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Original Research Article

Chitosan in Science and Industry: A Versatile Biopolymer

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ABSTRACT
Chitosan has gained significant attention for its unique properties and applications, reflected in the growing number of patents and publications. However, its limited solubility in basic and neutral fluids restricts its use. Another challenge stems from its natural origin chitosan are a diverse family of molecules that vary in size, composition, and monomer distribution, affecting its technical and biological performance. This review examines how chemical modifications can enhance chitosan's properties and improve solubility. We also discuss its key biological characteristics and their relationship to physicochemical attributes. Furthermore, we explore two green applications: chitosan as a support for biocatalysts and its role in the eco-friendly synthesis of metallic nanoparticles. Lastly, we highlight how chitosan's technical properties contribute to the development of innovative drug delivery systems.

1. Introduction

Chitosan, a remarkable natural polysaccharide derived from chitin, consists of β-(1→4)-linked D-glucosamine and N-acetyl-D-glucosamine. Its unique biological and physicochemical properties including biocompatibility, biodegradability, antimicrobial activity, and antioxidant capabilities position it as an exceptional material across various industries, including pharmaceuticals, food processing, biotechnology, and environmental sciences.

As the primary precursor of chitosan, chitin is one of the most abundant biopolymers in nature, mainly found in the exoskeletons of crustaceans, insects, fungi, and certain algae. Chitosan is primarily produced through the chemical deacetylation of chitin, and the degree of deacetylation (DD) plays a crucial role in determining its solubility and biological activity as shown in figure 1. The growing interest in chitosan both commercially and scientifically arises from its vast array of applications, establishing it as a valuable resource for drug delivery systems, antimicrobial agents, and biocatalyst support [1].

Nonetheless, chitosan faces several challenges. Its limited solubility in neutral and basic media can restrict its use in certain applications. Additionally, as a naturally derived polymer, chitosan exhibits variability in molecular weight, degree of acetylation, and structural properties, which can influence its biological and technological performance. Recent research efforts have been directed toward modifying chitosan's chemical structure to enhance its solubility, stability, and bioactivity. This paper provides a comprehensive overview of chitosan's fundamental properties, its technological applications, and its future prospects. Particular emphasis is placed on its role in sustainable processes, including the synthesis of metallic nanoparticles and biocatalysis, along with its significant potential in drug delivery systems.

1.1 Physicochemical properties of chitosan

1. Crystallinity of Chitosan

Chitosan is classified as a semi-crystalline biopolymer, indicating that it contains both crystalline and amorphous sections. The degree of crystallinity is primarily affected by the degree of deacetylation (DDA), molecular weight, and the conditions under which it is processed. A higher DDA (greater than 85%) promotes the formation of more crystalline areas due to enhanced hydrogen bonding, while a lower DDA (less than 50%) leads to an amorphous structure that demonstrates improved solubility [3].

The crystallinity of chitosan influences its mechanical properties, solubility, and bioactivity. Crystalline chitosan exhibits greater strength and stability, making it suitable for use in biomedical membranes and scaffolds. Conversely, amorphous chitosan is more soluble, making it preferable for applications in drug delivery and coatings.

Techniques such as X-ray diffraction (XRD), FTIR spectroscopy, and DSC can be utilized to analyze the crystallinity of chitosan. Modifications like crosslinking or blending can be performed to tailor its crystallinity for particular uses [4].

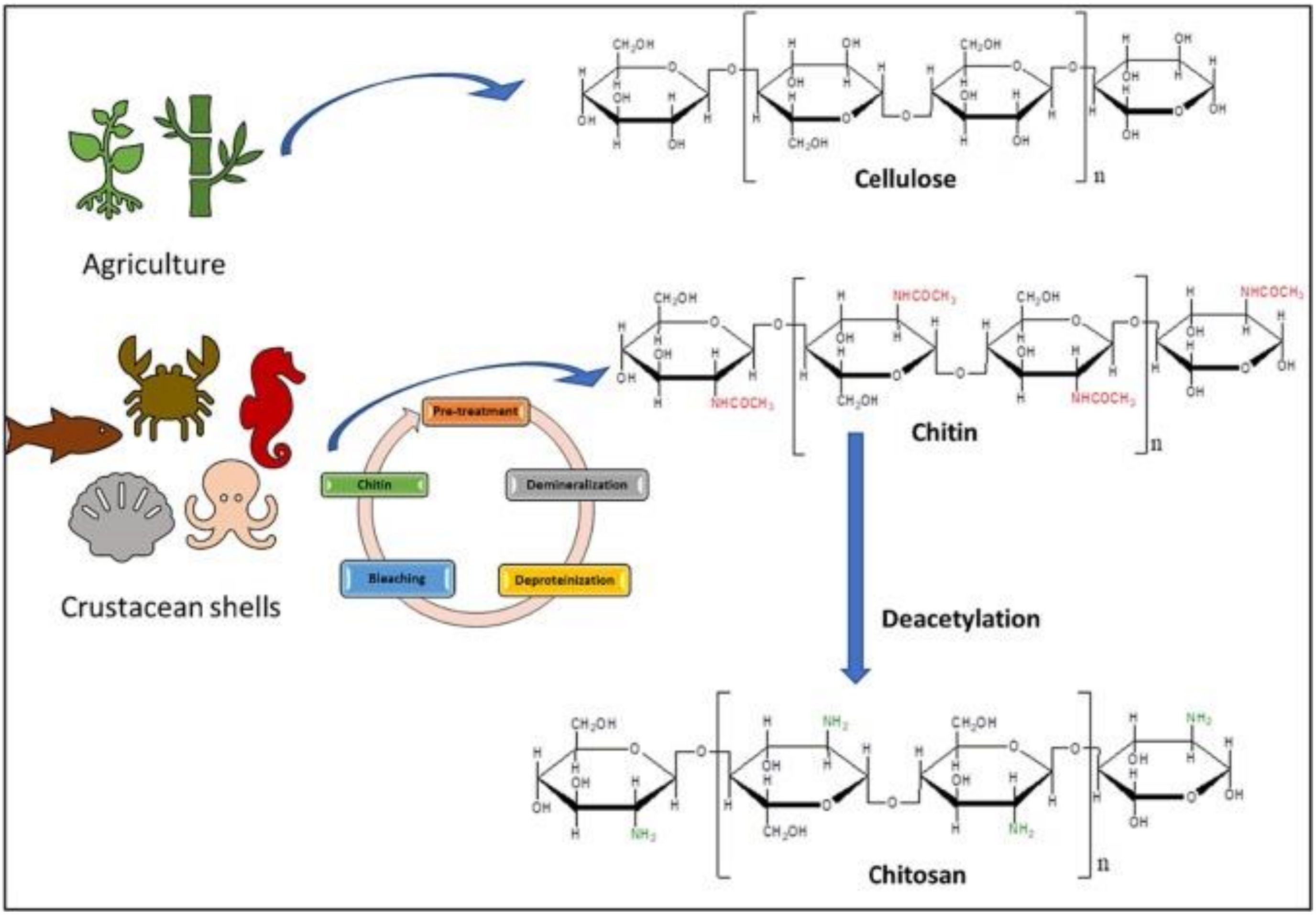

Figure 1: Chitosan in Science and Industry [2].

2. Moisture Absorption of Chitosan

Chitosan possesses a significant capacity for moisture absorption attributed to the presence of hydrophilic functional groups (-OH and -NH_2) within its structure. This characteristic enables it to hold onto water, making it advantageous for applications such as wound dressings, food packaging, and drug delivery systems.

Several factors influence the moisture absorption of chitosan, including:

- **Degree of Deacetylation (DDA):** An increased DDA enhances hydrophilicity, resulting in greater moisture absorption.
- **Molecular Weight:** Chitosan with a lower molecular weight tends to absorb more moisture due to an increased surface area.
- **Environmental Humidity:** Chitosan readily takes in moisture in humid conditions.

While moisture absorption can boost biodegradability and bioactivity, excessive water uptake may compromise mechanical stability. Therefore, techniques such as cross-linking or blending with hydrophobic materials are employed to manage water retention for various applications [5].

3. Solubility

Chitosan's solubility is a vital property, influencing its range of applications across different fields. While it is insoluble in both water and organic solvents, it can dissolve in acidic solutions (pH < 6.5) due to the protonation of amino groups. However, high molecular weight chitosan can still remain difficult to dissolve, even in acidic environments.

The degree of acetylation (DA) and molecular weight (MW) play a critical role in determining the solubility of chitosan. Chitosan oligomers, which have lower molecular weights, are soluble over a wider pH range, rendering them more suitable for biomedical applications. To address solubility challenges, researchers have developed water-soluble chitosan derivatives such as carboxymethyl chitosan, N-trimethyl chitosan, and sulfated chitosan.

4. Viscosity

The viscosity of chitosan is an important consideration, which is influenced by its molecular weight and degree of deacetylation. Chitosan with a higher molecular weight creates more viscous solutions, which can be difficult to manage in industrial settings. Additionally, the viscosity of chitosan solutions is affected by pH, with lower pH values leading to increased expansion of the polymer chain due to electrostatic repulsion among protonated amino groups.

5. Chemical Modifications

Chitosan is capable of undergoing various chemical modifications to enhance its solubility, stability, and functional characteristics [6].

Significant modifications include:

Phosphorylation: Enhances solubility in water and introduces chelating capabilities.

Quaternization: Improves solubility in neutral and basic environments, boosting its antimicrobial properties.

Sulfonation: Increases water solubility and enhances antioxidant capabilities.

Depolymerization: Produces low-molecular-weight chitosan and chitooligosaccharides, which exhibit superior bioactivity.

6. Degree of Deacetylation (DDA) of Chitosan

The degree of deacetylation (DDA) indicates the percentage of acetyl groups (-$COCH_3$) that have been removed from chitin to generate chitosan. It is a crucial factor that impacts solubility, biocompatibility, crystallinity, and biological effectiveness.

- **High DDA (over 85%)** results in freer amine (-NH_2) groups, allowing chitosan to be highly soluble in acidic environments and more biologically active.
- **Low DDA (under 50%)** retains a greater number of acetyl groups, leading to increased crystallinity and reduced solubility.

DDA can be assessed through techniques such as FTIR spectroscopy, NMR, and titration methods. Managing DDA allows for the customization of chitosan for applications ranging from drug delivery and wound healing to water purification and food preservation.

7. Molecular Weight of Chitosan

The molecular weight (MW) of chitosan is a significant factor that affects its solubility, viscosity, mechanical strength, and biological activity. Chitosan is categorized into three groups based on its molecular weight:

- **Low Molecular Weight (LMW, <50 kDa):** Exhibits high solubility, lower viscosity, and improved bioavailability, making it suitable for drug delivery and antimicrobial coatings.
- **Medium Molecular Weight (MW, 50–300 kDa):** Shows balanced properties, often applied in food packaging and biomedical fields.
- **High Molecular Weight (HMW, >300 kDa):** Characterized by greater viscosity and superior mechanical properties, making it ideal for use in wound healing and scaffolds.

Molecular weight can be determined using gel permeation chromatography (GPC) and can be manipulated through depolymerization or enzymatic degradation. Tailoring these properties enables the optimization of chitosan for specific applications. The physiochemical properties if chitosan is graphically shown in Figure 2.

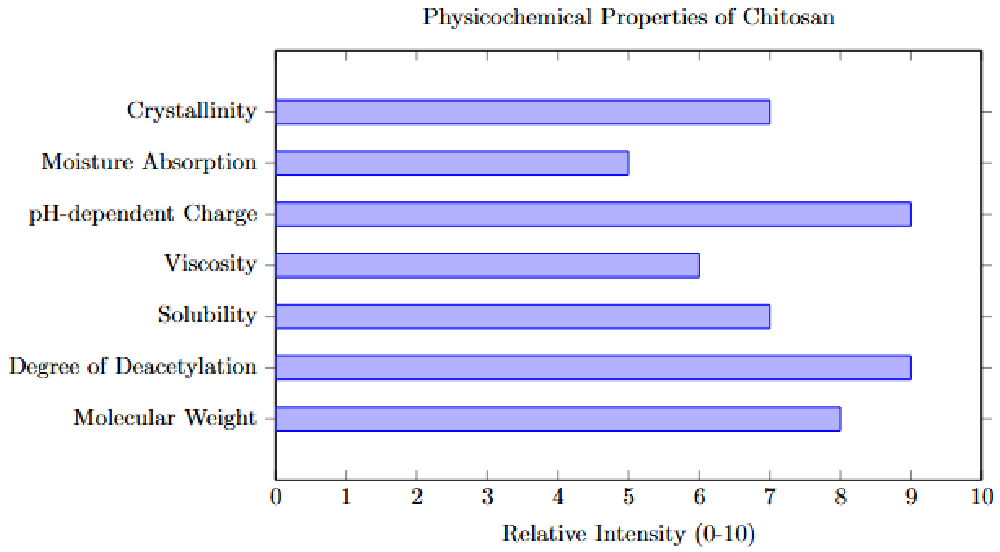

Figure 2: Physicochemical properties of chitosan.

1.2 Biological properties of chitosan

The biological properties if chitosan is graphically shown in Figure 3.

1. Biocompatibility

Biocompatibility refers to a material's ability to safely interact with biological systems without causing any toxicity or adverse reactions. Chitosan is recognized for its high biocompatibility, which makes it ideal for use in biomedical and pharmaceutical fields.

Factors Influencing Chitosan's Biocompatibility:

Natural Source: As it is derived from chitin, it is considered safe for biological applications.

Non-Toxic & Non-Immunogenic: It does not provoke significant immune responses.

Biodegradability: It decomposes in the body into non-toxic byproducts over time.

Hydrophilicity & Functional Groups: It has strong interactions with biological tissues and cells.

2. Antimicrobial properties

Chitosan possesses strong antimicrobial effects against a range of bacteria, fungi, and viruses. Its antimicrobial action is believed to involve:

Electrostatic Interactions: The positively charged chitosan binds to the negatively charged membranes of microbial cells, resulting in cell leakage and death.

Inhibition of RNA/DNA Synthesis: Chitosan can penetrate microbial cells and disrupt the replication of genetic material.

Nutrient Deprivation: It creates a barrier on microbial surfaces that hinders the uptake of essential nutrients. The effectiveness of chitosan's antimicrobial properties is influenced by factors such as molecular weight, degree of deacetylation, concentration, and environmental pH. Low molecular weight chitosan tends to be more effective against Gram-negative bacteria, while higher molecular weight variants are more effective against Gram-positive bacteria.

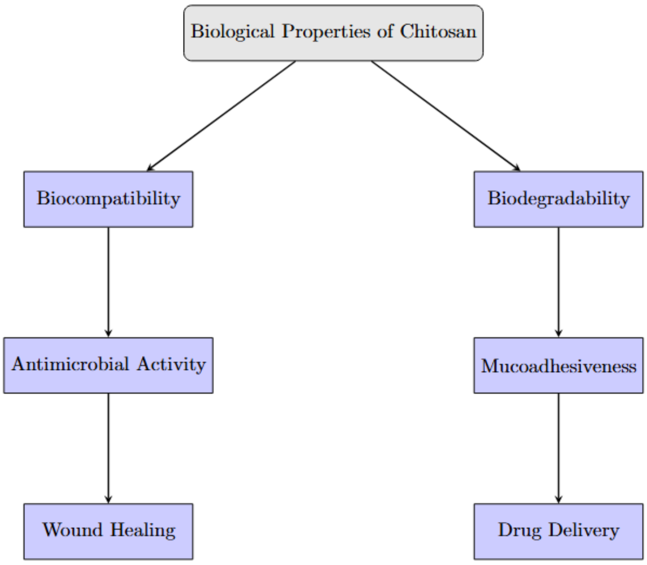

Figure 3: Biological properties of chitosan.

3. Antioxidant properties

Chitosan displays the ability to scavenge free radicals, primarily due to its hydroxyl and amino groups. Its antioxidant effects can be enhanced through chemical modifications, like adding gallic acid or phenolic compounds. Research indicates that low-molecular-weight chitosan derivatives exhibit better antioxidant abilities than their high-molecular-weight counterparts.

4. Anti-inflammatory properties

Chitosan and its derivatives show promising anti-inflammatory effects by regulating cytokine release and blocking inflammatory pathways. Particularly, chitooligosaccharides have been shown to decrease pro-inflammatory mediators such as Nitric Oxide (NO) and Tumor Necrosis Factor-alpha (TNF-α). The anti-inflammatory properties of chitosan make it a compelling candidate for managing inflammatory diseases [7].

5. Muco adhesiveness of chitosan

Mucoadhesiveness refers to a material's ability to stick to mucosal surfaces, such as those found in the gastrointestinal tract, nasal passages, eyes, and mouth. Chitosan, being a natural mucoadhesive polymer, is extremely useful in drug delivery, wound healing, and tissue engineering.

Chitosan's ability to adhere to mucosal surfaces can be attributed to:

- **Electrostatic Interactions:** The positively charged (-NH-) groups in chitosan interact with the negatively charged mucins present in the mucus layer.
- **Hydrogen Bonding & Hydrophilicity:** This property enhances its retention on mucosal surfaces.
- **Bioadhesive Polymer Network:** It forms a gel-like structure that improves drug absorption.

1.3 Chitosan in green processes

The green process of chitosan is graphically shown in Figure 4.

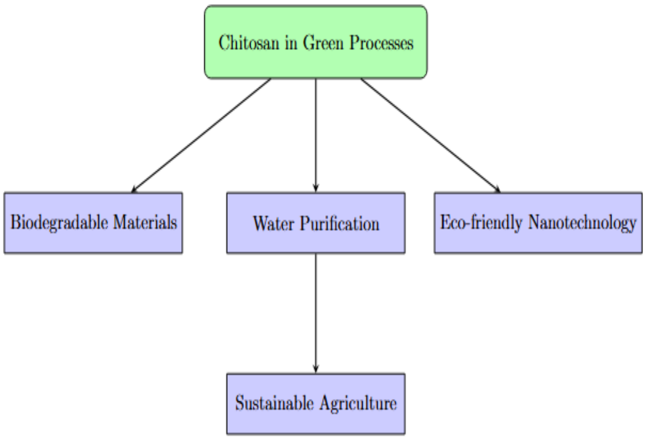

Figure 4: Green process of chitosen.

1. Biodegradable materials

Chitosan is extensively utilized in biodegradable products, acting as a substitute for synthetic plastics in packaging, biomedical frameworks, and coatings, thus supporting environmental sustainability. It is biodegradable and decomposes into harmless byproducts, finding applications in biodegradable films, packaging, and biomedical scaffolds, effectively replacing synthetic plastics in eco-friendly packaging solutions.

2. Water purification

In the realm of water treatment, chitosan serves as a potent bioadsorbent, effectively extracting heavy metals, dyes, and contaminants through flocculation and filtration, which enhances the eco-friendliness of wastewater treatment processes. It acts as a bioadsorbent for eliminating heavy metals and pollutants from wastewater and is incorporated in filtration membranes to boost water purification effectiveness. Chitosan-based flocculants facilitate the coagulation of pollutants.

3. Eco-friendly nanotechnology

Chitosan also plays a crucial role in environmentally friendly nanotechnology, participating in the synthesis of metallic nanoparticles like silver, gold, and copper. By acting as a natural reducing and stabilizing agent, it removes the necessity for toxic chemicals in nanoparticle production, making it suitable for applications such as antimicrobial, catalytic, and biomedical uses.

This area includes:

- Synthesis of Metallic Nanoparticles Chitosan functions as a reducing and stabilizing agent in the environmentally conscious creation of metallic nanoparticles (e.g., silver, gold, and copper nanoparticles).
- Biocatalysis Chitosan serves as a support framework for enzymes, enhancing their stability and reuse. It is utilized in biodegradable catalysts for green chemical reactions.

Examples of chitosan-based metallic nanoparticles include:

Silver Nanoparticles (AgNPs)**:** Employed for antibacterial coatings, wound healing, and biosensing purposes.

Gold Nanoparticles (AuNPs)**:** Used in drug delivery, imaging, and catalysis.

Palladium and Platinum Nanoparticles: Applied in catalytic processes and fuel cell advancements.

The characteristics such as size and stability of metallic nanoparticles are influenced by the molecular weight and acetylation level of chitosan. Lower molecular weight chitosan offers better stabilization, resulting in smaller and more uniform nanoparticles [8].

4. Sustainable agriculture

Chitosan-based innovations greatly enhance sustainable agriculture. It functions as a natural biopesticide, boosting plant resistance to pathogens, and is incorporated into seed coatings and biofertilizers to promote plant growth and improve soil health. By integrating chitosan into these eco-friendly applications, industries can transition toward sustainable practices, decreasing reliance on synthetic chemicals and favoring biodegradable alternatives.

5. Analysis: Improving chitosan's properties with chemical modifications

Chitosan, a biopolymer derived from chitin, is recognized for its excellent biocompatibility, biodegradability, and antimicrobial properties. However, its practical applications are often restricted due to its limited solubility, especially under neutral and basic conditions. Chemical modifications provide a robust approach to enhance the physicochemical characteristics of chitosan, particularly its solubility, thereby broadening its uses in biomedicine, food, pharmaceuticals, and material sciences.

6. The solubility challenge of chitosan

Chitosan is naturally soluble in acidic solutions (pH < 6.5) due to the protonation of its amine (-NH-) groups; however, it becomes insoluble in neutral and alkaline environments. This limitation restricts its application in various fields, particularly in drug delivery and biomedical settings where physiological pH (7.4) is essential. To tackle this issue, researchers have investigated different chemical modifications that introduce new functional groups, enhancing solubility across a broader pH spectrum and improving specific functionalities like antibacterial effectiveness, bioadhesion, and controlled drug release.

Table 1: Chemical modifications of chitosen.

Modification	Chemical group added	Effect on solubility	Other benefits
Carboxymethylation	-CH-COOH	Soluble in neutral and basic pH	Enhances water retention, bioavailability
Quaternization	Quaternary ammonium ($-NR_4^+$)	Soluble in a wider pH range	Improves antimicrobial and mucoadhesive properties
Sulfonation	-SO-H	Water solubility increases	Enhances anticoagulant activity
Phosphorylation	-PO-	Partial solubility improvement	Boosts osteoconductive (useful in bone regeneration)
Thiolation	-SH	Improves muco adhesion	Facilitates controlled drug release
PEGylation (Grafting of polyethylene glycol)	PEG chains	Improves solubility and biocompatibility	Reduces immunogenicity for drug delivery

2. Key chemical modifications and their effects

1. Applications of Modified Chitosan

By altering the structure of chitosan, researchers have effectively customized it for various applications as seen in table 1, including:

Drug Delivery Systems: Modified chitosan improves its solubility and enhances the precision of drug delivery.

Wound Healing and Tissue Engineering:Carboxymethylated chitosan increases biocompatibility and encourages cell attachment.

Water Treatment: Sulfonated and phosphorylated chitosan exhibit superior capacity for metal ion adsorption.

Food Industry: Chitosan derivatives enhance food preservation by boosting antimicrobial properties [9].

3. Chitosan as a support for biocatalysts and its role in the eco-friendly synthesis of metallic nanoparticles

Chitosan, a biopolymer obtained from chitin, is increasingly recognized as a sustainable support material for biocatalysts and in the environmentally friendly synthesis of metallic nanoparticles (MNPs). Its biodegradability, non-toxic nature, strong chelating ability, and potential for functionalization make it ideal for these uses [11].

3.1 Chiotosan as a support for biocatalysts

Biocatalysts, such as enzymes and microorganisms, often need stable and reusable supports to maximize their effectiveness in industrial processes. Chitosan provides several advantages:

1. High Porosity and Surface Area This feature facilitates the immobilization of enzymes.

2. Biocompatibility Chitosan helps maintain enzyme activity without causing denaturation.

3. Amino and Hydroxyl Functional Groups ($-NH_2$, -OH) These groups permit chemical modifications that can enhance stability.

4. Reusability Chitosan improves the lifespan of enzymes and lowers costs.

3.1.1 Chitosan-based biocatalyst systems

Chitosan can be modified or cross-linked to create stable carriers for enzymes as seen in Table 2.

Table 2: Biocatalyst system.

Modification	Effect	Application
Glutaraldehyde Crosslinking	Increases enzyme binding stability	Industrial bioreactors
Carboxymethylation	Enhances solubility	Drug synthesis
Magnetic Chitosan	Allows magnetic separation	Wastewater treatment

Example: Chitosan immobilized lipase is used in biodiesel production with higher efficiency than free enzymes.

3.2 Chitosan in the eco-friendly synthesis of metallic nanoparticles

Traditional methods for synthesizing metallic nanoparticles (MNPs) often rely on toxic chemicals and harsh reaction conditions. Chitosan offers a sustainable alternative due to its properties:

Natural Reducing Agent It aids in the reduction of metal ions.

Chelating Ability Chitosan stabilizes MNPs by binding with metal ions.

Biodegradability and Non-Toxicity Its safety makes it suitable for biomedical and environmental applications.

Synthesis Process of Chitosan-Based Metallic Nanoparticles as seen in Table 3.

1. Dissolve chitosan in a mild acid.
2. Introduce a metal salt precursor (e.g., $AgNO_3$ for creating silver nanoparticles).
3. Reduction and stabilization take place as chitosan functions as both the reducing and capping agent.
4. This results in the formation of stable nanoparticles with controlled dimensions.

Table 3: Stable nanoparticles.

Metallic nanoparticle	Function of chitosan	Application
Silver (AgNPs)	Reducing & stabilizing agent	Antimicrobial coatings
Gold (AuNPs)	Nanoparticle template	Drug delivery
Iron (FeNPs)	Magnetic support	Water purification
Zinc Oxide (ZnONPs)	Encapsulation for stability	Sunscreen & UV filters

Example: Chitosan-AgNPs show high antimicrobial activity and are used in wound dressings and food packaging.

3.3 Sustainable and industrial implications

Pharmaceuticals → Enzyme carriers for drug synthesis.

Bioremediation → Magnetic chitosan-FeNPs for wastewater treatment.

Green Catalysis → Chitosan-supported metal NPs for organic reactions.

Antimicrobial Coatings → Chitosan-AgNPs for medical textiles and packaging.

4. Chitosan's technical properties and their role in innovative drug delivery systems

Chitosan has proven to be a potent biopolymer in the field of drug delivery, thanks to its biodegradability, biocompatibility, mucoadhesive characteristics, and capacity to improve drug absorption. These properties facilitate the creation of sophisticated drug delivery systems that are controlled, targeted, and capable of sustained release [11].

4.1 Key technical properties of chitosan for drug delivery

The drug delivery of chitosan is shown in Figure 5. Table 4 shows properties of drug delivery of chitosan [12].

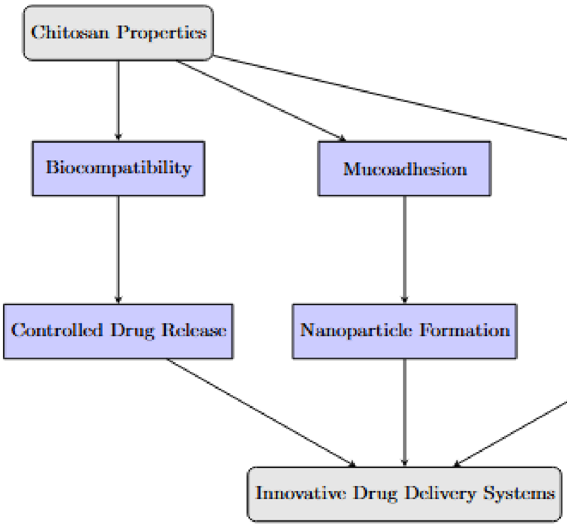

Figure 5: Drug delivery system.

Table 4: Chitosan properties for drug delivery.

Technical property	Role in drug delivery
Biodegradability and biocompatibility	Safe for human use, minimizes toxicity
Mucoadhesive nature	Enhances retention time on mucosal surfaces (oral, nasal, ocular)
pH-Sensitive solubility	Facilitates targeted drug release in acidic environments (e.g., stomach)
Permeation-enhancing ability	Opens tight junctions in epithelial cells for better drug absorption
Controlled drug release	Allows sustained release for prolonged therapeutic effects
Nanoparticle formation capability	Enables encapsulation of drugs for targeted delivery

4.2 Chitosan in gene and peptide delivery

- **Gene therapy:** Chitosan's cationic nature enables complexation with negatively charged DNA/RNA, facilitating gene delivery.
- **Peptide delivery:** Protects peptides and proteins from degradation, allowing efficient intracellular uptake.

5. Conclusions and future prospects

Chitosan is a highly adaptable biopolymer with significant applications across biomedical, pharmaceutical, and environmental fields. Its properties, including antimicrobial, antioxidant, and biocompatibility, make it an excellent choice for drug delivery, wound healing, and biocatalysis. Moreover, chitosan serves an important function as a support for biocatalysts and a stabilizer for nanoparticles, underscoring its sustainability in various industrial and environmental applications.

A major benefit of chitosan is its contribution to green chemistry, as it replaces harmful synthetic chemicals, facilitating eco-friendly biotechnological solutions [13]. Chemical modifications are vital for addressing solubility issues, which enables a broader spectrum of applications. Future research is expected to concentrate on sustainable modification methods aimed at enhancing solubility, bioactivity, and mechanical properties simultaneously.

However, the broader utilization of chitosan faces several challenges, including:

- Inconsistent quality: Variations in molecular weight and degree of acetylation can impact reproducibility.
- Limited solubility: Its poor solubility in neutral and alkaline conditions restricts some biomedical applications.
- High production costs: The expense of large-scale production of high-purity chitosan remains a barrier.

To overcome these challenges, future research should aim at optimizing production techniques, creating innovative chitosan derivatives, and broadening its applications in emerging areas suchas nanomedicine and bioprinting. With ongoing advancements, chitosan has the potential to transform multiple industries, promoting a sustainable and eco-friendlyfuture.

Authors' contributions

The author read and approved the final manuscript.

Conflicts of interest

The author declares no conflict of interest.

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Data availability

No new data were created.

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