PROPERTIES OF CHITOSAN AND ITS DERIVATIVES FOR BIOMEDICAL APPLICATIONS

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ABSTRACT

Deacetylation of naturally occurring chitin yields the biopolymer chitosan. Because of its insolubility in water and other common organic solvents, chitosan has very limited application and use. Chitosan, however, has reactive functional groups inside it, thus it may be chemically modified to produce chitosan derivatives. Furthermore, discussed are the uses of chitosan derivatives as an antibacterial, slow-release, targeting, and delivery method. Future medication research using chitosan derivatives has the potential to make a significant impact in biomedicine. Applications of chitosan in medicine are the focus of the current article. Chitosan is a polysaccharide that has several medical applications, including as a medication delivery mechanism, and also for its antioxidant, anti-cancer, wound-healing, and anti-microabial capabilities.

Keywords: *Chitin, Chitosan, Derivative, Biomedical, Application*

INTRODUCTION

As nanotechnology has progressed, chitosan derivatives such nanoparticles, hydrogels, microspheres, and micelles have been created. Derivatives of chitosan have use as drug delivery vehicles, vaccine adjuvants, and vaccine carriers. As a result, chitosan nanoparticles and chitosan derivatives have vast potential for usage and expansion in a variety of disciplines. In this article, we'll take a look at three of the most common ways that chitosan derivatives are used in medicine: as drug transporters, as drug materials, and to boost mucosal immunity. This study focuses on the development of methods for generating chitosan derivatives with desirable qualities like as solubility, pH sensitivity, targeting, and mucosal adherence, as these characteristics are what ultimately decide a material's potential uses. Chitin, which is made up of (14) linked 2-acetamido-2-deoxy -DGlucose, is the second most abundant natural polysaccharide on the planet. Because it is not produced by cellulose-containing organisms, chitin is often understood to be a cellulose derivative. Similar to cellulose, chitin's structure is only different at the C2 locations, where acetamide groups are found instead of hydroxyls. This chitin is converted into chitosan by a dose-dependent N deacetylation process. In 1859, while investigating the chitin's chemical and mechanical properties, Rouget stumbled onto chitosan. The linear polymer chitosan consists of α(1→4) linked 2-amino-2-deoxy-β-D-Glucopyranose that is connected together through glycosidic bonds. See Figure 1 and Figure 2 for an illustration of the molecular structure of chitin and chitosan, respectively. Deproteinization, demineralization, decolorization, and deacytelation are the four processes used to create chitosan from chitin. Throughout these procedures, chitosan goes through a number of changes, two of the most important being N acetylation and the Schiff's base reaction. Chitosan becomes very basic and soluble in aqueous acidic solution with deacetylation. By interacting with other classes of compounds, they give rise to a wide array of derivatives, including aldimines, ketimines, N-carboxymethyl chitosan, N-carboxybenzy chitosan, etc.

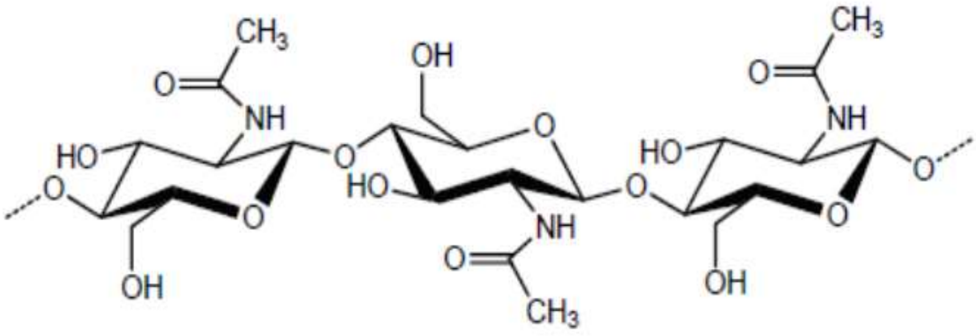

Figure 1: Structure of chitin

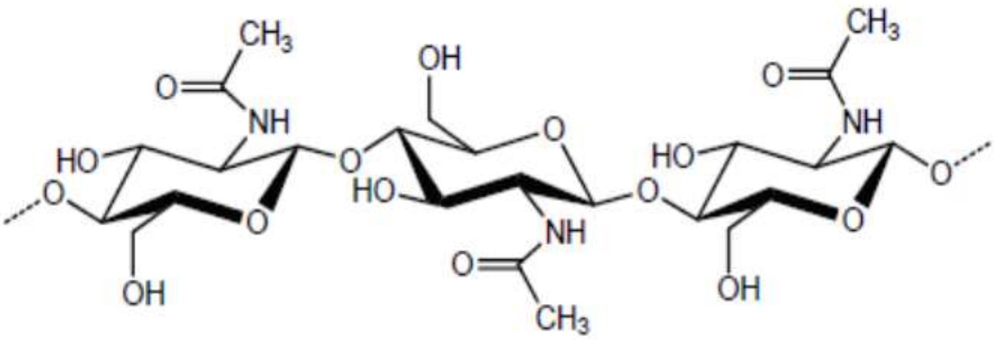

Figure 2: Structure of Chitosan

LITERATURE REVIEW

Suyeon Kim (2018) The alkaline deacetylation of chitin results in the formation of chitosan and the conversion of acetamide groups into primary amino groups. Extensive research into the vast range of biological activities of chitosan and its derivatives has led to a proliferation of potential uses, particularly in biomedicine. The solubility of chitosan in water and other solvents is crucial to its biological properties. Chitosan's bioactivities are mostly determined by its deacetylation degree (DDA) and molecular weight (MW), since the amino groups at its core are responsible for its interactions with other molecules. At higher DDA and lower MW, chitosan and its derivatives were more effective against bacteria and free radicals, and they showed promise against cancer. Chitosan oligosaccharides (COS) with a low polymerization degree are gaining a lot of attention in the medical and pharmaceutical fields because they are more water soluble and have a lower viscosity than chitosan. Chitosan and its derivatives are discussed in this review article for its antibacterial, antioxidant, anticancer, and antiinflammatory properties. Bioactivities, as well as the effects of chitosan's physicochemical properties as DDA and MW, are discussed.

Zhao, Dongying et al. (2018) Chitosan is a natural polymer that has the benefits of being biodegradable, nontoxic, and biocompatible. The medical industry is only one of several that may benefit from this. It has unparalleled potential as a delivery carrier and is simply not comparable to any other polymer. While chitosan is very impossible to dissolve in water, it does dissolve in acidic solutions. Since it is insoluble in water, it can't be used in many medicinal applications. Chitosan derivatives may be made using a variety of chemical reactions, including acylation, alkylation, sulfation, hydroxylation, quaternization, esterification, graft copolymerization, and etherification. As compared to unmodified chitosan, the chemical characteristics of modified chitosan are much better. Nanoparticles made from chitosan derivatives, for instance, have the stability and biocompatibility to be employed as drug delivery vehicles. The characteristics of chitosan, its derivatives, and their origins as nanoparticles are the primary topics of discussion in this paper. Other uses for chitosan-based nanoparticles include their use in antimicrobials, medication administration, vaccine distribution, and callus and tissue regeneration. In conclusion, chitosan-based nanoparticles have significant promise for future nano-vaccine and nano-drug development.

Gaurav Lodhi,et al (2014) Chitin is a polysaccharide found in nature that has an important function. Chitin is second only to cellulose in terms of the number of species that produce it annually. To produce chitosan, the most valuable chitin derivative, chitin is partly deacetylated in alkaline conditions or hydrolyzed enzymatically. Even though chitin and chitosan have been found to have important functional properties, their low solubility makes them unsuitable for use in food and medicine. Degradation products of chitosan and chitin are chitooligosaccharides (COS), which may be produced by enzymatic or chemical hydrolysis of chitosan. Researchers are keen to find ways to put COS and its derivatives to use in the medical field because of their high solubility and low viscosity. This study focuses on the synthesis and biological activities of chitin, chitosan, COS, and its derivatives because to the current interest in their biomedical applications.

Yogesh et al (2011) Many biological features important to medicinal chemistry have shown oxindole's use as a pharmacologically beneficial scaffold. Further supporting oxindole's value in the field of innovative drug development are the relative ease with which it may be synthesized and the frequency with which it occurs in plant-based alkaloids. It was discovered that molecules containing the oxindole moiety were widespread in plant-derived chemicals after their first isolation from Uncaria tomentosa, the so-called cat claw's plant, which grew in abundance in the Amazon jungle. Since it may be changed by a wide variety of chemical groups to develop unique biological functionalities, oxindole serves as a chemical scaffold for the fabrication and design of biological pharmacological agents. This article will summarize all current development investigations on oxindole-derived compounds and provide a broad chemical description based on existing relevant structure-activity correlations (SARs). Many different oxindole derivatives are being studied for their potential as anticancer drugs; however, some of these compounds have also demonstrated antimicrobial, -glucosidase inhibitory, antiviral, antileishmanial, antitubercular, antioxidative, tyrosinase inhibitory, PAK4 inhibitory, antirheumatoid arthritis, and intraocular pressure lowering activities. In this study, we highlight the importance of finding medications with an oxindole core, which are demonstrating and providing greater effectiveness in clinical practice, and potential benefits of developing novel oxindole compounds with wider pharmacological applications.

Atanasov, A.G., Zotchev, S.B., Dirsch, V.M. et al (2021) Traditional pharmacotherapy, notably for cancer and infectious disorders, has benefited greatly from natural compounds and their structural counterparts. Nevertheless, natural compounds have technological impediments to screening, isolation, characterisation, and optimization that have led the pharmaceutical industry to focus less on them since the 1990s. Improved analytical techniques, genome mining and engineering methodologies, and microbial culture advancements are only some of the current technical and scientific discoveries that are meeting these problems and creating new possibilities. This has resulted in a renewed focus on natural compounds as potential therapeutic leads, especially in the fight against antimicrobial resistance. In this article, we provide a brief overview of the technical advances that have opened the door to medication discovery based on natural products, before discussing some of the most promising avenues for future research.

CHITOSAN APPLICATIONS AND ITS DERIVATIVES IN THE TREATMENT OF SKIN AND SOFT TISSUE DISEASES

To clarify, chitosan is a byproduct of chitin deacetylation and is hence a naturally occurring cationic polysaccharide. Chitosan's notable antibacterial activity has led to its widespread usage in the medical community as a wound dressing. Chitosan, on the other hand, is not very water-soluble and is known to degrade quickly in the presence of moisture. These derivatives were created by synthesis modifications that improved upon the physical and chemical properties of chitosan while keeping its useful biological properties intact. Hydrogels, sponges, microspheres, nanoparticles, and thin films are only a few of the medicinal applications for chitosan and its derivatives. Because to their varied qualities, these compounds are utilized to treat a broad range of conditions, particularly those affecting the skin and other soft tissues.

Diseases of the skin and soft tissues include wounds, infections, and malignant growths on the epidermis, dermis, and fascia. Chitosan and its derivatives may be used to treat wounds caused by trauma to the skin, muscles, blood vessels, and nerves. Infected wounds may be dressed with chitosan or a derivative since bacteria and fungi are the most common causes of soft tissue infections including those of the skin and subcutaneous tissues. The most frequent kind of malignancy affecting fatty tissue, fascia, muscles, lymph nodes, and blood vessels, soft tissue sarcomas always have a dismal prognosis owing to their stealthy growth and quick spread to distant organs. The anticancer effects of chitosan and its derivatives suggest they may have use as components of medication delivery systems for the management of sarcoma. Soft tissue injuries have also been treated using chitosan-based nanoparticles, sponges, films, hydrogels, and scaffolds. The use of chitosan and its derivatives in the treatment of skin and soft tissue diseases has not yet been thoroughly evaluated, despite the field's obvious promise. This page gives a brief history of chitosan and its derivatives, structures, biological properties, and use as drug carriers. New developments in the use of chitosan and its derivatives in the prevention and treatment of skin and soft tissue damage, infection, and tumors are also covered.

Properties of Chitosan for Biomedical Applications

As a natural polysaccharide, chitin is second only to cellulose in frequency over the world. The purity of chitosan is dependent on the purity of the chitin used to make it, the method of separation, and the level of deacetylation. Both chitin and chitosan come from a wide variety of aquatic and terrestrial organisms, as well as certain bacteria. Biowaste is a byproduct of seafood processing that is converted into chitosan and chitin. This includes seafood including shrimp, lobster, crab, and squid. Nevertheless, seasonal and irregular raw material availability, ambiguity, and problems in processing conditions have hampered commercial synthesis of chitosan from biological waste generated by aquatic organisms. To this end, chitosan, a partly deacetylated polymer, has been extracted from terrestrial species including crabs, mushrooms, and insects. Out of all the land-dwelling animals, it was the silkworm and the honeybee that were singled out as potential sources of chitosan and chitin for industrial-scale use. Microorganisms that contain both chitin and chitosan include yeasts, molds, some chrysophyte algae, ciliates, and certain bacteria, most notably streptomycetes pores and Prosthecate bacterium stalks. It seems that chitosan synthesis from microorganisms is a viable alternative, since the method may be modified to produce a pure, uniform product meeting desired specifications. While many species of micro- and macro-organisms, both terrestrial and aquatic, are capable of producing chitosan and chitin, only a select handful have any commercial value.

Chitosan's unique qualities, as seen in Figure 3, make it a promising biomaterial for a wide range of medicinal uses. Chitosan's ability to prevent severe inflammation and immune system activation is one of its most remarkable features. All molecular weights and degrees of deacetylation of chitosan are safe to use. Chitosan's bactericidal capabilities stem from the polymer's cationic composition, which causes it to bind to the positively charged surfaces of bacteria and so alter the permeability of the cell membrane, thereby inhibiting bacterial growth. Deacetylated chitosan with a low pH is more effective against bacteria. Antibacterial action is enhanced against Gram-negative bacteria while exerting a lesser impact on Gram-positive bacteria when the molecular weight is decreased. To interact with the bacterial cell, chitosan needs a hydrophilic cell wall, which may be why it causes only mild damage to human cells. The mucoadhesive characteristics of chitosan are also noteworthy, as they pave the door for novel mucosal drug delivery methods and facilitate the adsorption of molecules that have no natural affinity for mucus. Chitosan increases medication uptake via epithelia by easing tight epithelial connections. When platelets and amino groups on the surface of chitosan interact, wounds heal more quickly, it has also been frequently employed in coagulation research.

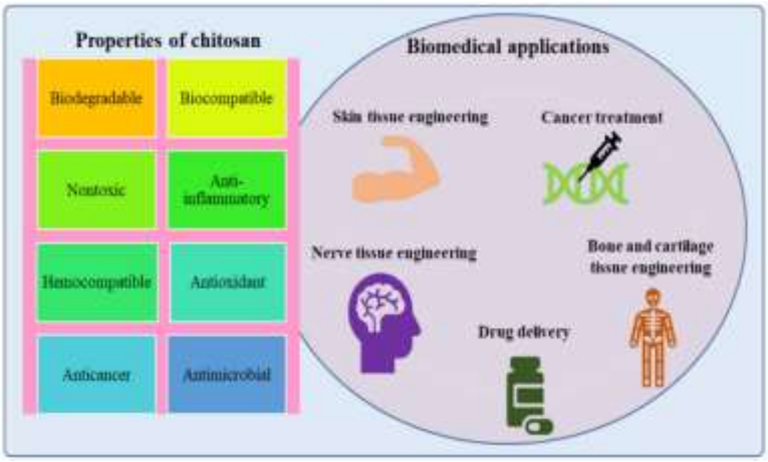

Figure 3: Nanoparticles based on chitosan and their potential medicinal uses

Chitosan is a semi-crystalline polysaccharide that is composed of linearly arranged N-acetyld-glucosamine and d-glucosamine residues. The inclusion of an amino group (-NH2) in its chemical structure gives it cationic characteristics. By luring in negatively charged molecules like proteoglycans, this positive charge facilitates the assembly of the extracellular matrix. Moreover, Hydroxyl groups (-OH) in a molecule's structure attract and bind other, positively charged molecules. Other than its electrostatic attraction, chitosan is modified with the help of various functional groups, leading to improved mechanical and physical properties, new functional features, and compelling therapeutic significance.

Biomedical applications of chitosan

This is a discussion of the many biomedical uses of chitosan, including its antibacterial and antioxidant properties as well as its use in burn treatments, ophthalmology, and other fields.

i. **Antimicrobial activity:** Recent years have seen a lot of research on the antibacterial properties of chitosan and its derivatives. It has been hypothesized that chitosan's antibacterial properties are shown through one of two mechanisms: (i) electrostatic stacking of polycationic chitosan disrupts bacterial metabolism, and (ii) chitosan prevents RNA from being transcribed into DNA. The acetylation and molecular weight of chitosan, however, are largely responsible for its antibacterial action.

ii. **Antioxidant activity:** the growing need to protect the human body from oxidative stress has led to an exhaustive quest for any and all naturally occurring antioxidants. Chitosan, for example, may be extracted from abundant and inexpensive sources like shrimp shell, crab shell waste, etc., and serves as a natural antioxidant.

iii. **Antitumor activity:** Chitosan has many biological functions, including anticancer action. Chitosan's membrane disrupting potential and apoptosis inducing actions are responsible for its anticancer efficacy. Cancer cell lines including Sarcoma-180 and mouse hepatoma H22 were used in experiments demonstrating chitosan's antitumor potential.

iv. **Wound healing:** With its homeostasis-maintaining properties, healing stimulation, antibacterial potential, nontoxicity, biocompatibility, and biodegradability, chitosan has found widespread use in wound therapy ever since its discovery. Many studies have been done based on these.

v. **Drug delivery system:** One or more pharmacologically active agents, together with an appropriate carrier, make up drug delivery systems. Ideal delivery systems should be able to route the active agent exclusively to the site of action in the body and administer the correct dosage at a consistent, acceptable rate during the prescribed time period.

A VERSATILE PLATFORM FOR BIOMEDICAL APPLICATIONS: CHITOSAN NANOPARTICLES

In the fields of nanomedicine and biomedicine, particles in the size range of 1-1000 nm are of interest because of their versatility in terms of both substance and size. Both top-down methods, like sonication and high-pressure homogenization, and bottom-up methods, including solvent displacement and reactive precipitation, may be used to create nanoparticles. Being much more diminutive than their mass counterparts, they possess special qualities. Nanoparticles with tailor-made characteristics are therefore attainable. Organic and inorganic nanoparticles are both available, however inorganic nanoparticles are more often used due to their resilience under severe processing conditions. Among inorganic materials, Nanoparticles made of metal oxides, such as zinc oxide, magnesium oxide, silver oxide, and titanium oxide, have received a lot of attention due to their versatile optical properties and sturdy physical composition. Because of their superior electrical, metallurgical, and structural properties, organic materials including lipids, polymers, and carbon nanotubes find widespread use. Polymeric nanoparticles may be made from both natural and synthetic polymers due to their stability and surface modifiability. In addition to their already impressive list of benefits, biopolymeric nanoparticles are also biodegradable, biocompatible, and relatively non-toxic. As an added bonus, these nanoparticles may be easily obtained from their natural environments. Chitosan is a white, inelastic polysaccharide that is biodegradable and compatible with living organisms. Carbohydrate backbone structure similar to cellulose, formed by deacetylating chitin; glucosamine and N-acetyl glucosamine repeating units linked by a 1-4-glycosidic linkage. It has several applications, including those in agriculture, the food business, biomedicine, water purification, pollution prevention, photography, and paper production.

The benefits of chitosan are combined with those of nanoparticles in chitosan nanoparticles (ChNP). Chitosan's low cost and ease of availability make it a promising material for a variety of medical applications, including wound healing and the creation of drug delivery systems. Because of chitosan's mucoadhesive properties, ChNP may be administered through a wide variety of transmucosal routes. These include the nasal, ocular, vaginal, tracheal, and pulmonary systems. In addition to its usage in food coatings, chitosan is a key ingredient in agricultural fertilizers. In addition to its usage in cosmetics as a skin moisturizer, guar gum is promoted in several countries, including the United States, as a dietary fiber to decrease fat absorption. Changing the basic structure of chitosan to create polymers with unique characteristics is critical for expanding the range of possible uses.

Polymeric nanoparticles containing chitosan, for instance, have been used for drug administration through several methods. Nanoparticles derived from chitosan have a positive surface charge and mucoadhesive qualities that allow them to bind to mucous membranes and slowly release their payload. ChNP are useful for the treatment of a wide variety of conditions, including those affecting the eyes, the digestive tract, the respiratory system, and even cancer. In light of these facts, we propose that chitosan is the most promising naturally occurring material for application in nanomedicine.

CONCLUSION

We can say that chitosan is a natural polymer that has the benefits of being biodegradable, nontoxic, and biocompatible. The medical industry is only one of several that may benefit from this. Cosmetics, farming, food production, the paper industry, and textiles are just a few of the many places you might find chitosan at work. In addition to this, they find extensive usage in biological contexts on account of their malleability (allowing them to be shaped into almost any form) and nontoxicity. When used as carriers of specific pharmaceuticals, chitosan nanoparticles may increase drug stability while keeping the biological features of chitosan. In comparison to lipid-based nanoparticles, chitosan nanoparticles have more favorable drug-loading and biological dispersion profiles.

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