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A Brief Review on Chitosan and Application in Biomedical Field

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ABSTRACT

Chitosan is a linear polysaccharide composed of randomly distributed β-(1-4)-linked D-Glucosamine (deacetylated unit) and N-acetyl D-Glucosamine (acetylated unit). It is made by treating shrimp and other crustacean shells with the alkali, sodium hydroxide. Chitosan has some therapeutic activities like lowering cholesterol, antiulcer, and wound healing and antimicrobial activity. Recently electrospinnanofibers based on chitosan have been widely researched. Chitosan have many physicochemical properties like colorless, white hard, inelastic, nitrogenous polysaccharide. It chelate with many transitional metal ion .The degree of substitution of hydroxyl and amino group also influence the mechanical and biological properties of chitosan samples. In recent year a lots of biological, medical and commercial applicability are being used. The amino group in chitosan has a pKavalue of ~6.5, leads to a protonation in acidic to neutral solution with a charge density dependent on pH. This makes chitosan water-soluble. Though the drug delivery by chitosan is not approved by FDA, purified form are available for biomedical application. This review gives clear information about introduction properties processing and applications of chitosan.

Keywords: Chitosan, Electrospin, Amino Group, Purified Form, Chelate, Protonation.

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INTRODUCTION

Chitosan is a linear polysaccharide composed of randomly distributed β-(1-4) linked D-glucosamine and N- acetyl-D-glucosamine. It is made by treating shrimp and other crustacean shells with the alkali, sodium hydroxide[1]. It is also naturally present in some microorganisms and fungi such as yeast. The term chitosan is used to describe a series of chitosan polymers with different molecular weights (50kDa- 2000kDa), viscosity (<2000mPaS), and degree of deacetylation (48%-98%).

Chitosan is also known as soluble chitin. Chitin consists of un branched chains of β-(1-4)-2-acetamido -2-acetamido-2-deoxy-D-glucose. It is similar to cellulose, in which hydroxyl group are replaced by acetamido residue. Chitin is practically insoluble in water, dilute acid and alcohol depending on the origin of the product [1, 2]. Chitosan forms salt with inorganic and organic acids like glutamic acid, lactic acid, hydrochloric acid and acetic acid[2]. The structures of chitin and chitosan are shown in Figure 1 and 2.

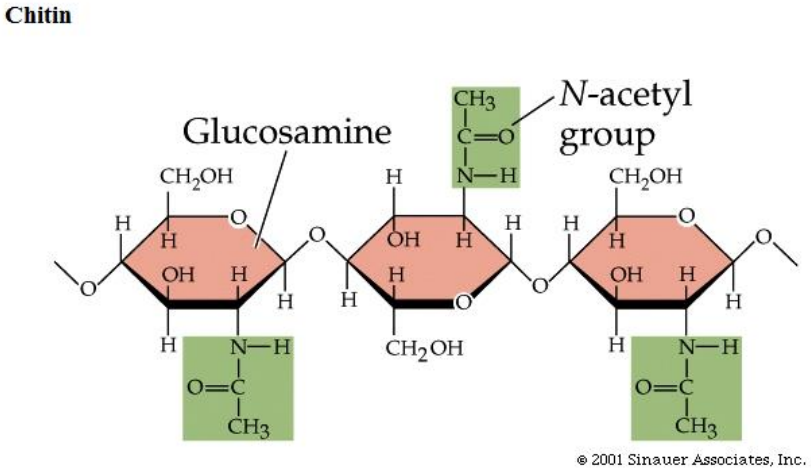

Figure 1: chemical structure of chitin

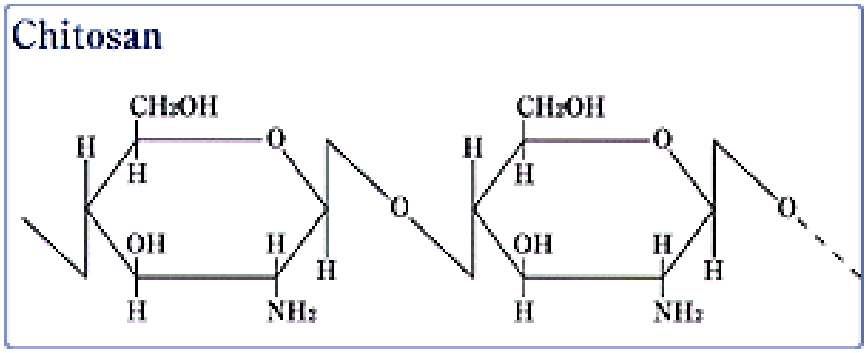

Figure 2: chemical structure of chitosan

Commercially chitin and Chitosan are having high percentage of nitrogen (6.89) compared to their substituted cellulose. Hence it can be used as chelating agent. Recently much attention has been paid to Chitosan as a potential polysaccharide resouraces[3]. Chitosan has some therapeutic activities like lowering cholesterol, anti ulcer, wound healing and anti microbial activity, it is used as a drug carrier owing to biocompatibility, biodegradable and non toxic character[4]. Recently, elecrospunnanofibers based on chitosan have been widely researched and various nanofibers products containing chitosan have been produced by elecrospinning. These nano fibers yield potential applications in various area[5].

Properties

Naturally occurring polymers like cellulose, dextrin, pectin, alginic acid and agar are naturally acidic in nature, whereas chitosan is an example of highly basic polysaccharide. Chitosan properties like solubility, viscosity, polyelectrolyte behavior ability to form films.

Physico-Chemical properties:

The physic-chemical properties of chitosan are as follows

- Chitosan is a colorless, off white, hard, inelastic, nitrogenous polysaccharide.
- The chitin molecular weight average range from 1.03×106 to 2.5×105 Daltons. But the formed chitosan by deacetylation reduces it to 1×105 to 5×105 Daltons.
- Chitin can easily process into gels, powders, membranes, fibers, colloids films, and beads.
- Chitosan is a linear polymer
- Chitosan having Reactive amino groups and hydroxyl groups they are easily substituted by other groups.
- Because It is a polysaccharide it chelate with many transitional metal ions. [6]

Biological properties

- Biocompatible- they have no antigenic property thus the compatible with animal and plant tissue.
- Natural obtained polymer
- Biodegradable to normal body temperature
- Safe and non toxic
- Binds to mammalian and microbial cells
- Regenerative effect on connective gum tissue
- It acts as a Haemostatic[3], hypocholesteroloemic, radical scavenging activity, anti coagulant property.

Processing of chitosan

Chitin can be isolated from crustacean shells by chemical process. It involves some processing steps as follows

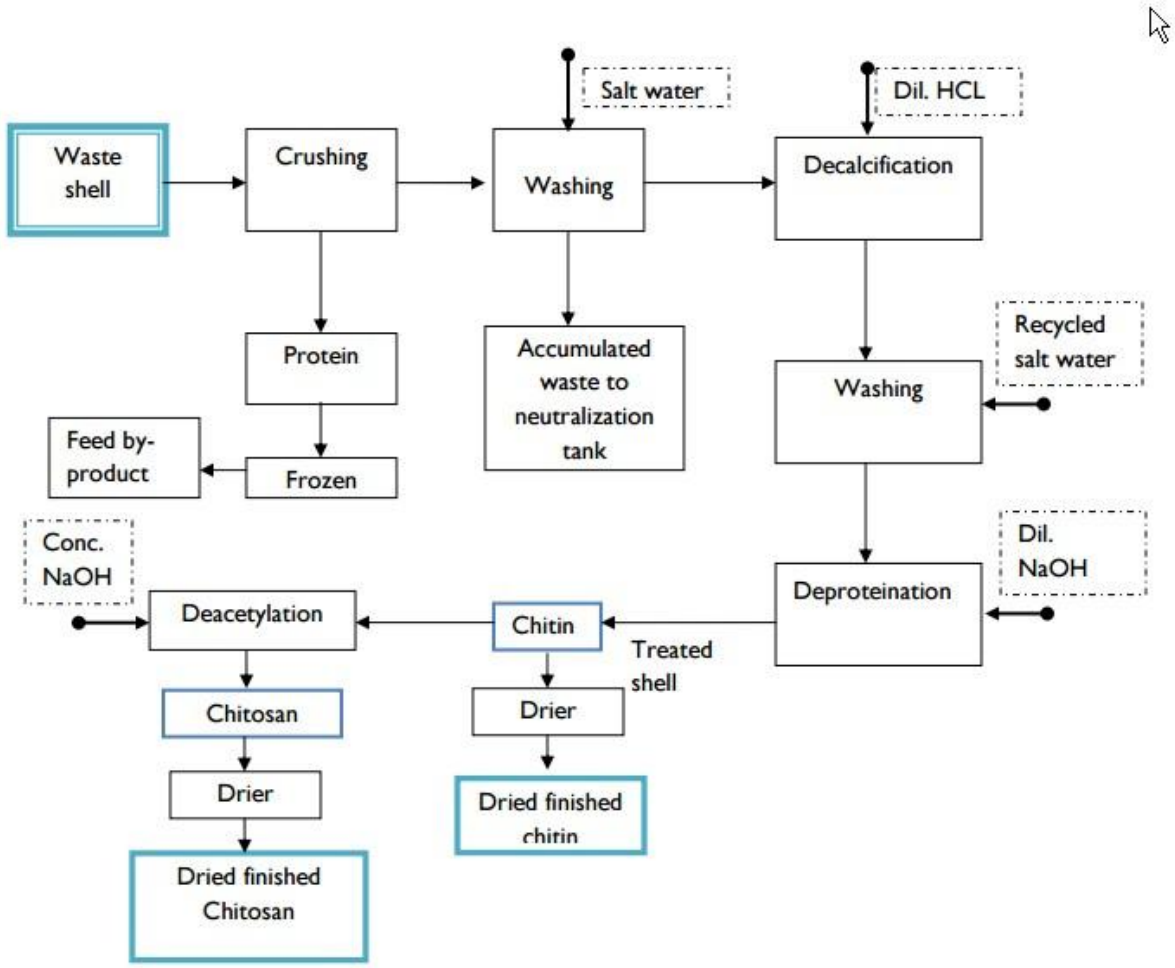

Figure 3: Manufacturing process[7]

a) Demineralization: it involves acid treatment (HCl) which removes the inorganic matter mainly calcium carbonate.

b) Deproteinization: in includes the extraction of protein matter in alkaline medium (NaoH).

c) Decoloration: it involves bleaching of the product by chemical reagents to achieve colorless product[8].

History

Chitosan (pronounced Kite-O-San) has long been considered as the "fat magnet". Researchers have it that it is simply a fat inhibitor which appears to work miracles for those in search of a safe way to lose that body fat.

Some 20 years later, there was a man who authored an article on insects in which he noted that similar substance was present in the structure of insects as well as the structure of plants. He then called this amazing substance as "chitin". Basically, the name chitin is derived from Greek, meaning "tunic" or "envelope". The concept was further known in 1843 when Lassaigne demonstrated the presence of nitrogen in chitin[1].

Rouget discussed the deacetylation form of chitosan different researches have been discussed the need of understand and studying the material from better production, purification methods, to the modifications of basic structure and its applications. Chitosan as a source of potential bio active material, but it also has several limitations to be utilized in biological systems, including its poor solubility under physiological conditions to overcome these researchers focused on the Derivatisation of chitosan by chemical modifications. These modifications results in increased solubility in water as well as an organic solvents[9].

Uses

Chitosan, primarily for increasing the plant defense, are based on how this amine containing polymer influence on te bio-chemical and molecular biology of the plant cell.

Chitosan is typically used as a natural seed treatment and plant growth enhancers and as eco friendly bio pesticides substances that boosts the inhere ability of plant to defend themselves against further infections.

APPLICATIONS:

As diluents:

chitosan with 2- hydroxyethyl starch due to the interactions taking place between their reactive hydroxyl and amino groups miscible blends by using these combination we can get the some controlled release formulations. It is because of the combination of diffusion and disintegration of the formed matrix tablet [2, 9].

Adnan A. Badwan, et al.Pharmaceutical applications of chitin and chitosan and their derivatives as effective excipients can be aligned for DC processing. The diversity of Physico-chemical properties of semi-crystalline nature, DDA, and MW enhance beneficial use as such and as a co-processed excipient in pharmaceutical preparations. Moreover, their high surface area, porous structure, and plastic deforming nature enhance necessary particle bonding and tabletability in the DC mode with low sensitivity upon lubrication. Optimal use as a single multifunctional excipient can be established when chitin and chitosan are co-processed with other excipients.[10]

As Mucoadhesive excipient:

Bioadehesion is type of controlled drug delivery system mainly targeted for GI track. A comparison of chitosan and other polymer indicates that the cationic polymer has higher bioadehesion property compared to other natural polymer[10]. The Mucoadhesive property of chitosan is due to the presence of OH and amine group gives rise to hydrogen bonding. The occurrence of the mucoadhesion causes prolonged residence time of drug. There by enhanced absorption and bioavailability in gastrointestinal track[11].

As controlled drug delivery system

Chitosan is a cationic polymer used for controlled drug delivery. It forms polyion complexes as a result of its interactions with anionic polymers. The poly ion complexes and their basic properties have been used for pharmaceutical purpose [8, 11].

As permeation enhancer

Chitosan having cationic nature is capable of opening tight junctions in a cell membrane. This property has led to a number of studies to investigate the use of chitosan as a permeation enhancer for hydrophilic drugs that may otherwise have poor oral bioavailability, such as peptides. Yu-jie Zhang et al investigated the permeation enhancing effect of various chitosan formulations was estimated by using the permeation coefficient of fluorescein isothiocyanate recombinant hirudin-2 across the excited rabbit nasal epithelium in vitro. It conclude that Chitosan with or without some enhancers was able to effectively promote the nasal absorption of recombinant hirudin, while not resulting in severe mucosal ciliotoxicity. A chitosan formulation system would be a useful approach for the nasal delivery of recombinant hirudin[12].

Enhanced bone formation by transferring growth factor

Chitosan composite micro granules were fabricated as bone substitutes for the purpose of obtaining high bone forming effects Lee JY el al. (2002) done a research on porous chitosan matrices were dealt with in this research. Porous chitosan matrix was fabricated by freeze- drying and cross linking aqueous chitosan solution. All chitosan based devices demonstrated improved bone forming capacity by increasing mechanical stability and biocompatibility. Release of platelet-derived growth factor-BB from these matrices exerted significant osteoinductive effect in addition to the high osteoconducution capacity of the porous chitosan matrices. These results may expand the feasibility of combinative strategy of controlled local drug delivery concept and tissue engineered bone formation in constructive therapy in the field of periodontics, orthopedics and plastic surgery[13].

Wound healing properties

Efficacy of chitosan in the promotion of wound healing was reported in 1978. Chitosan acetate had the advantage of good oxygen permeability, high water absorptive and slow enzyme degradation. They are tough and protective. Chitosan also used as coating on normal biomedical material. Catgut sutures coated with regenerated chitin or chitosan show wound healing activity only slightly lower than all chitin- fibers. Surgical gauze coated with regenerated chitin demonstrates a substantially greater amount of activity.[14]

In Vaccines delivery

The potential use if chitosan as delivery systems for inactivates influenza vaccines given intra nasally has been studied. Investigations tells that the ability of low molecular weight chitosan in the form of nano particles as new long term nasal vaccine delivery vehicle[15].

Chitosan microparticles are able to associate with large amount ovalbumin (model vaccine for diphtheria toxoid) chitosan microparticles are not disintegrated in an acidic environment and protect the antigen against degradation by entrapping it into their porous structure. The chitosan microparticles transport the associated ovalbumin into the peyer's patches. Since the uptake of antigen by Peyer's patches is an essential step in oral vaccination, these porous chitosan microparticles are a very promising vaccine delivery systems[16].

As Parenteral delivery

As highly purified chitosan fractions was found neither toxic nor hemolytic, that they have the ability to complex DNA and nuclease degradation and that low molecular weight chitosan can be administered IV route without liver accumulation suggest there is potential to investigate further low molecular weight chitosan as components of a synthetic gene therapy system[17,18].

Chitosan in fuel cell

Fuel cells are electrochemical devices which convert energy into electrical energy. Fuel cells have attracted attention due to their potential as a promising alternative to traditional power sources. More recently, efficient and environmentally being biopolymer chitosan have been extensively investigated as a novel material for its application in fuel cell. This biopolymer can be used in both membrane electrolyte and electrode in various fuel cells such as alkaline polymer electrolyte fuel cell, direct methanol fuel cells and bio fuel cells[19,20].

Gold chitosan particles for heavy metal sensing

In the year 2005, a research done an innovative strategy for using gold nano particles capped with chitosan for sensing heavy metal ions was suggested. Chitosan is poly cationic in nature due which the polymer can be attached to the negatively charged gold nano particles surfaces through

electrostatic interactions. Chitosan chelating properties and gold nano particles optical properties have been used to detect low concentrations of heavy metal ions in water [21].

Chitosan as a food additive

Chitosan have film forming and barrier property, thus making it a potential raw material for edible films or coating. Due to its antibacterial or anti fungal properties and anti film forming property of chitosan make it an ideal for use as biodegradable antimicrobial packaging material that can be to improve the storage of destructible foods. Various researches clearly states that chitosan can be used as an effective film forming or preservative for improvement of quality and shelf life of various food. US FDA approved chitosan as a food additive in United States[22].

Cosmetic industry

Cosmetic compositions are disclosed the treatment of hair or skin, characterized by a content of new quaternary chitosan derivatives of the formula. The chitosan derivatives have a good substantively, particularly to hair keratin, and prove to have hair strengthening and air conditioning characteristics. Chitosan used in oxidation hair-coloring composition, hair setting lotions, gel form and skin creams[23].

Colon specific drug delivery

Since chitosan gets eliminated in colon, enteric coating materials are used for colon, enteric coating materials are used for colon specific drug delivery. Drugs, such as sodium diclofenac, an anti inflammatory drug, are entrapped inside the core of the chitosan microspheres. These microspheres are then coated with enteric coating, which is then used for drug delivery. In colon, sodium diclofenac is found to be released over the period of time of nearly 12 hours[24].

Other application

Deuchi et al. (1994) reported that chitosan reduces fat digestibility in rats and chickens when fed at 5% and 1.5% of the diet respectively. Bokura and kodayashi (2003) worked especially in elderly women and suggested that chitosan in safe and significantly reducing serum total cholesterol. The effect of chitosan on decreasing total LDL cholesterol is mild. [24, 25]

- Used as a drug carrier in microparticulate system
- Used a films containing drug [26]
- Preparation of hydrogels, agent for increasing viscosity in solutions
- Wetting agent, and improvement of dissolution of poorly soluble drug substances Disintegrant Bioadhesive polymer [27]

- Site-specific drug delivery (e.g. to the stomach or colon) Absorption enhancer (e.g. for nasal and oral drug delivery [28, 29].

CONCLUSION

Chitosan is a natural polymer having properties of color less hard inelastic polysaccharide. It is a biodegradable, safe and non toxic linear polymer. The basic core material for preparation of chitosan is chitin which is obtained from shrimp and other crustacean shells. Chitosan having so many applications in pharmaceutical field as diluents in tablets manufacturing, Mucoadhesive excipient, as permeation enhancer and having wound healing property. Recently chitosan was used in vaccine delivery systems. Other than pharmaceutical field chitosan is used as fuel agent, used as anti dot in metal sensing. This Review gives clear information about properties and applications of chitosan.

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