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Chitosan: A versatile biopolymer in pharmaceutical and drug delivery applications

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Abstract
Chitosan is one of the leading natural biomaterial after cellulose. In biomolecules delivery, it stands out for its superior oxygen permeation ability and mucoadhesive capacity. Due to their improved structural and functional properties as well as biocompatibility, biodegradability, and nontoxicity, chitosan and its nanoparticles are currently grasping the interest of researchers. In this work, a critical review is performed covering its conventional and novel applications, specially focused on pharmaceutical area, providing a clear picture of the current state of art to serve as a basis to direct future research in this field.

Keywords: Chitosan, chitin, bioactive molecules; polysaccharides, biomedical applications

1. Introduction
Ayurveda is one of the oldest systems of medicine in the world, and its foundations rest heavily on the use of herbs, minerals, and plant-based medicines. Ayurvedic texts like the CharakaSamhita and SushrutaSamhita document the medicinal properties of hundreds of plants and their use in therapeutic treatments [1]. A biopolymer is a type of polymer that is produced naturally by living organisms. These polymers are made up of monomer units that are linked by covalent bonds and are usually derived from renewable sources, such as plants, animals, and microorganisms. Chitosan (CS), a naturally derived biopolymer, has attracted considerable interest due to its remarkable versatility, wide availability, and distinctive properties, making it a promising material for various medical applications. CS iscomposed of *N*-acetyl-glucosamine and glucosamine units obtained by the deacetylation of chitin, generally under alkali conditions at relatively high temperature [2]. Henri Braconnot is credited with the discovery of chitin in 1811, marking the beginning of research in this area. Chitosan, a derivative of chitin, first emerged in 1859 through the pioneering work of Charles Rouget. The term 'chitosan' was introduced later, in 1894, by Felix Hoppe-Seyler [3]. Various methods for extracting chitin and chitosan lead to materials with unique properties, which can be tailored further to enhance their biological activities. Chitosan-based drug delivery systems have been developed for a variety of administration routes, such as oral, ophthalmic, transdermal, nasal, and vaginal, offering enhanced drug targeting and sustained release. Due to its versatility, chitosan plays a key role in a broad spectrum of applications across food and pharmaceutical sectors. Its biodegradability, non-toxicity, and biological activity make it especially valuable in medical, pharmaceutical, agricultural, and environmental sectors.

2. Physicochemical and Biological properties of Chitosan biopolymer
Chitosan's unique combination of physico-chemical and biological properties makes it an incredibly versatile material with a wide range of applications across various industries. It has a wide range of physicochemical and biological properties, which are listed in Table 1 [4].

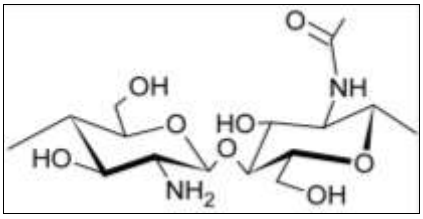

Fig 1: Chemical structure of chitosan: this figure shows the ability of chitosan to have a different functional group that gives diverse applications of chitosan.

Table 1: Physicochemical and biological properties of chitosan biopolymer

Physical properties	Chemical properties	Biological properties
• High molecular weight (1.2 × 105 g mol^{-1}) • White yellow in color • Weak base (powerful nucleophile, pKa 6.3) • Flakes, bead or powder • Intermolecular hydrogen bonding • Optical clarity. • Amorphous solid • Density 0.18-0.33 g/cm^3 • Soluble in diluted aqueous acid solution • Insoluble in water • Conductivity	• Rigid D-glucosaminestructure • Degree of acetylation range 70-95% • Cationic polyamine • At pH <6.5, a high charge density • Forms gels with Poly-anions Polyelectrolyte • Adheres to negatively charged surfaces • Amiable to chemical modification • Additive in paper industry • Filmogenic properties • Linear polyamine • Numerous reactive groups (amino and hydroxyl) • Linear amino-polysaccharide with high nitrogen content	• Biocompatibility • Bacteriostatic • Wound management • Anticancerogen • Accelerates bone formation • Accelerates the formation of osteoblast • Antioxidant • Biodegradable • Homeostatic • Natural polymer • Bone formation • Safe and non-toxic

3. Extraction techniques

The extraction of chitosan involves a multi-step process that requires careful control of conditions like pH, temperature, and reaction time. The quality of the extracted chitosan depends on the degree of deacetylation and the effectiveness of removing proteins and minerals from the raw material. This biomolecule can be extracted from seafood industry waste, such as shrimp shells, using both traditional and sustainable green extraction methods [5]. Here's a step-by-step overview of the typical extraction process:

3.1. Raw Material Selection (Chitin Source)

Chitosan is extracted from chitin, which is primarily sourced from crustacean shells, insects, or some fungi. Crustacean shells (shrimp, crab, etc.) are the most common source, as they are rich in chitin [6].

3.2. Demineralization (Removal of minerals)

To remove inorganic materials, mainly calcium carbonate ($CaCO_3$) and calcium phosphate ($Ca_3(PO_4)_2$) from the raw material [7].

1. The shells are first cleaned to remove dirt and other impurities.
2. The shells are then immersed in a diluted hydrochloric acid (HCl) solution for several hours, which dissolves the calcium carbonate and other mineral content.
3. After demineralization, the shells are washed with distilled water to remove any residual acid.

3.3. Deproteinization (Removal of Proteins)

To remove the protein content (mainly the proteins in the shell) from the demineralized chitin to leave the pure chitin, the following procedure adapted:

1. The demineralized chitin is treated with a strong alkaline solution, typically sodium hydroxide (NaOH), at a concentration of 2-5%.
2. The solution is heated to 60-100°C for several hours. The alkali breaks down the proteins and removes them from the chitin structure [8].
3. The treated chitin is then washed thoroughly with distilled water to neutralize the alkaline solution and remove any residual proteins.

3.4. Deacetylation (Conversion of Chitin to Chitosan)

To remove the acetyl groups (-$COCH_3$) from chitin to convert it into chitosan, it will undergo

1. The purified chitin is treated with a concentrated sodium hydroxide (NaOH) solution, typically 40-50% in concentration [9].
2. The mixture is heated at temperatures between 100-120°C for several hours to promote the deacetylation reaction.
3. The degree of deacetylation can be controlled by adjusting the NaOH concentration, temperature, and reaction time.
4. After deacetylation, the chitosan is washed with distilled water to remove the residual alkali and neutralize the chitosan.

3.5. Drying

- After the extraction process, the chitosan is usually a wet solid or slurry. It is then dried to obtain the final chitosan powder.
- Drying can be done by air drying, freeze-drying, or oven drying at a low temperature (50-60°C) to prevent degradation [10].

3.6. Final Purification

The chitosan may undergo filtration, bleaching, or washing to achieve the desired purity and consistency [11].

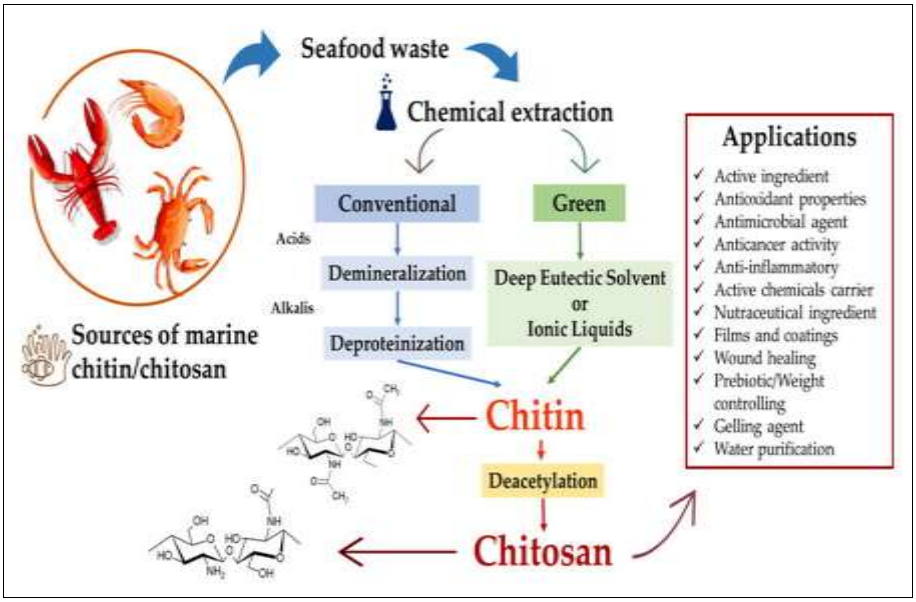

Fig 2: Diagrammatic representation of chitosan preparation from natural source in which natural and chemical processing are utilized.

4. Pharmaceutical characteristics

The biological activity of chitosan and its derivatives is highly versatile. Chitosan is effective against a wide variety of bacteria, filamentous fungi, and yeasts [12]. The below section provides a brief overview of chitosan's bioactivities.

4.1. Antibacterial Activity

Chitosan exhibits potent antibacterial activity due to its ability to interact with bacterial cell membranes, inhibit essential bacterial processes, and disrupt cellular structures. The degree of deacetylation, molecular weight, pH, and bacterial strain all play important roles in determining its effectiveness. The amino groups (-NH_2) on chitosan are positively charged in acidic conditions, which allows chitosan to interact with the negatively charged components of bacterial cell membranes (such as phospholipids and lipopolysaccharides). This electrostatic interaction causes structural changes in the bacterial membrane, making it more permeable and leading to leakage of intracellular contents (e.g., proteins, nucleic acids, ions), which disrupts cellular functions and results in bacterial death. Low molecular weight chitosan can penetrate bacterial cell walls, interact with DNA, and inhibit DNA transcription and mRNA synthesis. In contrast, high molecular weight chitosan binds to negatively charged components on the bacterial cell wall, forming an impermeable barrier, altering cell permeability, and preventing the transport of substances into the cell. This hypothesis was further supported by this studies [13]. Its antibacterial activity is also pH-dependent. It is more effective at acidic pH levels (below 6) because its amino groups are protonated, making chitosan positively charged and more able to interact with bacterial membranes. Chitosan exhibits a broad spectrum of activity and a high killing rate against both Gram-positive and Gram-negative bacteria. This antimicrobial effect is due to interactions between chitosan and its derivatives with bacterial cell wall components. The studies referenced in this section highlight a strong correlation between antibacterial activity and the hydrophilicity of the cell wall, indicating that the action is targeted and results in reduced toxicity toward mammalian cells [14].

4.2. Antifungal Activity

The antifungal activity of chitosan is influenced by its molecular weight and degree of acetylation, with these effects varying depending on the type of fungus. Chitosan forms a physical barrier on the surface of the fungal cell, which prevents the germination of fungal spores and inhibits fungal growth [15]. This is especially useful in the control of plant pathogens or preventing fungal contamination in food products. Chitosan can inhibit certain fungal enzymes, such aschitinaseand glucanase, which are important for cell wall synthesis and the breakdown of structural components. By interfering with these enzymes, chitosan weakens the fungal cell wall, making it more vulnerable to external stresses. The degree of deacetylation (DD) of chitosan determines its solubility and ability to interact with fungal cells. Chitosans with a higher degree of deacetylation tend to exhibit stronger antifungal activity due to the increased availability of amino groups, which are responsible for interacting with the fungal membrane [16].

4.3. Antiviral Activity

Chitosan exhibits promising antiviral activity through multiple mechanisms, including blocking viral entry, disrupting viral membranes, and inhibiting viral replication. It is particularly effective against enveloped viruses, but its effectiveness can vary based on factors such as the virus type, degree of deacetylation, molecular weight, and pH conditions. The antiviral activity of chitosan is primarily attributed to its molecular structure and its ability to interact with viral particles, preventing them from infecting host cells. Chitosan can interact with the surface proteins of viruses, preventing them from binding to host cells. Viruses typically use surface glycoproteins (such as spikes or receptors) to attach to specific receptors on the surface of host cells. Chitosan's positively charged amino groups (-NH_2) can electrostatically interact with the negatively charged components on the viral surface, blocking the virus's ability to bind to the host cell's receptors. This prevents the initial attachment of the virus to the host cell, which is a crucial step in viral infection [17]. Chitosan's mucoadhesive properties enable it to remain on the mucus surface of the host for prolonged periods, where it can exert

its antiviral effects. Studies have shown that chitosan with high molecular weights (50-1000 kDa) and a degree of acetylation between 10% and 30% inhibits the replication of bacteriophage, tobacco mosaic virus, murine norovirus, and feline calicivirus. Furthermore, reducing the polymerization degree of low molecular weight chitosan enhances its antiviral activity. Chitosan with a molecular weight below 10 kDa has also been reported to exhibit antiviral effects against several influenza virus subtypes, indicating that molecular weight plays a significant role in antiviral efficacy.

4.4. Anti-Tumor Activity

Chitosan exhibits potent antitumor activity through several mechanisms, including inducing apoptosis, inhibiting cell proliferation, reducing angiogenesis, and enhancing the immune response. Its use in combination with chemotherapy, as a nanocarrier for drug delivery, and in tissue regeneration shows its potential as an effective tool in cancer treatment. Chitosan and its derivatives have demonstrated antitumor activity in both *in vitro* and *in vivo* models. Tokoro *et al* have found that the antitumor effect of chitosan derivatives is linked to the increased secretion of interleukin-1 and interleukin-2, which promote the maturation and infiltration of cytolytic T-lymphocytes [18]. This finding is further supported by *in vivo* study which showed that chitosan enhanced lymphokine production and stimulated the proliferation of cytolytic T-lymphocytes [19]. One of the key mechanisms by which chitosan exerts its antitumor effects is by inducing apoptosis in cancer cells. Apoptosis is a controlled and regulated form of cell death, and its induction is crucial for eliminating malignant cells. Chitosan triggers apoptosis by activating various signaling pathways such as the mitochondrial pathway (via cytochrome c release and caspase activation) and death receptor pathways (through activation of caspase-8 and other pro-apoptotic proteins). Additionally, chitosan may upregulate the expression of pro-apoptotic proteins (like BAX) and downregulate anti-apoptotic proteins (like Bcl-2), promoting programmed cell death in cancer cells.

4.5. Anti-Oxidant and Anti-Inflammatory Activities

The antioxidant activity of chitosan is primarily attributed to its ability to scavenge free radicals and reduce oxidative stress. Oxidative stress, caused by an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them, is linked to various chronic diseases, including cancer, cardiovascular disease, diabetes, and neurodegenerative disorders. Chitosan contains amine (-NH_2) and hydroxyl (-OH) groups that allow it to act as an effective free radical scavenger. These groups can interact with and neutralize reactive oxygen species (ROS) like hydroxyl radicals (•OH), superoxide anions ($O_2^{\bullet -}$), and hydrogen peroxide (H_2O_2), which are harmful to cells and tissues. By neutralizing these free radicals, chitosan helps reduce oxidative damage to lipids, proteins, and DNA, thus preventing cellular damage and aging [20].

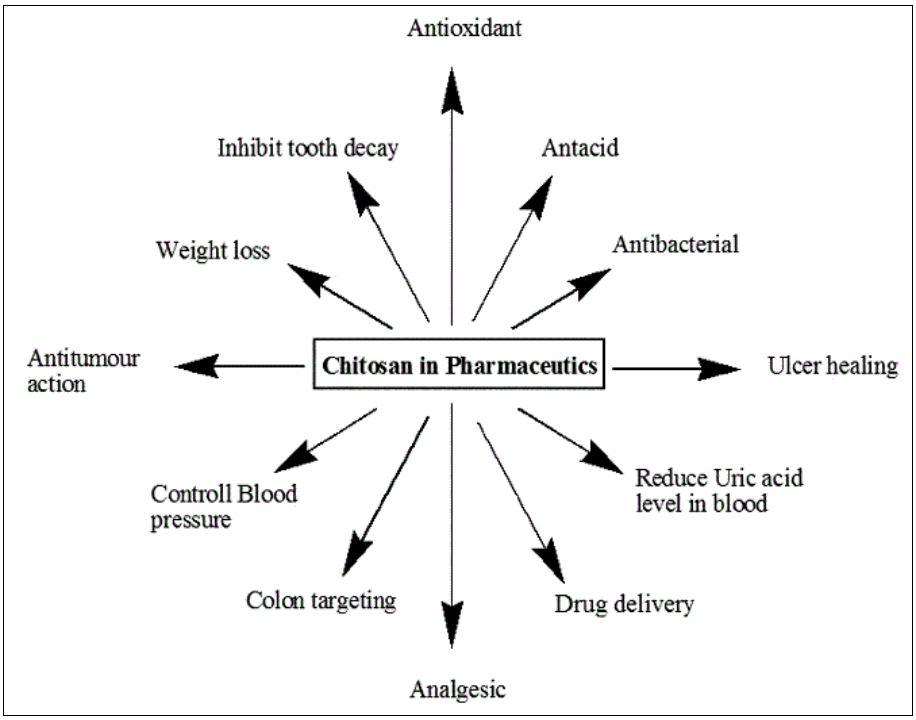

Fig 3: Pharmaceutical Characteristics of Chitosan

5. Applications

Chitosan and chitosan-based systems have been shown potential applications in drug delivery as well as pharmaceutical field.

5.1. Drug Delivery Applications: Chitosan has garnered significant attention in drug delivery applications due to its biocompatibility, biodegradability, and unique physicochemical properties [21]. Some key drug delivery applications of chitosan include:

5.1.1. Oral Drug Delivery: Chitosan is used as a carrier for oral drug delivery due to its ability to improve the bioavailability of poorly soluble drugs. It can form nanoparticles or microparticles that protect drugs from degradation in the gastrointestinal tract, enhance absorption,

and enable controlled or sustained release [22].

5.1.2 Targeted Drug Delivery: Chitosan can be modified to improve its targeting abilities, such as by conjugating with ligands that recognize specific cell surface receptors [23]. This allows for targeted drug delivery to specific tissues or cells, including cancer cells, improving therapeutic efficacy while minimizing side effects.

5.1.3 Nanoparticles and Nanocapsules: Chitosan-based nanoparticles or nanocapsules are widely used for drug encapsulation. The small size of these particles enables efficient drug loading and targeted delivery to specific sites in the body. They also facilitate sustained or controlled release profiles, enhancing drug stability and reducing dosing frequency [24].

5.1.4 Transdermal Drug Delivery: Chitosan is used in transdermal drug delivery systems, such as patches or gels, because of its ability to enhance drug penetration through the skin. It acts as a penetration enhancer and can facilitate the delivery of a wide range of drugs, including proteins, peptides, and small molecules.

5.1.5 Inhalation Drug Delivery: Chitosan is also explored in inhalation drug delivery systems for targeting the lungs [25]. Chitosan-based microparticles can be used for the delivery of vaccines, antibiotics, or other therapeutics to the respiratory system, offering potential benefits in treating lung infections or diseases.

5.1.6 Gene Delivery: Due to its positive charge, chitosan can form complexes with negatively charged DNA or RNA, making it a suitable vector for gene delivery. Chitosan-based formulations are used in gene therapy to deliver genetic material to target cells for the treatment of genetic disorders or cancers [26].

5.1.7 Hydrogels for Drug Delivery: Chitosan-based hydrogels can be used as carriers for controlled drug release [27]. These hydrogels can be designed to respond to environmental factors like pH, temperature, or enzymatic activity, allowing for localized drug release and enhanced therapeutic outcomes.

5.1.8 Wound Healing and Localized Drug Delivery: Chitosan has also been utilized in wound healing applications, where it can deliver antibiotics or other drugs locally to promote healing and prevent infection. It can be incorporated into dressings or hydrogels that release drugs in a controlled manner at the wound site [28].

5.2. Biomedical Applications

5.2.1. Bone Regeneration

- **Bone Tissue Engineering:** Chitosan-based scaffolds are used for bone regeneration and repair. Its porous structure allows for cell attachment and growth, and it can be combined with other bioactive materials like hydroxyapatite or growth factors to enhance bone formation.
- **Osteoporosis Treatment:** Chitosan has been explored for use in the treatment of osteoporosis due to its ability to enhance bone mineralization and stimulate osteoblast activity, supporting bone health and regeneration.

Chitosan is often used to create 3D porous scaffolds that support bone regeneration. These scaffolds provide a physical matrix for bone cells (osteoblasts) to attach and proliferate, helping to guide the formation of new bone tissue. Porosity is an essential feature, as it ensures that nutrients, oxygen, and growth factors can reach the cells within the scaffold. The scaffold also facilitates the migration of cells into the defect site [29]. Chitosan can be functionalized by incorporating osteo-inductive agents such as growth factors (e.g., bone morphogenetic proteins (BMPs), vascular endothelial growth factor (VEGF)) or mineral compounds (such as hydroxyapatite (HA) or tricalcium phosphate (TCP)) to enhance its ability to stimulate bone growth.

5.2.2. Cartilage Tissue Regeneration

Chitosan has shown significant potential in cartilage tissue regeneration due to its biocompatibility, biodegradability, and ability to support cell growth and differentiation. Cartilage regeneration is a critical area in regenerative medicine, especially for conditions like osteoarthritis or traumatic cartilage injury [30]. Chitosan, alone or in combination with other materials, is widely used in cartilage tissue engineering to promote the repair and regeneration of damaged cartilage. Here's how chitosan is applied in cartilage tissue regeneration:

- **Porous Scaffolds:** Chitosan can be used to create 3D scaffolds with a porous structure that mimics the extracellular matrix (ECM) of cartilage [31]. These scaffolds allow for the attachment, proliferation, and differentiation of chondrocytes (cartilage cells), providing a supportive environment for cartilage regeneration.
- **Customizable Properties:** Chitosan-based scaffolds can be tailored in terms of porosity, mechanical strength, and degradation rate to suit the needs of cartilage tissue. This customization helps in providing an appropriate environment for cell migration and tissue formation [32].
- **Combination with Other Biomaterials:** Chitosan is often combined with other materials like hydroxyapatite, collagen, or alginate to improve the mechanical properties and enhance cartilage regeneration. Hydroxyapatite, for example, mimics the mineral content of bone, while collagen provides structural support for chondrocyte growth.

5.2.3. Cardiac Tissue Regeneration

Cardiac tissue regeneration is an area of intense research, particularly for patients with heart disease, myocardial infarction (heart attack), or other forms of cardiac injury. The heart has a very limited capacity to regenerate damaged tissue, leading to permanent scarring and a decline in heart function. Chitosan, a natural biopolymer derived from chitin, has garnered significant interest in the field of cardiac tissue engineering due to its biocompatibility, biodegradability, anti-inflammatory properties, andability to support cellular activity. Chitosan's ability to create supportive scaffolds for cardiomyocytes (heart cells) and stem cells is one of its key roles in promoting cardiac tissue regeneration [33].

- **3D Scaffolds:** Chitosan can be processed into 3D scaffolds with a porous structure that mimics the extracellular matrix (ECM) of cardiac tissue [34]. These

scaffolds provide a supportive environment for cell attachment, proliferation, and differentiation, allowing for the regeneration of functional cardiac tissue.

- **Structural Support:** The scaffolds serve as a structural framework for the regeneration of the myocardium (heart muscle). Chitosan's ability to form hydrogels or fibrous matrices makes it ideal for creating scaffolds that can support the growth of heart cells and tissue.
- **Customization of Properties:** Chitosan-based scaffolds can be customized in terms of pore size, mechanical strength, and degradation rate to closely match the properties of native heart tissue. This ensures that the scaffold remains in place long enough to promote tissue regeneration before gradually degrading [35].

5.3. Gene Delivery

Gene delivery is the process of introducing genetic material, such as DNA or RNA, into cells to modify their function or behavior. Chitosan's cationic charge allows it to interact with the negatively charged DNA through electrostatic interactions [36]. The chitosan-DNA complexes protect the nucleic acids from degradation by nucleases and enhance their stability in biological environments. Chitosan can be used to prepare nanoparticles that encapsulate DNA or RNA, forming chitosan/DNA nanoparticles. These nanoparticles have several advantages for gene delivery, including improved cellular uptake, controlled release, and targeted delivery.

- **Gene Therapy:** Chitosan is widely used for gene therapy applications, such as the delivery of genes to treat genetic disorders (e.g., cystic fibrosis, muscular dystrophy) and cancers. Chitosan-based delivery systems can facilitate the transfer of therapeutic genes to specific tissues, thereby offering targeted treatments with reduced side effects (Li, B *et al* 2020) [37].
- **Vaccine Development:** Chitosan-based systems can be used to deliver DNA or RNA vaccines [38]. The ability of chitosan to protect and deliver antigens or genetic material directly to immune cells makes it a potential candidate for developing new vaccine delivery systems.
- **Stem Cell Therapy:** In stem cell-based therapies, chitosan is used to deliver genes that enhance stem cell differentiation, proliferation, or homing to specific tissues [39]. This can improve the therapeutic efficacy of stem cell therapies in tissue regeneration.
- **Cancer Therapy:** Chitosan has been used for delivering genes that can induce apoptosis (programmed cell death) in cancer cells or enhance the immune response against tumors. By using chitosan to deliver tumor-suppressor genes or therapeutic proteins, targeted cancer therapies can be developed [40].

References

1. Aranaz I, Alcántara AR, Civera MC, Arias C, Elorza B, Heras Caballero A, *et al*. Chitosan: An overview of its properties and applications. Polymers. 2021;13(19):3256.
2. Yanat M, Schroën K. Preparation methods and applications of chitosan nanoparticles with an outlook toward reinforcement of biodegradable packaging. Reactive and Functional Polymers. 2021;161:104849.
3. Huq T, Khan A, Brown D, Dhayagude N, He Z, Ni Y. Sources, production and commercial applications of fungal chitosan: A review. Journal of Bioresources and Bioproducts. 2022;7(2):85-98.
4. Madni A, Kousar R, Naeem N, Wahid F. Recent advancements in applications of chitosan-based biomaterials for skin tissue engineering. Journal of Bioresources and Bioproducts. 2021;6(1):11-25.
5. Joseph SM, Krishnamoorthy S, Paranthaman R, Moses JA, Anandharamakrishnan C. A review on source-specific chemistry, functionality, and applications of chitin and chitosan. Carbohydrate Polymer Technologies and Applications. 2021;2:100036.
6. Pellis A, Guebitz GM, Nyanhongo GS. Chitosan: sources, processing and modification techniques. Gels. 2022;8(7):393.
7. Kou SG, Peters LM, Mucalo MR. Chitosan: A review of sources and preparation methods. International Journal of Biological Macromolecules. 2021;169:85-94.
8. Issahaku I, Tetteh IK, Tetteh AY. Chitosan and chitosan derivatives: Recent advancements in production and applications in environmental remediation. Environmental Advances. 2023;11:100351.
9. Kumari S, Kishor R. Chitin and chitosan: origin, properties, and applications. In: Kumari S, editor. Handbook of chitin and chitosan. Amsterdam: Elsevier; 2020. p. 1-33.
10. Hahn T, Tafi E, Paul A, Salvia R, Falabella P, Zibek S. Current state of chitin purification and chitosan production from insects. Journal of Chemical Technology and Biotechnology. 2020;95(11):2775-2795.
11. Tang RH, Li M, Liu LN, Zhang SF, Alam N, You M, *et al*. Chitosan-modified nitrocellulose membrane for paper-based point-of-care testing. Cellulose. 2020;27(7):3835-3846.
12. Yan D, Li Y, Liu Y, Li N, Zhang X, Yan C. Antimicrobial properties of chitosan and chitosan derivatives in the treatment of enteric infections. Molecules. 2021;26(23):7136.
13. Yilmaz Atay H. Antibacterial activity of chitosan-based systems. In: Jana S, editor. Functional chitosan: drug delivery and biomedical applications. Amsterdam: Elsevier; 2020. p. 457-489.
14. Kong Y, Zhang W, He T, Yang X, Bi W, Li J, *et al*. Asymmetric wettable polycaprolactone-chitosan/chitosan oligosaccharide nanofibrous membrane as antibacterial dressings. Carbohydrate Polymers. 2023;304:120485.
15. Li J, Feng Y, Chen W, Zhang S, Ma J, Chen S, *et al*. Electroactive materials: innovative antibacterial platforms for biomedical applications. Progress in Materials Science. 2023;132:101045.
16. Zhao Q, Fan L, Liu Y, Li J. Recent advances on formation mechanism and functionality of chitosan-based conjugates and their application in o/w emulsion systems: A review. Food Chemistry. 2022;380:131838.
17. Karadeniz F. *In vitro* anti-HIV-1 activity of chitosan oligomers N-conjugated with asparagine and glutamine. BioTech. 2023;12(1):18.
18. Lima BV, Oliveira MJ, Barbosa MA, Goncalves RM, Castro F. Immunomodulatory potential of chitosan-based materials for cancer therapy: a systematic review of *in vitro*, *in vivo* and clinical studies. Biomaterials Science. 2021;9(9):3209-3227.

19. Mohyuddin SG, Qamar A, Hu CY, Chen SW, Wen JY, Liu XX, *et al*. Effect of chitosan on blood profile, inflammatory cytokines by activating TLR4/NF-κB signaling pathway in intestine of heat stressed mice. Scientific Reports. 2021;11(1):20608.
20. Jhaveri J, Raichura Z, Khan T, Momin M, Omri A. Chitosan nanoparticles-insight into properties, functionalization and applications in drug delivery and theranostics. Molecules. 2021;26(2):272.
21. Farinha I, Freitas F. Chemically modified chitin, chitosan, and chitinous polymers as biomaterials. In: Kumari S, editor. Handbook of chitin and chitosan. Amsterdam: Elsevier; 2020. p. 43-69.
22. De Gaetano F, Marino A, Marchetta A, Bongiorno C, Zagami R, Cristiano MC, *et al*. Development of chitosan/cyclodextrin nanospheres for levofloxacin ocular delivery. Pharmaceutics. 2021;13(8):1293.
23. De Gaetano F, d'Avanzo N, Mancuso A, De Gaetano A, Paladini G, Caridi F, *et al*. Chitosan/cyclodextrin nanospheres for potential nose-to-brain targeting of idebenone. Pharmaceuticals. 2022;15(10):1206.
24. Kantak MN, Bharate SS. Analysis of clinical trials on biomaterial and therapeutic applications of chitosan: A review. Carbohydrate Polymers. 2022;278:118999.
25. Peers S, Montembault A, Ladavière C. Chitosan hydrogels for sustained drug delivery. Journal of Controlled Release. 2020;326:150-163.
26. Trombino S, Curcio F, Poerio T, Pellegrino M, Russo R, Cassano R, *et al*. Chitosan membranes filled with cyclosporine A as possible devices for local administration of drugs in the treatment of breast cancer. Molecules. 2021;26(7):1889.
27. Patta ACF, Mathews PD, Madrid RR, Rigoni VL, Silva ER, Mertins O. Polyionic complexes of chitosan-N-arginine with alginate as pH responsive and mucoadhesive particles for oral drug delivery applications. International Journal of Biological Macromolecules. 2020;148:550-564.
28. Pellá MCG, Simão AR, Lima-Tenório MK, Tenório-Neto E, Scariot DB, Nakamura CV, *et al*. Chitosan hybrid microgels for oral drug delivery. Carbohydrate Polymers. 2020;239:116236.
29. Ryu JH, Choi JS, Park E, Eom MR, Jo S, Lee MS, *et al*. Chitosan oral patches inspired by mussel adhesion. Journal of Controlled Release. 2020;317:57-66.
30. Vasdev N, Chaudhari N, Polaka S, Rajpoot K, Gondaliya P, Sayyed AA, *et al*. Current progress in preservative-free topical ophthalmic formulations. Journal of Drug Delivery Science and Technology. 2023;79:103996.
31. Zamboulis A, Nanaki S, Michailidou G, Koumentakou I, Lazaridou M, Ainali NM, *et al*. Chitosan and its derivatives for ocular delivery formulations: Recent advances and developments. Polymers. 2020;12(7):1519.
32. Algharib SA, Dawood A, Zhou K, Chen D, Li C, Meng K, *et al*. Preparation of chitosan nanoparticles by ionotropic gelation technique: Effects of formulation parameters and *in vitro* characterization. Journal of Molecular Structure. 2022;1252:132129.
33. Dubashynskaya NV, Golovkin AS, Kudryavtsev IV, Prikhodko SS, Trulioff AS, Bokatyi AN, *et al*. Mucoadhesive cholesterol-chitosan self-assembled particles for topical ocular delivery of dexamethasone. International Journal of Biological Macromolecules. 2020;158:811-818.
34. Elkomy MH, Ali AA, Eid HM. Chitosan on the surface of nanoparticles for enhanced drug delivery: A comprehensive review. Journal of Controlled Release. 2022;351:923-940.
35. Eid HM, Naguib IA, Alsantali RI, Alsalahat I, Hegazy AM. Novel chitosan-coated niosomal formulation for improved management of bacterial conjunctivitis: A highly permeable and efficient ocular nanocarrier for azithromycin. Journal of Pharmaceutical Sciences. 2021;110(8):3027-3036.
36. Fang G, Yang X, Wang Q, Zhang A, Tang B. Hydrogels-based ophthalmic drug delivery systems for treatment of ocular diseases. Materials Science and Engineering C. 2021;127:112212.
37. Li B, Wang J, Gui Q, Yang H. Drug-loaded chitosan film prepared via facile solution casting and air-drying of plain water-based chitosan solution for ocular drug delivery. Bioactive Materials. 2020;5(3):577-583.
38. Bao Z, Yu A, Shi H, Hu Y, Jin B, Lin D, *et al*. Glycol chitosan/oxidized hyaluronic acid hydrogel film for topical ocular delivery of dexamethasone and levofloxacin. International Journal of Biological Macromolecules. 2021;167:659-666.
39. Jeong WY, Kwon M, Choi HE, Kim KS. Recent advances in transdermal drug delivery systems: A review. Biomaterials Research. 2021;25:1-15.
40. Phatale V, Vaiphei KK, Jha S, Patil D, Agrawal M, Alexander A. Overcoming skin barriers through advanced transdermal drug delivery approaches. Journal of Controlled Release. 2022;351:361-380.