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Mini Review Article

Medical application of Chitosan

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Abstract

By using the deacetylation method, chitin is converted into bioproduct chitosan. Deacetylation can be accomplished using chemical or biological mechanisms. Due to its biocompatibility, nontoxicity, biodegradability, natural origin, and resemblance to human macromolecules, it is useful in medicine. Chitosan may have antibacterial and antioxidant properties. Additionally, it could be used in biotechnology, agriculture, gene therapy, food technology, medication delivery, cancer therapy, and other fields. The objective of the current review was to list the most significant applications of Chitosan in the biomedical field.

Keywords Deacetylation, Antibacterial, Antioxidant, Biodegradability, Agriculture, Gene therapy

Introduction

The field of biomaterials gave natural polymers a lot of attention. They could be immediately recognized through the bio environment and quickly metabolized for producing residues that are naturally removed and noncytotoxic due to their structural similarity to biological macromolecules (Ramya et al., 2012). In terms of natural materials employed as treatments for human diseases, marine resources have been at the forefront. Recently, interest in using the second-most prevalent polymer in nature—the marine biopolymer chitin for medical purposes has surged. Chitin is a biopolymer that is extracted from crustaceans. Under highly alkaline conditions, partial deacetylation of chitin converts it into Chitosan (Babu & Ramesh, 2017). (Fig.1). Chitosan is an N-acetyl-D-glucosamine and D-glucosamine copolymer. The copolymer contains varying quantities of N-acetyl-D-glucosamine and D-glucosamine residues based on varying degrees of deacetylation (Reshad et al., 2021), (Rinaudo, 2006). Because Chitosan has a positive ionic charge, it might bind to materials that have a negative charge, such as negatively charged proteins, ions, lipids, and fat. In addition, Chitosan is nontoxic and possesses superior bioavailability and biodegradability.

Due to these characteristics, it could be utilized for various applications, including the treatment of wounds, as a medication carrier, chelating agent, dietary supplement, food packaging, biomaterial, and pharmaceutical uses, among others (Gallo et al., 2016), (Reshad et al., 2021).

Medical application of Chitosan

Antioxidant activity

It has been established that antioxidants are good for health. They prevent the body's reactive oxygen radical molecules from destroying proteins, DNA, and membrane lipids (Zhao et al, 2018). Having an unpaired electron on their outer orbit, free radicals are extremely unstable substances that are reactive in their search for another electron. Free radicals are substances that could be found in the environment, drugs, smoke, poisonous substances, sun's UV radiation, packaged foods, and other sources. Antioxidants could protect the organism from the purported negative effects of free radicals while also preventing the degradation of lipids and other food components (Kurniasih & Dewi, 2018). Recently, biological polysaccharides have received much attention as a result of their availability, nontoxicity, and strong antioxidant action.

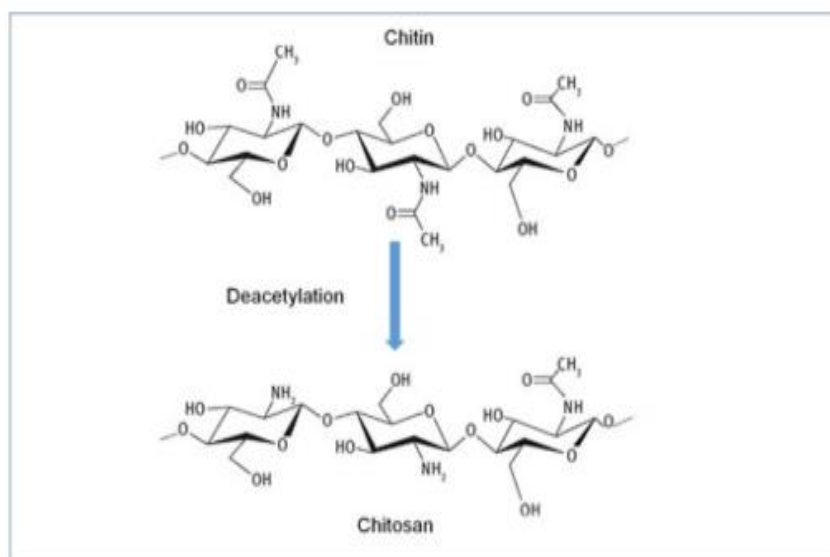


Fig. 1 Conversion of chitin to chitosan (Reshad et al., 2021)

For instance, polysaccharides from marine species and Chitosan from shrimp both exhibit strong antioxidant effects (Hao et al., 2021). Chitosan's antioxidant property is one of its well-known uses. In dietary and biological systems, Chitosan inhibits ROS and prevents lipid oxidation, according to numerous studies. The antioxidant effect of Chitosan has been attributed to several different mechanisms. By giving a hydrogen atom or lone pairs of electrons as donations, Chitosan can neutralize free radicals or bind metal ions. Chitosan's interaction with metal ions may include several complex mechanisms, such as chelation, adsorption, and ion exchange (Rajalakshmi et al., 2013). Research has been done both in vitro as well as in vivo on Chitosan's antioxidant abilities. Liu examined Chitosan's antioxidant effects on the oxidation of lard and crude rapeseed oil. The researcher found that Chitosan can considerably decrease serum levels of malondialdehyde and free fatty acids, increase superoxide dismutase (SOD) and show the activities of glutathione peroxidase and catalase, the body's primary antioxidant enzymes (Liu, 2018). This shows that Chitosan could be used as one of the alternatives to synthetic antioxidants like butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) since it controlled the activities of antioxidant enzymes and reduced lipid peroxidation (Avelelas et al., 2019). Chitosan can block the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical with an inhibition range of 28.37 to 38.03 % at doses between 0.125 and 1.0 mg/mL, according to a study by (Kumar Kuppusamy & Karuppaiah, 2013). Chitosan may be thought of as a potential natural antioxidant for stabilizing foods containing lipids to increase shelf life because it can chelate metal ions. Chitosan may prevent the oxidation of lipids by chelating ferrous ions already present in the system and removing their prooxidant or conversion into ferric ions (Mustafa, 2018).

Drug carrier

Serious side effects emerge from a significant portion of the medication being delivered spreading throughout healthy organs or tissues which aren't involved in the pathological process. A viable solution to this critical problem is the development of systems of targeted drug delivery, which release bioactive substances or medications at the desired location of the action. Three elements make up the targeted drug delivery system: a carrier system, a targeting moiety, and a therapeutic substance. The medicine can enter the carrier system either through passive absorption or chemical conjugation. The pharmacokinetics of the medications is greatly influenced by the carrier molecule, making it of utmost relevance. Here, the cationic polysaccharide chitosan has gained prominence in the pharmaceutical and medicinal fields because of its widespread availability, distinct mucoadhesive, innate pharmacological characteristics, and other advantageous biological traits like biodegradability, biocompatibility, low-immunogenicity, and nontoxicity (Ramya et al., 2012; Kumar et al., 2004). Amphiphilicity, a necessary quality for the production of self-assembled NPs which might be exploited for drug delivery applications, has been added to Chitosan through chemical modification. The hydrophobic cores regarding the NPs might serve as reservoirs or micro-containers for different bioactive compounds. Due to their small size, NPs could be employed for targeted drug delivery via intravenous injection. By attaching the targeting molecules to the surface regarding drug-loaded NPs, the therapeutic efficiency of the medication could be improved (Dufes et al., 2004). Low molecular medications, genes, and peptides are routinely delivered by using Chitosan. Arrange of hydrophobic and hydrophilic drugs could be loaded into the NPs throughout the creation process, with the efficiency of the loading based on the physicochemical features of the drug (Ramya et al., 2012).

Antimicrobial activity

Recently, there was a lot of interest in the antibacterial activity of Chitosan, chitin, as well as its derivatives against several types of micro-organisms, including yeast, bacteria, and fungi (Mustafa, 2018). Chitosan is a broad-spectrum antibacterial agent because it has an inhibiting effect on many different types of bacteria. Numerous variables, including molecular weight, metal ion concentration, deacetylation level, and solvent PH, have an impact on Chitosan. The interaction of metal ions may reduce anti-microbial activity regarding Chitosan itself while boosting the overall antibacterial activity of the chitosan-based dressings because of the interaction between metal-chelating molecules. The antibacterial efficacy of Chitosan diminishes as the degree of deacetylation rises. Chitosan exhibits more antibacterial action in solvents with a pH of 6 than it does in those with other pH values (Zhang et al., 2020; Chen et al., 2008). A variety of theories provide insight into various mechanisms. One of the most widely recognized theories holds that Chitosan's antibacterial properties are produced by a positively charged amino group. The negatively charged microbial cell membrane interacts with the positively charged amino group. This contact results in the release of several proteins and other bacteria' biological components (Reshad et al., 2021; Sahariah & Måsson, 2017). The positive charge of the polymer chain will adhere to the surfaces of bacteria, changing the permeability of the membrane wall to prevent microbial development (Goy et al., 2009). Gram-negative bacteria's cell membranes were subjected to chitosan treatment, and Helander et al. found evidence of considerable cell surface modifications, including thickening and the creation of vesicular structures on *E. coli* and *Salmonella Typhimurium* outer membranes (Helander et al., 2001). They concluded that Chitosan attaches to Gram-negative bacteria's outer membrane and alters its barrier characteristics, most likely via forming a complex with different lipopolysaccharides (Ramya et al., 2012). On a wide variety of fungi, including *Botrytis cinerea*, *Trichophyton equine*, *Fusarium oxysporum*, *Piricularia oryzae*, and others, antifungal chitosan properties have been noted. Chitosan might demonstrate many fungi-inhibiting methods. Chitosan, for instance, may prevent *Saccharomyces cerevisiae* from making proteins and influence *Candida Albicans* intracellular ultrastructures and membrane integrity, preventing the growth of the two fungi (Xing et al., 2015).

Antitumor

Cancer continues to be a major public health concern as one of the main causes of morbidity on a global scale (Abedian et al., 2019). Recent investigations showed that Chitosan and its derivatives have antitumor effects in the in vivo as well as the in vitro settings. The anticancer properties of chitosan derivatives are mediated by increased IL-2 and (IL)-1 secretion that leads to infiltration and maturation of the cytolytic T-lymphocytes (Zhao et al., 2018). Studies employing mice that had consumed low-Mw Chitosan showed that the substance significantly reduced Lewis's lung cancer metastatic spread (Mustafa, 2018). Numerous research on Chitosan's anticancer properties states that its mechanism

involves membrane disruption and apoptosis induction. Chitosan's antiproliferative effects on the human monocytic leukemia cell line (THP1) and some human breast cancer cell lines have led researchers to hypothesize that it has anticancer potential (Abedian et al., 2019). According to research done by Qi et al. on the anticancer effects of Chitosan on hepatocellular carcinoma, the antitumor process was triggered by changes in the potential of the mitochondrial membrane, an increase in the amount of lipid peroxidation in the membrane, and the neutralization of charge on the cell surface (Qi et al., 2007). Takimoto et al. had shown that the Chitosan caused apoptosis by altering the expression of death receptors and triggering caspase-8 (Takimoto et al., 2004). However, Hasegawa et al. demonstrated that Chitosan activated caspase-3, causing bladder tumor cells to die apoptotically (Hasegawa et al., 2001).

Anticholesterol

Hypercholesterolemia represents one of the main global risk factors for mortality and morbidity. Hypercholesterolemia is a term used to describe blood cholesterol levels that are higher than the normal limit of 200 mg/mL (Oksal et al., 2020). The use of nanoparticles in pharmaceutical areas is a rapidly growing subject of technology nowadays. The most effective materials for mucosal administration of medications and antigens are those with nanoparticle sizes (Rampino et al., 2013). Chitosan is a natural substance that is used to create drug-containing nanocarriers. Chitosan is a great starting point for the creation of nanoparticles since it is harmless and biocompatible (Oksal et al., 2020). Chitosan has been proposed to lower cholesterol in several different ways. This could be a result of the effect of Chitosan, which reduces the absorption of fat and cholesterol. Chitosan is broken down into various sugars in the intestine, increasing viscosity and decreasing fat and cholesterol absorption (Aldulimy et al., 2021). The presence of 3 types of reactive functional groups, including the primary hydroxyl group (OH) at the C-3 position, the amino group NH₂ at the C2 position, and the secondary hydroxyl group (OH) at C-6 positions in its structure, controls electrostatic force between chitosan and anion compounds, like bile acids and fatty acids (Mustafa, 2018). Chitosan has the power to lower levels of cholesterol in the blood, which reduces the absorption of fats in the small intestine and lowers fat and weight, hence lowering the risk of heart disease in general. As a result, it combats some metabolic conditions and alterations and lowers obesity brought on by food (Aldulimy et al., 2021).

Conflict of Interest

The author hereby declares no conflict of interest

Consent for publication

The author declares that the work has consent for publication

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