Chitosan - A Potent Bioplymer of Biomedical, Biochemical and Industrial Research

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Natural biomolecules have been the starting point for the discovery of many important modern medicines, nutraceuticals and biomaterials. This fact has led to biochemical and pharmacological investigations and general biological screening programme for natural products all over the world. In recent times, there is a lot of interest in drugs from marine origin with potential benefits. Marine organisms produce many bioactive substances, which are having a lot of potential applications. Chitosan is an important polysaccharide of marine origin prepared from the shells of crustaceans, clams, krills, oysters, squid, fungi and insects (Cardenas *et al.*, 2001).

Chitosan is a linear polysaccharide composed of randomly distributed β-(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucosamine (acetylated unit) (Fig. 1) and it is chemically similar to that of the plant fiber, cellulose (Fig. 2). Positive charge is carried on the acetyl remnants and when solubilized in an acid

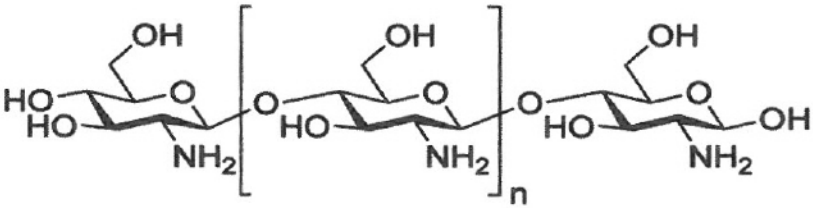

Fig 1. Structure of chitosan

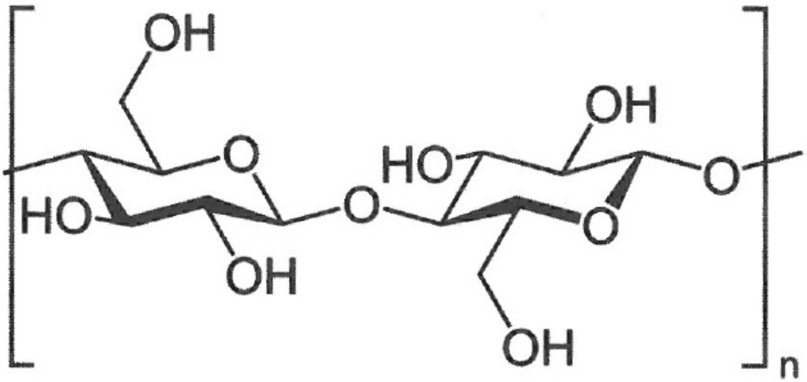

Fig 2. Structure of cellulose

environment, polymers will bind to negatively charged molecules such as lipids and fats. Generally crude chitosan is completely soluble in aqueous 2% w/v acetic acid. The solubility of the chitosan depends on the level of protonation in the NH_2 functional group moiety at C-2 position of the D-glucosamine repeating unit through conversion of marine polysaccharide into a polyelectrolyte in acidic media (Roberts, 1992). It is a special marine biopolymer possessing excellent characteristics such as biodegradability, biocompatibility, and antibacterial activity (Vimaladevi *et al.*, 2015). Hence it is considered as an interesting novel type functional biomaterial of nutraceutical and biomedical importance. The presence of NH_2 groups in chitosan is one of the major reasons for its greater potential in various applications as compared to chitin (Fig. 3). Chitosan is the only pseudonatural cationic polymer and thus has many applications in different fields.

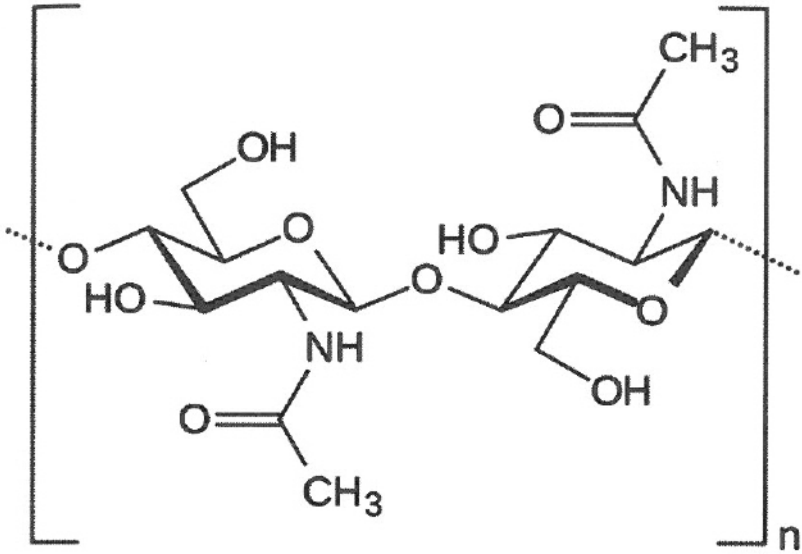

Fig 3. Structure of chitin

Chitosan as a vehicle improves the transport of polar drugs across epithelial surfaces, and is biocompatible and biodegradable. Some of the potential applications of chitosan and its derivatives are in the areas of medicine, water treatment, drug delivery, hydrogels, membranes, antioxidants, adhesives, food packaging and biosensors. Chitosan has been reported to possess immunological, antibacterial, antiulcer and wound healing properties (Vimaladevi *et al.*, 2015; Anandan *et al.*, 2004). Chitosan is also an effective and adequate hemostatic agent even under the most severe conditions of anticoagulation. It has been reported to possess antilipidemic (Santhosh *et al.*, 2006), antioxidant (Xie *et al.*, 2008) and membrane stabilizing properties (Filipovic-Grcic *et al.*, 2001). Experimental studies (Van Bennekum *et al.*, 2005; Sumiyoshi and Kimura, 2006) have shown that it behaves as a fibre in the gastrointestinal tract and increases the amount of fat eliminated in the stool. Han *et al.* (1999) reported that supplementation of chitosan is capable of attenuating high fat diet-induced hyperlipidemia in experimental animals. Reports by Filipovic-Grcic *et al.* (2001) indicated the membrane stabilizing property of chitosan. Administration of chitosan solution is found to exert beneficial actions in treating "athlete's foot" conditions. Earlier Anandan *et al.* (2004) observed the antiulcerogenic potential of chitosan against HCl-ethanol-induced gastric ulcer in rats. Reports by Sumiyoshi and Kimura (2006) have shown that the dietary supplementation of chitosan is capable of ameliorating high fat diet-induced hyperlipidemia in experimental animals. The reactive oxygen species quenching capable of chitosan and its derivatives has also been studied in detail (Xing *et al.*, 2005). As the chemical nature of chitosan tends to wrap solid particles in liquids to bring them together and agglomerate, it is efficiently exploited in the controlled release of various drugs (Dutta *et al.*, 2004). Recently, it has attracted more attention as a biomedical material, owing to its unique biological activities, which include antitumor, immune-enhancing effects and antibacterial activity in combination with its non-toxic nature (Kim *et al.*, 2003). Chitosan has profound applications in the fields of agriculture, clarification and purification, paper and textiles, chromatography, photography, food and pharmaceutical, nutrition and cosmetics, biotechnology and medicine (Senel and McClure, 2004; Santhosh *et al.*, 2006). Both hard and soft contact lenses can be made from chitosan.

In agriculture, chitosan and its derivatives are used mainly in seed treatment and plant growth stimulation. It also functions as an ecological friendly biopesticide substance, which enhances the innate ability of plants to defend themselves against fungal infections (El Hadrami *et al.*, 2010). Application of chitosan is found to increase photosynthesis, nutrient uptake, seed germination, sprouting and vigor in plants (Bhaskara Reddy *et al.*, 1999). Trimethylated chitosan is used in non-viral gene delivery into plant genome (Liu *et al.*, 2010). It is reported that the bio-control action of chitosan elicits natural innate defense responses within the plant to resist against insects, pathogens, and soil-borne diseases. Agricultural applications of chitosan can reduce environmental stress due to drought and soil deficiencies, strengthen seed vitality, reduce decay of vegetables, fruits and citrus crops, and increase yields (Rabea *et al.*, 2003).

Biodegradable flexible composite films prepared from gelatin and chitosan have homogeneous matrix, good water barrier, stable structure and mechanical properties (Gómez-Estaca *et al.*, 2010). The novel biodegradable films prepared from the mixture of chitosan and poly (lactic acid) solution using film-casting method exhibit interesting qualities especially in the field of bioactive packaging due to the antimicrobial properties of chitosan films and the excellent mechanical properties of PLA (Xie *et al.,* 2008). Chitosan may also be used as a coating material in the form of nanocomposite silica-chitosan coatings (Sharma *et al.*, 2009). Chitosan is also used as a coating material in fruits for effectively extending the shelf life. Chitosan is also used in the preparation of biosensors. Chitosan and its derivatives are appropriate for tissue engineering applications because of their gel forming, porous structure properties, biodegradability, ease of chemical modification, biocompatibility, high affinity to *in vivo* macromolecules and antibacterial activity (Jiang *et al.*, 2007; 2009).

Investigations by Zhong *et al.* (2012) have shown that the antimicrobial properties of acetyl, chloroacetyl, and benzoyl thiourea derivatives of chitosan against four bacterial species are much better than that of the parent chitosan. Antifungal actions of the chloroacetyl thiourea derivatives of chitosen is potentially higher than that of the acetyl and benzoyl thiourea derivatives. Chitosan/nylon-6 blended membranes with silver are antibacterial against both gram-negative and gram-positive bacteria (Ma *et al.*, 2008). The antimicrobial value of chitosan in lipid emulsions as well as in aqueous solutions is very much efficient in producing formulations with improved activity in terms of reducing the number of microorganisms (Tsai and Su, 1999).

Chitosan has been used as an adsorbent due to its high contents of amino and hydroxyl functional groups. Cross-linked chitosan has been prepared and stabilized in acid medium. A novel cross-linked chitosan resin has been functionalized with a threonine moiety through the extension arm of chloromethyloxirane and its potential assessed for application in a solid-phase extraction method (Katarina *et al.*, 2009). The introduction of azide and lactose moieties into chitosan provides much better water solubility at neutral pH values. These types of chemicals have been used as a biological adhesive for soft tissues (Ono *et al.*, 2000). Adhesive strength augments with increasing molecular mass of the chitosan samples used and number of amino groups available (Varshosaz *et al.*, 2006).

Nutraceutical and therapeutical interventions of water soluble vitamins has been known for long and recently they are being widely supplemented in food formulations. Especially phenolic acid-grafted chitosan derivatives can serve as exceptional biofunctional encapsulating materials for water soluble vitamins. Studies by Chatterjee *et al.* (2016) have shown that thiamine and pyridoxine loaded ferulic acid-grafted chitosan microspheres is capable of exerting enhanced anti-inflammatory activity in experimental animals. Coronary heart disesase is one of the major public concerns in both developed and developing countries. In recent times, there is growing interest in biomedical applications of marine biopolymers in the field of cardiovascular research. Experimental investigations (Anandan *et al.,* 2012; 2015) have demonstrated that the salubrious effect of dietary chitosan supplementation in attenuating experimentally-induced myocardial infarction condition is probably ascribable to its antioxidant defense and membrane-stabilizing properties.

Aging has been defined as the changes that occur in living organisms with the passage of time that lead to functional impairment and ultimately to death. Free radical-induced oxidative damage has long been thought to be the most important consequence of the aging process. Studies by Anandan *et al.* (2013) have suggested that chitosan could be an effective therapeutic agent in treatment of age-associated disorders where hypercholesterolemia and oxidative stress are the major causative factors. Investigations by Santhosh *et al.* (2007) have shown that dietary supplementation of chitosan is capable of attenuating the antitubercular drugs-induced hepatoxicity in rats.

Chitosan as a natural biopolymer has been extensively used in membrane applications because of its good film-forming character, high hydrophilicity and excellent chemical resistance properties. Since it is a cycloaliphatic biopolymer, it contains hydroxyl groups and active amino acids that can be chemically modified by several chemicals. Chitosan-based membranes have been used for ultrafiltration of biomaterials, protein separation or adsorption and pervaporation (Jayakumar *et al.*, 2011). Sodium alginate and chitosan have been used for preparation of enantioselective membranes (Meng *et al.*, 2010). These materials possess significant number of chiral active sites required for fine hydrophilicity. An ion-exchange membrane matrix prepared by grafting of poly (MAA) onto epichlorohydrin and poly (methacrylic acid) cross-linked chitosan membranes are found to be useful as an ion exchange adsorbent for the separation of basic proteins from biological fluids (Huang *et al.*, 2006). Among the diverse biodegradable polymers used for the development of controlled-release formulations, chitosan has been reported to be advantageous since it is a natural, biocompatible, non-toxic product with the potential for biodegradability (Santos *et al.*, 2007).

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