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# Chitosan as classic biopolymer: A review

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## Abstract

Chitosan which is derived from chitin is a naturally occurring biopolymer, pretends to have a large number of pharmaceutical application. Chitosan offers good biocompatibility and also low toxicity which makes it a good pharmaceutical excipient in both conventional and novel applications**.** It is that this uniqueness makes it significant for the Pharma industry. Here a large number of its pharmaceutical application, history, origin, chemistry and its method of preparation have been studies to provide a reliable means of information.

Keywords: Chitosan, Polymer, Excipients, Applications.

## Introduction

Chitosan is a natural positively charged (cationic) biopolymer derived from the hydrolysis of the polysaccharide chitin.[1] Chitin is an amino polysaccharide (combination of sugar and protein) abundantly available natural biopolymer found in the exoskeletons of crustacean like shrimp, crab, lobster and other shellfish[2].Partial deacetylation of chitin to remove acetyl groups present in chitin gives chitosan[3].After cellulose the chitosan is second most abundantly available polysaccharide[4]. Chitosans used as an excipient in pharmaceuticals is relatively new approach[5]. Chitosan has several desirable qualities for the biomedical field and is found biocompitable. The chitin was discovered in mushrooms in early 19th century by Henry Braconnot when he observed a substance (chitin) insoluble in sulphuric acid[6].Later this substance was found in insects as well. Chitin is Greek name meaning envelope.Scientist Rouget discovered chitosan during experiments with chitin.It was established that specific chemical and heat treatment can make chitosan soluble.Scientist Ledderhose identified that chitin was made of glucosamine and acetic acid.Continued study of several researchers have resulted in discovery of new uses of chitin (chitosan) as they find different forms including crab shells and fungi in nature.

There are some general properties of a polymer for specific drug delivery system and polymer should possess certain desirable properties useful in pharmaceutical formulations as mentioned below:

- Chelates many translational metal ions.
- Unique ability to attach itself to other molecules.
- Ability of specific cellular action for target drugs
- Biocompatible and biodegradable to non toxicexcretable fragments within desirable time
- Economic and can be easily processed in manufacturing the formulations
- It has bacteriostatic and fungistatic effect

## Orgin

Chitin the basic component of the exoskeletons of crustacean and other species like mollusca, insects and fungi. Chitosan is mainly obtained from crustacean chitin and from crabs and shrimp shell wastes. The major (about 70%) organic component is chitin in such shells[7].Chitin occurs in three polymorphic forms a-chitin is used where hardness is required.In case where flexibility requires b and g chitins are used. Chitosan prepared from chitin is more reactive biopolymer.

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**Chemistry**

Chitosan [poly{(1,4)-2-amino-2-deoxy-D-glucopyranose}][8].Chitosan is isolated from the shells of shrimp, crab and lobuster etc. by treating the shell with 2.5N Sodium hydroxide at 75 deg centigrade and with 1.7N HCl at room temperature for 6 hours. The deacetylation is done with NaOH at high temperature. Increase in temperature or NaOH concentration increases the degree of deacetylation. Chitosan has hydrolysed N-acetyl groups as compared to chitin. Solubility and rheological properties of the biopolymer are affected by the degree of hydrolysis. The source of polymer affects the pKa of amino group from 5.5 to 6.5.The polymer is soluble at low pH makes the polymer unique for drug delivery applications.

**Preparation**

Chitosan is extracted from mycelia of *Mucor racemosus* and *Cunninghamella elegans* at different growth phases on yeast, peptone and dextrose medium. Chitosan is rapidly produced in both strains *M. racemosus and C. elegans*. Maximum yield of chitosan is obtained after 24 hours of cultivation in culture. The *M. racemosus* strain yield is about 40% higher than that of *C. elegans*. The D-glucosamine content in *M. racemosus* is about 48% and 90% in *C. elegans*. The degree of N-acetylation is different for both strains. Another process of preparation of modified carbohydrate polymer chitosan involves precipitation of dissolved chitosan from an acid solution by the stepwise addition of a neutralizing agent.The partially neutralized chitosan gel phase is subjected to shear agitation to a pH of about 6.9 to form a gel like suspension of discrete chitosan particles.

**Applications in Pharmaceuticals**

Chitosan having good biocompatibility and low toxicity has proved to be a good pharmaceutical excipient in both conventional and novel applications[9].It is a good diluent in direct compression of tablets, use binder for wet granulation, slow release of drugs from tablets and granules, film controlling drug release[10].It increases viscosity in solutions preparing hydrogels, improves the dissolution of poorly soluble drugs, absorption enhancer for nasal and oral drugs, biodegradable polymer for implants and carrier to vaccine delivery and gene therapy.[11]

Various experimentation study on application of chitosan and its derivatives:

- A novel mucoadhesive polymer prepared by template polymerization of acrylic acid in presence of chitosan for transmucosal drug delivery system. The polymer complex is formed through hydrogen bonding. The polyacrylic acid gets improved miscibility with chitosan through hydrogen bonding. The dissolution rate of PAA/chitosan polymer complex may be varied by pH and ratio of the two ingredients. The mucoadhesive property of the polymer complex was similar to carbopol.[12]
- As valuable excipient microcrystalline chitosan has high capacity for retaining water. This property is advantageous in development of slow release formulation, formulation of gels that control drug release. Microcrystalline chitosan is a hydrophilic excipient, controlling rate for drug release for mucoadhesive formulations for stomach.[13]
- Glycol chitosan polymer forms polymeric vesicle drug carriers. Chitosan polymers are suitable for fabricating a drug delivery system of orals and intranasal administration of gut labile molecules .Glycol chitosan with attachment of a specific number of fatty acids from unilamillar polymeric vesicles which are bio and haemocompatible and capable of entrapping water soluble drugs like Bleomycin.
- For the treatment of ulcerative colitis, 5-amino salicylic acid was encapsulated into chitosan capsule for colon specific delivery. The *in-vivo* study in colitis induced rats has shown that the capsules disintegrated in the large intestine as compared to the formulation without chitosan which absorbs in small intestines.
- A new polymer forming micelles in water named N-palmitolyl chitosan has the encapsulation capacity and controlled release ability of hydrophobic model drug Ibuprofen has been evaluated.
- In cancer therapy chitosan films were fabricated to deliver Paclitaxel at the tumor site in therapeutically relevant concentration. Paclitaxel formulated with 31%w/w in chitosan films were transluscent and flexible and the chemical integrity of the molecule was unaffected.
- Chitosan nanoparticles of hydrophobic drugs like Triclosan and Furosemide were made by complexation with Cyclodextran and further entrapment in the Chitosan nanocarrier.The resulting nanosystem was evaluated for its zeta potential ability to associate and deliver the complexed drugs. It is observed that the nanosystem with chitosan has potential for Transmucosal delivery (TMD) of hydrophobic compounds.

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- Antimicrobial, bacteriostatic and fungistatic activity of chitosan in lipid emulsions and solutions was investigated.It was found that 0.5% chitosan confirmed to the requirements of preservation efficiency, in emulsion formulations for mucosal as well as for parenteral applications[14].
- The examination of effects of chitosan oligomers on pulmonary absorption of interferon alpha resulted in significant increase in serum interferon-aloha concentration. The findings confirm the use of chitosan improves the pulmonary absorption of biologically active peptides.
- Sustained release chitosan microspheres of recombinant human interleukin-2 were evaluated. It was found that rIL-2 was released in a sustained manner. Chitosan microspheres were added to the cells at different concentrations.The assay of rIL-2 confirm that chitosan microspheres is a suitable sustained release carrier for rIL-2 delivery.
- Investigation of solubilising and absorption enhancing property of Naproxen chitosan and polyvinyl pyrrolidone(PVP)concluded that chitosan is more effective than PVP.Direct compression property and subilising power makes chitosan suitable for fast release solid dosage form of naproxen.
- Chitosan the cationic polymer has potential for DNA complexation and could be useful for non viral vectors for gene therapy. Chitosan protects DNA against DNAase degradation.[15]
- Glipizide microspheres containing chitosan exhibited a good mucoadhesive property in the in-vitro wash off test and showed higher percentage drug entrapment efficiency.
- Insulin chitosan nano particles prepared by inotropic gelation of chitosan glutamate and Triphosphate penta sodium and by simple complexation of insulin and chitosan.It were observed that the Insulin-Chitosan solution formulation was found to be more effective than the complex nanoparticle formulation.
- Chitosan is able to increase pre corneal residence time of ophthalmic formulations containing active ingredients when compared with simple aqueous solutions. The study was conducted on tear concentration of Tobramycin and Ofloxacin after topical application of chitosan based solutions.
- It was experimented to microencapsulate protein loaded chitosan nanoparticles using typical aerosol excipients such as mannitol and lactose producing protein loaded nanoparticles to the lungs.
- The nanoparticles showed good protein loading capacity (65-80%) providing the release of 75-80% insulin within 15minutes.

**Other related applications of chitosan**

1. Chitosan is used in the fields as diverse as health care to agriculture, dyes to fabrics as:
    a. Water waste treatment by removal of metal ions and coagulants like dyes etc.
    b. In food industry as preservative and color stabilizer.
    c. It is used in medical bandages, contact lenses and other equipments.
    d. Biotechnology-In enzyme immobilization, cell recovery chromatography.
    e. Agriculture-Seed coating, fertilizer, controlled agrochemical release.
    f. Pulp and paper, surface treatment photographic paper.
2. Chitosan is useful as a polymer carrier for catalysts and for intermediate products for synthesis of fine chemicals.[16]
3. Several researchers have documented the successful use of products made with chitosan as part of weight loss programme.
4. As a dietary supplement chitosan is marketed in Japan as a fat blocker and for Cholesterol control. When combined with a sensitive diet and moderate exercise chitosan can help in eliminating unwanted fat.

**Pharmacokinesis**

Chitosan attaches itself to fat in the stomach before it is digested, thus traooing the fat and preventing its absorption by digestive tract. Fat in turn binds to the chitosan fiber forming a mass which the body cannot absorb, which is then eliminated by the body. Chitosan fibers differ from other fibers in that it possess a positive ionic charge which gives it the ability to bind chemically with negatively charged lipids ,fats and bile acids[17].As such chitosan can absorb upto 4-6 times its weight in fat and prevent that fat from being absorb in the body.

## Conclusion

Chitosan exhibits desired bio-degradability, weak antigenicity and superior bio-compatibility as compared with other natural polymers[18]. The polysaccharide chitin is abundantly found in nature making chitosan, plentiful and

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relatively inexpensive product[19].Chitosan is used in design of many different types of drug carriers for various administration routes like oral, parenteral, nasal, buccal, transdermal, vaginal, topical etc. It can be formulated as nanoparticles, microspheres , membrane sponge etc. For drug delivery, special preparation techniques are used to prepare chitosan drug carriers by taking care such parameters as cross linker concentration, chitosan molecules weight and processing conditions all these effect release rate of the loaded drug[20].Chitosan seems to be the biopolymer for the development of new derivatives.[21]

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