspectives on chitosan should prioritize the development of advanced modification strategies to enhance its physicochemical stability, biodegradability, and targeted biological activity. Standardization of production parameters, together with comprehensive vivo and clinical evaluations, will be essential for its broader integration into biomedical, pharmaceutical, agricultural, and food-related applications. Interdisciplinary approaches are expected to accelerate the translation of chitosan-based systems from experimental studies to reliable and scalable technologies.

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Literatür: Mehmet Alperen Arık, Emine Yalçın, Tuğçe Kalefetoğlu Macar
Sonuç: Mehmet Alperen Arık, Oksal Macar
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Author Contributions: author contributions are below.
Introduction: Mehmet Alperen Arık, Emine Yalçın, Kültiğin Çavuşoğlu
Literature: Mehmet Alperen Arık, Emine Yalçın, Tuğçe Kalefetoğlu Macar
Conclusion: Mehmet Alperen Arık, Oksal Macar
1st author's contribution rate: %20, 2nd author's contribution rate: %20. 3rd author's contribution rate: %20, 4th author's contribution rate: %20. 5th author's contribution rate: %20.

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