Modification of Chitosan

Sohel J. Shaikh[1], Raviraj K. Dhawale[2], Sangmesh N. Yewange[3], Renuka R. Deshpande[4]
[1,2,3] *B.Pharmacy Final Year Student, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512, Maharashtra, India*
[4]*Assistant Professor, Department of Pharmaceutics, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512, Maharashtra, India*

***Abstract*- Today, chitosan (CS) is probably considered as a biofunctional polysaccharide with the most notable growth and potential for applications in various fields. Chitosans are recognized as versatile biomaterials because of their non-toxicity, low allergenicity, biocompatibility and biodegradability. This review presents the recent source and preparation chitosan. Some special biomedical applications are also highlighted.**

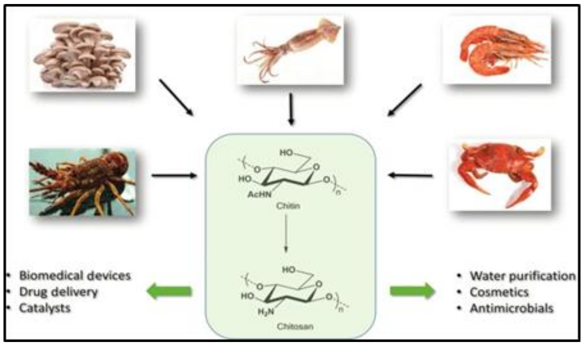
***Index terms*- chitosan, polysaccharide, biomedical applications**

INTRODUCTION

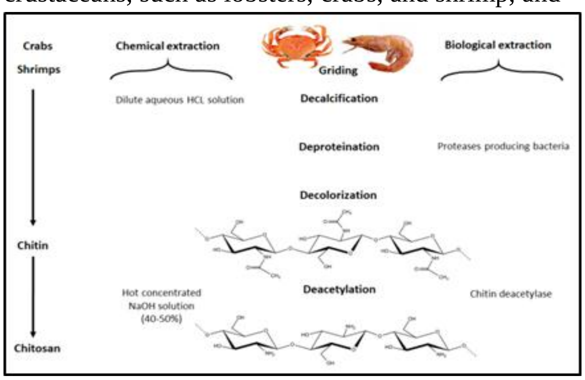
Chitin/Chitosan is a substance that can be found from nature, especially in crustaceans like crab, prawn, and insects. Chitin/chitosan is a substance needed by cells of living things in addition to the five main food groups needed by the body, namely carbohydrate, protein, fat, vitamins, and minerals. Chitin/Chitosan is, therefore, a food supplement that balances the use of the nutrients from the five main food groups. Chitin is the second most natural polysaccharide after cellulose on earth and is composed of β (1→4)-linked 2-acetamido-2-deoxy-β-D-glucose1 (N- acetyl glucosamine). It is often considered as cellulose derivative, even though it does not occur in organisms producing cellulose. It is structurally identical to cellulose, but it has acetamide groups (−NHCOCH3) at the C-2 positions. Similarly the principle derivative of chitin, chitosan is a linear polymer of α (1→4)-linked 2-amino-2-deoxyβ-D-glucopyranose and is easily derived by N-deactivation, to a varying extent that is characterized by the degree of DE acetylation, and is consequently a copolymer of acetylglucosamine and glucosamine.
Chitin is estimated to be produced annually almost as much as cellulose. It has become great interest not only as an under-utilized resource but also as a new functional biomaterial of high potential in various fields and the recent progress in chitin chemistry is quite significant. Chitin is a white, hard, inelastic, nitrogenous polysaccharide found in the exoskeleton as well as in the internal structure of invertebrates. The waste of these natural polymers is a major source of surface pollution in coastal areas. The production of chitosan from crustacean shells obtained as a food industry waste is economically feasible, especially if it includes the recovery of carotenoids. The shells contain considerable quantities of astaxanthin, a caroteniod that has so far not been synthesized, and which is marketed as a fish food additive in aquaculture, especially for salmon. The chitinous solid waste fraction of average Indian landing of shellfish was ranged from 60,000 to 80,000 t. The three parts of our motherland, India, are surrounded by ocean and its inner land is also very much rich with ponds, lakes, and logons. The proper utilization of those water resources (aquaculture) in terms of research in chitin and chitosan can bring the economic and academic prosperity of the nation.
Chitin and chitosan are now produced commercially in India, Poland, Japan, the US, Norway and Australia. A considerable amount of research is in progress on chitin/chitosan worldover, including India, to tailor and impart the required functionalities to maximize. (Caiqin Q, et al; 2006)

SOURCE OF CHITOSAN

Chitin is widely distributed in nature, constituting an important renewable resource. The main sources of chitin generally used are the crustacean wastes of the fishing industry. This chapter provides a brief account of the main processes employed in chitin isolation and the preparation of chitosan by extensive deacetylation of chitin. The common methods of characterization of chitin and chitosan, in terms of degree of acetylation and molecular weight, are discussed. Their crystalline structure and their solution properties are also described. The capacity of chitin and chitosan of forming complexes with metal ions is shown, and mention is made to some of its diverse applications.



The ability of chitosan to form polyelectrolyte complexes with polyanions, the cooperativity of this reaction and the properties of chitosan-based polyelectrolyte complex membranes, are also examined. The chapter ends with a review of the applications of chitin and chitosan in medicine, pharmacy, agriculture, the food industry, cosmetics, among others. The natural bio control active ingredients, chitin/chitosan, are found in the shells of crustaceans, such as lobsters, crabs, and shrimp, and



many other organisms, including insects and fungi. It is one of the most abundant biodegradable materials in the world.(Rinaudo M. 2006)

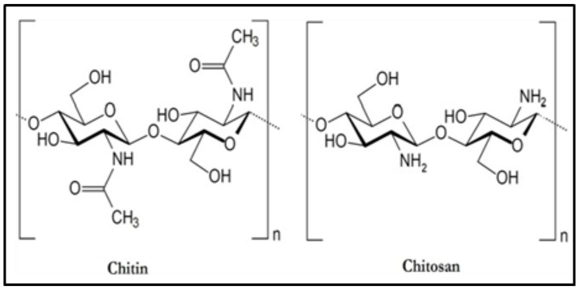
PREPARATION OF CHITOSAN

Although chitosan occurs naturally in some fungi and green algae, it is primarily produced industrially from chitin by chemical treatment using alkali. These methods are used extensively for commercial purpose of chitosan preparation because of their low cost and suitability to mass production. From a chemical point of view, alkalis can be used to deacetylate chitin. Commonly, in the heterogeneous method, chitin is treated with a hot concentrated solution of NaOH during a few hours, and deacetylated up to ~85%–99% and chitosan are produced. According to the homogeneous method, alkali chitin is prepared after the dispersion of chitin in concentrated NaOH (30 g NaOH/45 g H2O/ 3 g Chitin) at 25 °C for three hours or more, followed by dissolution in crushed ice around 0 °C. This method results in soluble chitosan with an average degree of acetylation of 48%–55%. Many parameters in the deacetylation reaction can limit the characteristics of the final chitosan. The results shown in Table 2, show the advantage of successive bathes compared to a single treatment of a long time the importance of the addition of NaBH4 preventing oxidation is clearly demonstrated.

PROPERTIES OF CHITOSAN

Chitin is a muco polysaccharide, derived naturally and found to be produced abundantly (second to cellulose) through biosynthesis. Chitins are characterized as white, non-elastic, hard, nitrogenous polysaccharides that have been estimated to be synthesized in approximately one billion tons annually. Chitosan is derived from the N-de acetylation form of chitin. Chitosan is composed of β (1→4)-linked 2-acetamido-2-deoxy-β-D-glucose (N-acetyl glucosamine). Chitin is structurally identical to cellulose, but it has acetamide groups (-NHCOCH3) at the C2-portion. On the other hand, chitosan is a linear polymer formed by α (1→4)-linked 2-amino-2-deoxy-β-D-gluco pyranose and derived by N-deacetylation, characterized by the degree of deacetylation, which is the copolymer of N-acetylglucosamine and glucosamine. Chitosans are the major elements derived from the shells of arthropods such as crabs, shrimps, lobsters, and insects, also produced extracellularly by the cell walls of fungi and brown algae.

Chitosan is rarely found in nature but does occur in dimorphic fungi, such as Mucor rouxii, by the action of the deacetylase enzyme on chitin. Chitosan is an aminopolysaccharide molecule with a strong positive electrical charge, which strongly attracts and bonds to negatively charged molecules. Chitosan-derived biomaterials have received considerable attention as an antimicrobial, functional, renewable, nontoxic, biocompatible, bioabsorbable, and biodegradable biopolymer agent. Chitosan is insoluble in water and organic solvents; it is soluble once mixed with acetic, nitric, hydrochloric, perchloric, and phosphoric acids. The solubility of chitosan derivatives can be observed



especially in aqueous acidic solutions, which has a pH ratio lowers than 6.5. At the same time, the solubility range also can be altered upon depolymerization, chemical modification of primary and secondary hydroxyl groups. (B.Sarmento et al 2007)

CHEMICAL STRUCTURE AND COMPOSITION OF CHITOSAN

The amine groups in chitosan become prorogated at acidic pH and transmit apositive charge to the chitosan chains. Most biological cell surfaces are anionic, and chitosan was thought to strongly adhere to the tissues at the site of a wound via electrostatic interactions due to its cationic characteristics. The solubilisation of chitin to produce chitosan in the acidic environment is found to take place via the protonation of an –NH2 function on the C2-position of the D-glucosamine repeat unit, whereby the polysaccharide is able to convert to a polyelectrolyte. Generally, chitosan has three types of reactive functional groups. Its amino groups have both primary and secondary hydroxyl groups at the C2-, C3-, and C6- positions.

These are the groups that permit the modification of chitosan-like graft copolymerization for specific applications in the tissue engineering field. The degree of deacetylation (DDA), crystallinity, and molecular weight (MW) are the main aspects in which chitosan can be modified to obtain different physiochemical properties. Chitosan consists of carbon (44.1%), hydrogen (6.84%), and nitrogen (7.97%), with an average MW of 5.3 × 105 Daltons.

Chitosan chemical properties are insoluble in most solvents but slightly soluble in diluted organic acids such as acetic, lactic, malic, formic, and succinic acids. The usage and benefits of chitosan are limited due to its insolubility in water, high viscosity, and aggregation of the protein molecules at the higher pH levels. Pyrolysis gas chromatography, gel permeation chromatography and ultraviolet spectrophotometry, titration, and separation spectrometry and near-infrared spectroscopy are the specific methods to detect the DDA of chitosan. Commercialized chitosan biomaterials possess DDA greater than 70% and with MW ranging from 1 × 105 Daltons to 1.2 × 106 Daltons. Chitosan derivatives with higher MW are potentially capable of providing better surface and film-forming properties due to its internal hydrogen bonding. Then again, it was reported that chitosan, with higher level of MW, possibly slows drug release.

At the same time, chitosan is contains nitrogen in comparison to cellulose and this property highly beneficial for metal chelation and polyoxysalt and film formations compared to cellulose. However, chitosan derivatives also potentially chelate metal ions such as iron, magnesium, and cadmium. The DDA of a chitosan biomaterial is the actual molarity of the glucosamine residue in the polymer chain to indicate the cationic charge on the molecule once diluted in acid solution. This is clearly evident from the proportion of free amino groups in the chitosan biopolymer. (Riccardo A.A. et al 2010)

BIOMEDICAL APPLICATIONS OF CHITOSAN

The design of artificial kidney systems has made possible repetitive haemodialysis and the sustaining life of chronic kidney failure patients. Chitosan membranes have been proposed as an artificial kidney membrane because of their suitable permeability and high tensile strength.

The most important part of artificial kidney is the semi permeable membrane and so far made from commercial regenerated cellulose and cuprophane. Since the primary action of the cellulose membrane is that of a sieve, there is little selectivity in the separation of two closely related molecules. These novel membranes need to be developed for better control of transport, ease of formability and inherent blood compatibility. A series of membranes prepared from chitin and its derivatives improved dialysis properties. One of the most serious problems of using these artificial membranes is surface induced thrombosis, where heparization of blood is needed to prevent clotting, and people who are liable to internal hemorrhage can be dialyzed only at great risk. Hence, these are the most challenging problem still to be resolved in the development of membranes which are inherently blood compatible. From these point of views, chitosan is hemostatic, i.e., causes clots.

1. Wound Healing/Wound Dressing.

Chitosan has been found to have an accelerator effect on wound healing/wound dressing process. Regenerated chitin fibres, non-woven mats, sponges and films exhibit an increase in wound healing by over 30 per cent. Chitin can also be used as a coating on normal biomedical materials. Standard silk and catgut sutures coated with regenerated chitin or chitosan show wound healing activities only slightly lower than the all-chitin fibres. Surgical gauze coated with regenerated chitin demonstrates a substantially greater amount of activity than an uncoated control group.

2. Burn Treatment.

Chitosan is a promising candidate for burn treatment. This is true since chitosan can form tough, water-absorbent, biocompatible films. These films can be formed directly on the burn by application of an aqueous solution of chitosan acetate. Another advantage of this type of chitosan treatment is that it allows excellent oxygen permeability. This is important to prevent oxygen-deprivation of injured tissues. Additionally, chitosan films have the ability to absorb water and are naturally degraded by body enzymes. This fact means that the chitosan needs not be removed. In most injuries (and specially burns), removing the wound dressing can cause damage to the injury site.

3. Artificial Skin.

The effect of treatment with chitosan and saline solution on healing and fibroplasia of wounds made by scalpel insersions in skin and subcutaneous tissue in the abdominal surface of dogs have been reported. The design for artificial skin, applicable to long-term chronic use focuses on a nonantigenic membrane which performs as a biodegradable template for the synthesis of neodermal tissue. It appears that chitosan polysaccharides having structural characteristics similar to glycosamino glycans can be considered for developing such substratum for skin replacement. Nowadays the investigation on brain-skull damage, plastic skin surgery is being made by the use of chitosan.

4. Ophthalmology.

Chitosan has replaced the synthetic polymers in ophthalmological applications. Chitosan possesses all the characteristics required for an ideal contact lens; optical clarity, mechanical stability, sufficient optical correction, gas permeability, partially towards oxygen, wettability, and immunologically compatibility. Contact lenses are made from partially depolymerized and purified squid pen chitosan by spin casting technology, and these contact lenses are clear, tough, and possess other required physical properties such as, modulus, tensile strength, tear strength, elongation, water content, and oxygen permeability. Antimicrobial and wound healing properties of chitosan along with excellent film forming capability make chitosan suitable for development of ocular bandage lens.

5. Drug Delivery Systems.

The applicability of natural polysaccharides such as, agar and pectin in the design of dosage forms for sustained release has been reported. Despite the medical applications of chitin/chitosan described above, they are still utilized in the pharmaceutical field. It is already known that compounds having a molecular weight lower than 2900 pass through membranes derived from chitosan. Since chitin and chitosan do not cause any biological hazard and are inexpensive, these polymers might be suitable for use in the preparation of dosage forms of commercial drugs. Controlled release technology emerged during the 1980s as a commercially sound methodology. The achievement of predictable and reproducible release of an agent into a specific environment over an extended period of time has many significant merits. The most significant merit would be to create a desired environment with optimal response, minimum side effect and prolonged efficacy. This is a relatively new technology and requires an interdisciplinary scientific approach. Chitin/chitosan controlled delivery systems are at developing stage and being used for a wide variety of reagents in several environments.

6. Weight Loss

Chitosan forms connective films, attaching to bile and fatty acids in the gut. The films then pass through your digestive system, increasing the amount of fat removed in the stool. In one clinical study, chitosan supplements reduced participants' weight by up to ~7 lbs. over three months. But let's not forget that placebo alone can work remarkably well – it helped people lose 4 lbs. In turn, chitosan's realistic contribution was only about 3 lbs., on average. Chitosan oligosaccharide might reduce inflammation, but clinical trials are still lacking.

7. Boosting Immunity

Chitosan may balance the immune system by affecting both the Th1 and Th2 response .As a reminder: the Th1 response is protective when in sync, but linked to autoimmunity in excess; Th2 over activity is predominantly linked to allergies. Chitosan nanoparticles – tiny, uniform, microscopic particles – increased Th1 and Th2 responses in mice in a balanced way. Nanoformulations are being investigated as "vaccine adjuvant," compounds that can enhance the effectiveness of vaccines.

8. Kidney Disease.

Chitosan supplements may help people with kidney disease or kidney failure, but the research to-date is sparse. In one older trial, chitosan given to 40 people with kidney failure improved strength, appetite, and sleep after 12 weeks. It also increased hemoglobin and reduced blood creatinine and urea levels, which points to its potential to improve kidney function additionally; high phosphorus levels are strongly linked with a higher risk of dying in people with chronic kidney disease. In rats, an iron-chitosan complex reduced blood phosphorus levels. This complex can bind phosphorus stronger than most other available phosphorus binders.

Chewing chitosan gum also became a popular method for reducing high phosphate levels in people with kidney disease.

However, chitosan gum is not as good as it sounds. In fact, it is probably downright ineffective. One 2009 study found that chitosan gum lowered phosphate levels after just two weeks of chewing. Recent studies failed to replicate the results. It turns out that the amount of chitosan in chitosan chewing gum is too low to have a phosphate-binding effect. And according to a detailed analysis, the 2009 study was poorly designed while the benefits boil down to a placebo effect.

9. Protecting the Brain.

Chitosan oligosaccharide may have some brain-protective properties. Supplementation with the oligosaccharide form reduced brain damage in rats with Alzheimer's and improved their memory and learning.

Additional research is underway, exploring its potential to prevent Alzheimer's and Parkinson's disease.

10. Binding Toxins & Heavy Metals.

Chitosan might bind to and help remove toxins. Since it eliminates bacteria (such as E.coli) and heavy metals from water, similar benefits from supplements are a possibility. Despite this, its effects on clearing toxins in humans have yet to be explored. In rats, chitosan protected against the buildup of a toxic heavy metal called cadmium. It reduced cadmium levels and protected the animals against damage. In one cell-based study; chitosan could bind to and filter out mold toxins.

11. Fighting Bacteria and Gum Disease.

Chitosan first sparked the interest of researchers in the 90s for its antimicrobial potential. Aside from being anti-inflammatory, scientists discovered it can destroy food-borne and other disease-causing bacteria. (Medically reviewed by Jonathan Ritter)

CONCLUSION

Drugs from marine sources are pharmacological activity as well as they play important role in designing the formulation. From this review it is suggested that Chitosan is biodegradable polymer which is pharmacologically active and play important role in designing the formulations such as sustained release, controlled release and interpenetrating polymer network.

REFERENCE

[1] Caiqin Q, Huirong L, Xiao Q, Liu Y, Juncheng Z, Yumin D, "Water-solubility of chitosan and its antimicrobial activity." Carbohydrate Polymers, 2006, 63, 367–374.

[2] Rinaudo M. Chitin and chitosan: Properties and applications. Prog. Polym. Sci. 2006;31:603–632. doi: 10.1016/j.progpolymsci.2006.06.001

[3] Chitin and Chitosan Sources, chemistry, biochemistry, physical properties and

applications, editors: Skjak-Braek, G., Anthonsen, T., Sand ford, P.A. Springer 1989
[4] Chitosan -Based Systems for Biopharmaceuticals, editors B.Sarmento and J. Das Neves, Wiley 2007
[5] Marine Chitin and Chitosan, editors : Riccardo A.A. Muzzarelli, MDPI Polymers, Special Issue 2010
[6] Medically reviewed by Jonathan Ritter, Pharm D, PhD (Pharmacology) | Written by Nina Goluskin | Reviewed by Ana Aleksic, MSc (Pharmacy).

AUTHOR PROFILE

Sohel J. Shaikh, Student of B.pharmacy 4th year, Latur College of Pharmacy, Hasegaon.

Raviraj K. Dhawale, Student of B.pharmacy 4th year, Latur College of Pharmacy, Hasegaon.

Sangmesh N. Yewange, Student of B.pharmacy 4th year, Latur College of Pharmacy, Hasegaon.

Renuka R. Deshpande, Assistant Professor, Department of Pharmaceutics, Latur College of Pharmacy Hasegaon,