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NARRATIVE REVIEW

Organic Modification of Chitosan: An Overview

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ABSTRACT

Alkaline deacetylation of chitin yields chitosan, a naturally occurring polymer with remarkable biological qualities like immunological, antibacterial, and Wound healing capabilities. Recently, there has been an increase in interest in modifying chitosan chemically to increase its solubility and expand its uses. The usual method for obtaining chitosan is to deacetylate chitin in an alkaline environment. Chitin is one of the most common organic molecules, generated by biosynthesis second only to cellulose yearly. Chitin plays a significant role in the exoskeleton of animals, particularly insects, mollusks, and crustaceans. It is also the main fibrillar polymer found in some fungi's cell walls. Composed of glucosamine and N-acetyl glucosamine units connected by β (1–4) glycosidic linkages, chitosan is a linear polysaccharide. The degree of deacetylation refers to the amount of glucosamine present. Actually, in a broad sense. This study reviews the major chitosan chemical changes that have been suggested in the literature. Furthermore, a vast variety of derivatives with a wide range of uses are produced by these chemical alterations. Instances of recent and pertinent instances of the various uses are provided, with a focus on tissue engineering, medication delivery, and environmental applications. Looking ahead, the future of chitosan modification appears bright, driven by advancements in smart polymers, green chemistry, and nanotechnology. These developments are facilitating the creation of tailor-made materials with diverse applications, further expanding the potential utility of chitosan in various fields.

Keywords: Chitosan, Organic modification, Graft copolymerization, Biodegradability

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INTRODUCTION:

Interestingcharacteristics ofchitosan includebiocompatibilityandbiodegradability[1], as well as non-toxic, non-immunogenic, and non-carcinogenic breakdown products [4,5]. Chitosan hence has potentialuses ina widerangeof industries, including flocculation, waste water treatment, biomedicine, and functional membranes. However, the limited solubility of chitosan in weak acid solutions restricts its potential uses [1 6]. The usual method for obtaining chitosan is to deacetylate chitin in an alkaline environment. Chitin is one of the most common organic molecules, generated by biosynthesis second only to cellulose yearly. Chitin plays a significant role in the exoskeleton of animals, particularly insects, mollusks, and crustaceans. It is also the main fibrillar polymer found in some fungi's cell walls. Chitosan is a linear polysaccharide consisting of glucosamine and N-acetyl glucosamine units connected by β (1–4) glycosidic linkages, as seen in Figure 1. The degree of deacetylation refers to the amount of glucosamine present. In fact, chitin is generally thought to become soluble in an aqueous acidic media when its deacetylation level exceeds around 50% [2,4]. To increase chitosan's solubility and expand its uses, there has been a rise in interest in chemically modifying the material recently [5]. Chitosan's solubility at neutral andalkaline pH values can besignificantly increased by derivatization, which involves adding tiny functional groups to the chitosan structure, such as carboxymethyl or alkyl groups without compromising the cationic character of the substance. Polymers having polyampholytic characteristics can be produced by substituting moieties containing carboxylic groups. Graft copolymerization has been the most popular modifying technique. Through the covalent attachment of a molecule, known as the graft, to the chitosan backbone, chitosan grafting enables the creation of functional derivatives [7,8]. This study will explain the primary techniques that have been utilized to chemically alter chitosan. There will be a few examples of the chemical reactions and experimental setups that are indicative of the field. Lastly, the most significant uses of these modified chitosan-based polymers in various industries are also covered.

Chemistry of Chitosan

Deacetylated chitin is a naturally occurring that is converted into chitosan. A linear polysaccharide consists of β-(1→4)-linked N-acetylglucosamine (GlcNAc) and glucosamine (GlcN) units [9]. Reactive functional groups, mainly amino (NH_2) and hydroxyl (OH) moieties, are dispersed throughout the polymer backbone of the compound in its chemical structure as shown in Figure 1. These functional groups operate as important sites for organic alterations and give chitosan its distinct chemical reactivity[10].

Amine Groups (NH_2): The glucosamine units of chitosan include the main amino groups, which give the polymer a basic character. A variety of changes are possible due to the amino groups' easy participation in nucleophilic substitution processes. The amine groups in chitosan are very reactive, which makes it possible to introduce a variety of functional entities including Schiff bases, amides, and esters [11].

Hydroxyl groups (OH): The hydroxyl groups that come fromthe GlcNAcand GlcN units help to make chitosan hydrophilic overall. These hydroxyl groups participate in hydrogen bonding interactions, especially those on the C-6 position of the glucosamine units. Furthermore, the hydroxyl groups have the ability to change chemically, introducing new functional groups like ethers and esters[12] .

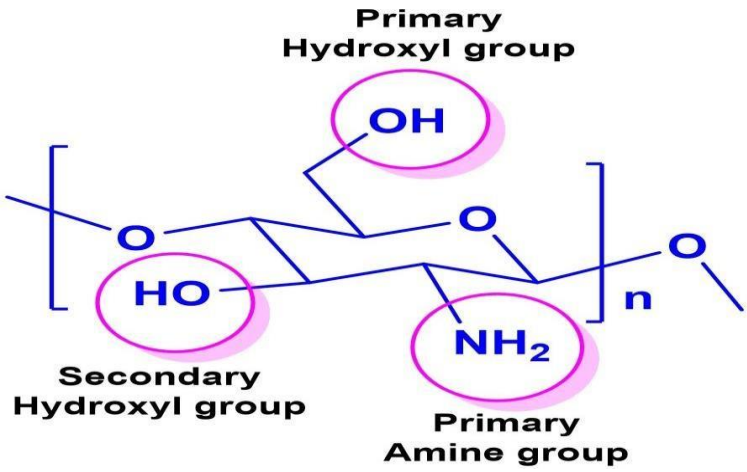
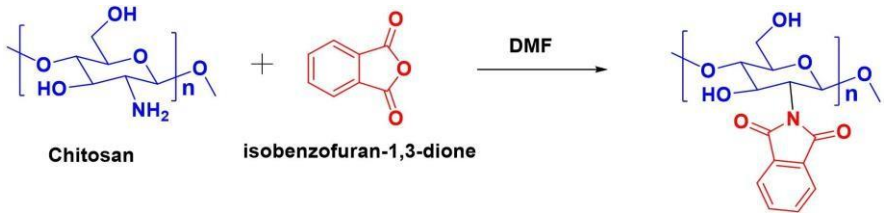


Figure 1 Structural representation of chitosan with active functional groups.

Chemical Reactivity and Protecting Groups

Chitosan's chemical reactivity results from the presence of reactive hydroxyl groups and nucleophilic amino groups. The production of amides and esters results from the interactions of the amino groups, which are nucleophiles, with electrophiles such acylating agents. On the other hand, the hydroxyl groups can react with other substances to generate ethers, esters, and other derivatives [13] . N-phthaloyl-chitosan, an essential soluble N-protected precursor for further controlled modification processes of chitosan, may be produced using a straightforward and practical process for chemoselectively protecting the amino groups of chitosan. While partial hydroxy group phthaloylation was a side consequence of typical N-phthaloylation of chitosan in N,N-dimethylformamide, the O-phthaloylation was successfully reduced by the addition of a tiny amount of hydroxy-containing substances [14] . Water was one of the most appropriate chemicals to study; as a consequence, chemoselectively N-phthaloylated chitosan was formed, devoid of any noticeable O-phthaloyl groups. The resultant N-phthaloyl-chitosan had a bulky substituent, yet it was nevertheless found to be crystalline. According to a solubility test, N-phthaloyl-chitosan showed a strong affinity for organic solvents as shown in Scheme 1[15] .



Scheme 1: Protection group for the selective reaction of hydroxyl groups [14].

METHODS OF MODIFICATION

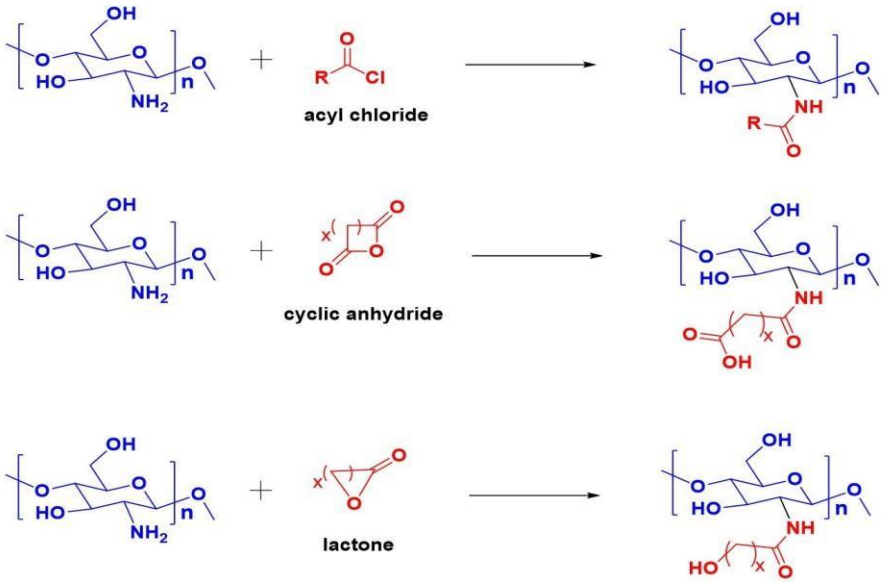
Chitosan's modification is significantly enhanced through various methods of attaching organic molecules. This allows researchers to tailor its properties for specific applications [16].

Acylation Reactions: Theprocess of acylationreactions includes addingacyl groups to chitosan, usually by means of interactions with carboxylic acids, anhydrides, or acid chlorides as shown in Scheme 2[17]. Commonly, acylation processes result in the formation of esters and amides. These changes affect the solubility, biodegradability, and interaction properties of chitosan.

Schiff Base Formation: The condensation process between the amino groups in chitosan and aldehydes or ketones form Schiff bases. The azomethine (-C=N-) connections that Schiff bases introduce to increase the uses of chitosan in bioconjugation, drug administration, and sensing[18] as shown in Scheme 3.

Amidation Coupling: Amide coupling involves the activation of carboxylic acid groups, typically facilitated by carbodiimide coupling agents, to enable their reaction with amino groups present in chitosan[19]. This process leads to the formation of amide bonds, resulting in the introduction of functional groups, as depicted in Scheme 4. The general reaction scheme for amidation coupling can be represented as follows:

Chitosan (NH_2) + Carboxylic Acid (COOH) → Amide Bond Formation



Scheme 2: Chitosan acylation with different acylating groups [17].

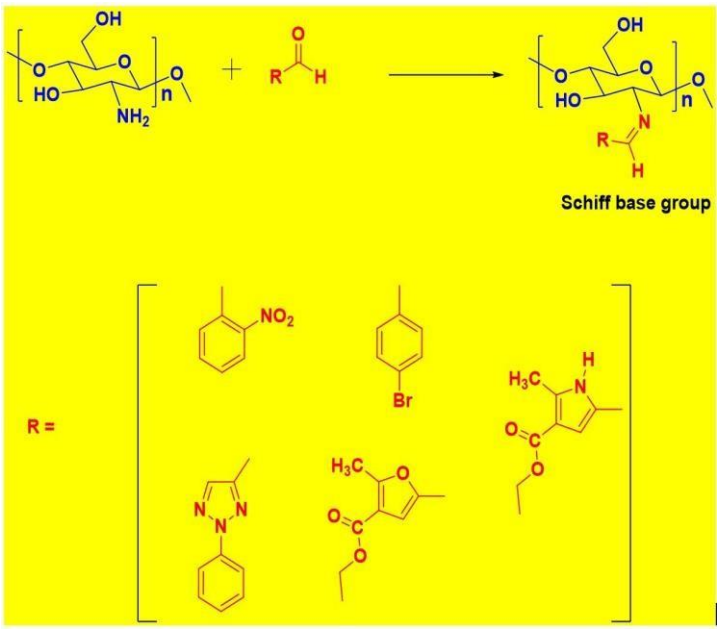
Carbodiimide coupling agents, such as N,N'-dicyclohexylcarbodiimide (DCC) or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC), are commonly used to activate the carboxylic acid groups, facilitating their reaction with the amino groups of chitosan [20].

Click Chemistry: For the modification of chitosan, click chemistry—in particular, copper-catalyzed azide-alkyne cycloaddition, or CuAAC—offers a bioorthogonal method[21,22] . Introduction of Functional Groups: Triazole linkages are created, which allow for exact control over the level of alteration while maintaining the original characteristics of chitosan as shown in Scheme 5[23] . The general reaction scheme for CuAAC can be represented as follows:

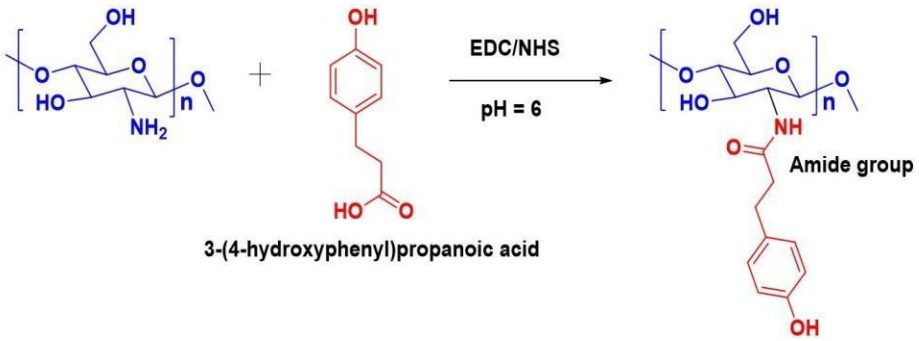
Chitosan-Alkyne + Azide ⟶ Triazole Linkage Formation

Enzymatic Modification: Usingenzymes likelipases or transaminasestocatalyzecertain reactions on chitosan is known as an enzymatic technique. Introduced Functional Groups [24] : The regioselective insertion of functional groups made possible by enzymatic modification minimizes unfavorable side effects and maintains the structural integrity of chitosan as shown in Figure 2[25] .

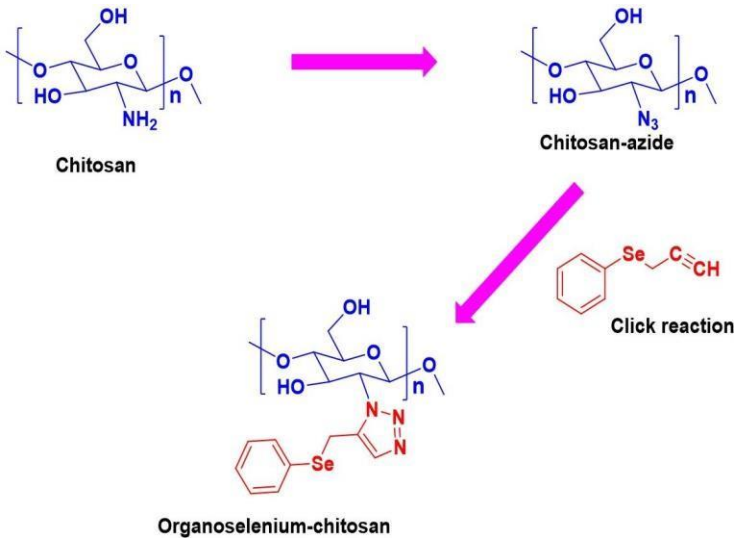
Polymer-Polymer Conjugation: There are several ways to conjugate chitosan with other polymers, such as mixing and graft copolymerization. Introduction of Functional Groups: By introducing various functionalities from the second polymer, this technique



Scheme 3: Reaction route of synthesis Schiff base group with amine group of chitosan[18] .



Scheme 4: Chitosan amide formation with acid group[20] .



Scheme 5: Click reaction of chitosan[23] .

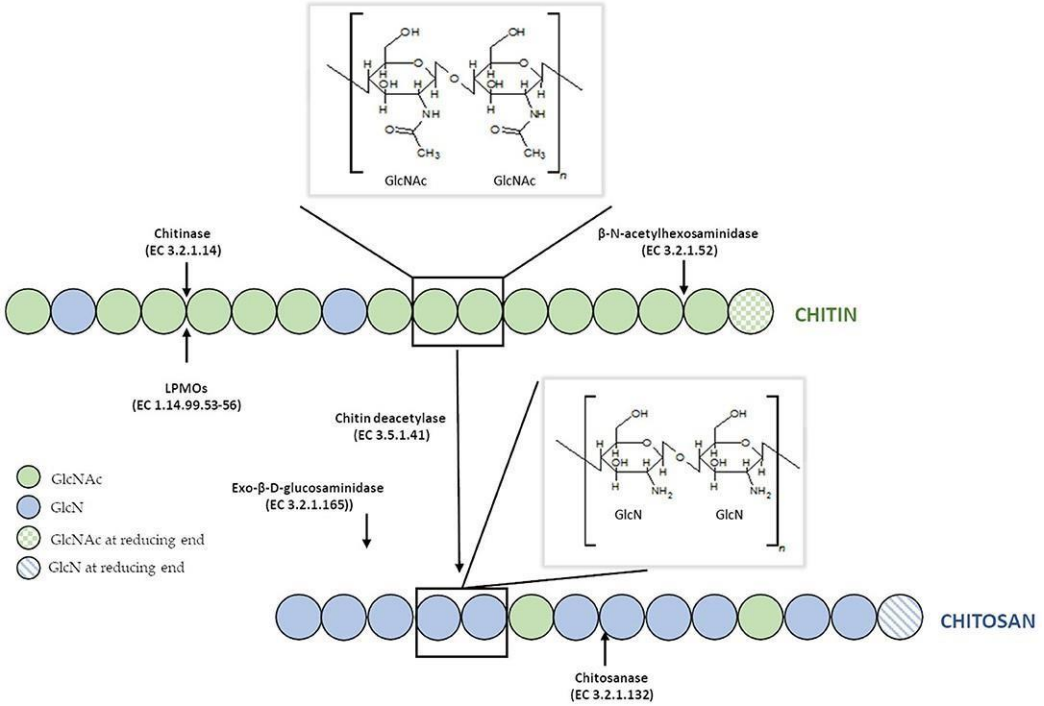
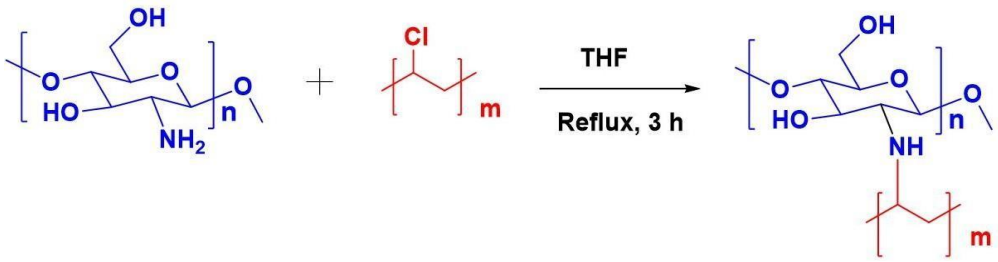


Figure 2 Enzymatic modification of chitosan [25] .

improves the mechanical, thermal, and biological characteristics of chitosan[26] . Chitosan's adaptability is enhanced by polymer-polymer connections, which go beyond the addition of functional groups and enable the development of complex materials with specific characteristics. Through a variety of techniques, chitosan may be integrated with other polymers to improve its mechanical, thermal, and biological properties [27] . By grafting polymer chains onto the chitosan backbone, a hybrid material is produced by graft copolymerization as shown in Scheme 6[28] . Grafting can be accomplished by enzymatic or free radical polymerization processes. Different functions are added by grafted polymers, which change the mechanical strength, thermal stability, and material compatibility of chitosan. This approach finds use in the creation of functional coatings, tissue engineering, and drug delivery materials [29] . After the preparation of the poly(vinyl chloride) (PVC)-chitosan thin films, the effect of filling nanoparticles on the lattice was examined[28] . Tetrahydrofuran (THF) was used to dissolve PVC and 15% nano-chitosan in order to create thin films through the casting process. Using a diffusive reflectance apparatus, the optical characteristics of the thin films were measured in the approximate wavelength range of 250–1300 nm. In addition, calculations were made for the dielectric constant, Urbach energy, transmittance, reflectance, refractive index, absorption, optical conductivity, and skin depth. Both plain and NPs-filled thin film absorbance various values [30] .



Scheme 6: Polymer-polymer modification of chitosan[28] .

Functional Groups and Their Introduction

Mainly the modification of chitosan by adding several functional groups to its chemical structures. This gives the biopolymer specific characteristics. Here, we examine the insertion of important functional groups into chitosan by their synthesis [31].

Synthesis Ester: When chitosan combines with derivatives of carboxylic acids, such as acid chlorides, anhydrides, or carboxylic acids, esters are frequently introduced through acylation reactions. Effect on Chitosan, the hydrophobicity, solubility in organic solvents, and film-forming properties of chitosan are improved by esters. Applications for modified chitosan esters include controlled release systems, medication administration, and wound healing [32] .

Synthesis Amides: When the amino groups in chitosan combine with the carboxylic

acid groups in a carbodiimide-mediated coupling process, amide groups result. Effect on the Chitosan, improvements in mechanical qualities, stability, and biocompatibility are all facilitated by amides. Biomedical applications such as medication delivery and tissue engineering frequently employ chitosan amides [33].

Synthesis Schiff Bases: The amino groups in chitosan condense with aldehydes or ketones to generate Schiff bases. Effect on Chitosan, Schiff bases form azomethine linkages, which improve chitosan's reactivity to out- side stimuli and open up new possibilities for imaging, biosensors, and drug administration [34].

Synthesis Aldehydes and Ketones: Either Schiff base production or regulated oxidation of chitosan can introduce aldehydes and ketones. Effect on Chitosan: The presence of aldehydes and ketones increases the chitosan's potential for further chemical alterations and speeds up cross-linking events, which affects how it is used to make hydrogels and transport drugs [35] .

Synthesis Quaternary Ammonium Salts: Reactions involving alkyl halides, epoxides, or other quaternizing agents add quaternary ammonium salts. Effect on Chitosan: Chitosan's antimicrobial qualities are strengthened by the addition of positively charged quaternary ammonium groups, which makes it appropriate for use in water treatment, antibacterial coatings, and wound dressings [36].

Synthesis Hydroxyl Derivatives: By reacting with different reagents, such as epoxides or isocyanates, hydroxyl derivatives can be introduced. Chitosan is impacted by hydroxyl derivatives because they improve hydrophilicity and provide more sites for chemical alteration. Tissue engineering, wound healing, and drug delivery are three areas where modified chitosan hydroxyl derivatives are useful [37].

Synthesis Thiol Groups: Through reactions with reagents containing thiols, thiol groups can be added. Effect on Chitosan: The presence of thiol groups allows chitosan to take part in thiol-disulfide exchange processes, which promotes the creation of materials that respond to stimuli and bio conjugation techniques [38]. A thorough understanding of the synthesis and effects of various functional groups leads to a customized modification of chitosan. This information may be used by researchers to create chitosan derivatives with carefully adjusted characteristics, increasing the material's versatility in a variety of applications. Figure 3 shows possible reactions to form various functional groups with chitosan.[39]

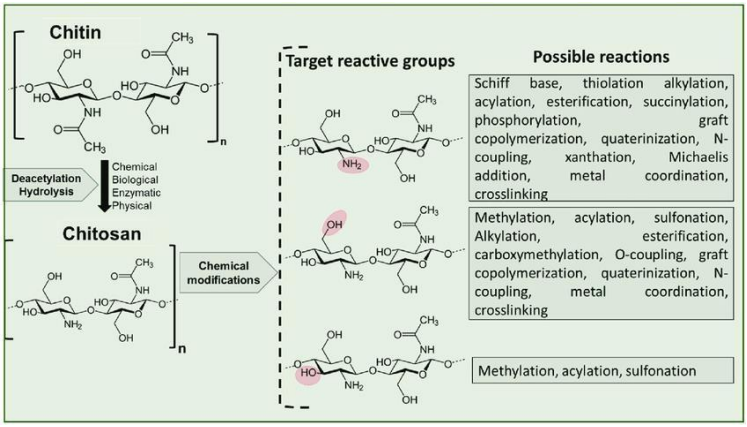


Figure 3 Possible reactions to form various functional groups with chitosan [39].

Challenges, and Future Perspectives:

In both medical and industrial applications, it is important to address the toxicity of modified chitosan[40,41] . This is because the original compound is biopolymer and biodegradable. However, this is not me the produced modified materials have the same characteristics. Another important issue should be addressed is the solubility of chitosan in common organic solvents. Thus, chitosan is either insoluble or very slightly soluble in the most of organic solvent.

CONCLUSIONS:

In conclusion, the area of chitosan organic modification is greatly expanded the range of using it in both medical and industrial applications. The desire to chemically alter chitosan to make it more soluble and extend its applications has grown recently. Chitin is typically obtained by deacetylating it in an alkaline solution to produce chitosan. One of the most prevalent organic compounds is chitin, which is produced annually via biosynthesis second only to cellulose. Animal exoskeletons, especially those of insects, mollusks, and crustaceans, heavily depend on chitin. It is also the primary fibrillar polymer present in the cell walls of some fungi. Chitosan is a linear polysaccharide made up of glucosamine and N-acetyl glucosamine units joined by β (1–4) glycosidic links. The quantity of glucosamine present is referred to as the degree of deacetylation. Well, broadly speaking. With advancements in green chemistry, smart polymers, and nanotechnology ready to open up new applications in tissue engineering, drug delivery, and other fields, the future of chitosan modification seems bright. To fully utilize this extraordinary biopolymer in a variety of scientific and industrial contexts, chitosan modification methods must be further investigated and improved.

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DECLARATIONS

Authors' contributions

Both authors contributed equally to the design, execution, and interpretation of the research, as well as the drafting and revision of the manuscript. All authors approved the final version of the manuscript and are responsible for its content.

Conflict of interest

The authors declare that they have no potential conflicts of interest.

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