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Review Article

A Review On Biomedical Application Of Chitin And Chitosan

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Abstract

Chitin is the second most available polysaccharide after cellulose. It is a fairly ubiquitous compound produced by many organisms: fungi and algae cell walls, insects, exoskeletons, endoskeleton of mollusks and crustacean shells. Annually, it has been estimated that on 10^{10} to 10^{11} tons are produced by living organisms. However, commercially chitin is mainly recovered from marine sources, *i.e.*, the crustaceans processing industries. More than 10,000 tons of chitin extracted from shellfish waste, which could provide sufficient raw material for develoopment of value-added processes and products. Chitosan, composing of randomly distributed β-(1→4) linked D-glucosamine and *N*-acetyl-D-glucosamine residues, is obtained by alkaline deacetylation of chitin. Due to its nontoxicity, good biocompatibility, and susceptibility to chemical modification, chitosan has gained significant interest for applications in biotechnology, wastewater, cosmetics, agriculture, food technology, textiles, medical and pharmaceutical research. The present review provides insight into the different biomedical application of chitin and chitosan.

Keywords: Chitin, Chitosan, Biomedical, Water treatment, Wound healing

INTRODUCTION

Chitin is the second renewable carbon source after lignocelluloses biomass and, in fact, about 1600 tons of chitin are annually produced. For industrial production, solid chitin is soaked in 40–50% (w/v) NaOH. This process removes more than 80% of the acetyl residues and converts N-acetyl-D-glucosamine into β-1,4-D-glucosamine. Complete deacetylation is possible by repeating the alkaline treatment. Therefore, the term "chitosan" is not uniquely related to a defined compound, but to a group of commercially available copolymers that are heterogeneous for deacetylation degree, molecular mass, polymerization degree and acid dissociation constant (pKa value). These different characteristics, in particular the degree of deacetylation and the molecular weight, influence the physicchemical properties (including viscosity and solubility), and they have a direct influence on the biological properties of the substance and the effects on pathogens. All these characteristics make chitosan very useful for several industrial applications, namely cosmetology, food, biotechnology, pharmacology, medicine and, more recently, agriculture.

Chitin

Chitin is the second most ubiquitous natural polysaccharides after cellulose on earth and composed of beta (1-2)-linked 2-acetamide-2-deoxy-beta-D-glucose (N-acetyl glucosamine). Chitosan is a linear polymer of alpha (1-4)-linked 2-amino-2-deoxy beta-D-glucopyranose and is easily derived by N-deacetylation to varying extent that is easily consequently a copolymer of N-acetyl glucosamine and glucosamine. Chitin is mainly used as a raw material to produce chitin-derived products, such as chitosans, chitin/chitosan derivatives, oligosaccharides and glucosamine. An increasing number of useful products derived from chitin continue to attract commercial development. The large number of patents filed involving chitin-derived products reflects the commercial expectations for these products. Presentlhy, Chitin and chitosan prepared from crab and shrimp shells are now available as commercial products throughout the world (Pal *et al*., 2014).

Chitin is highly hydrophobic and It is soluble in hexofluroacetone, and chloroalcohols in conjunction with aqueous solution of minerals acids and dimethyl acetomide containing 5% lithium chloride and insoluble in water and in most solvents because of its compact structure. Therefore, chemical modifications of chitin are performed to obtain more soluble analogs, among which, chitosan, derived by partial *N*-deacetylation of chitin, is the most common such derivative (Rudall and Kenching., 1967).

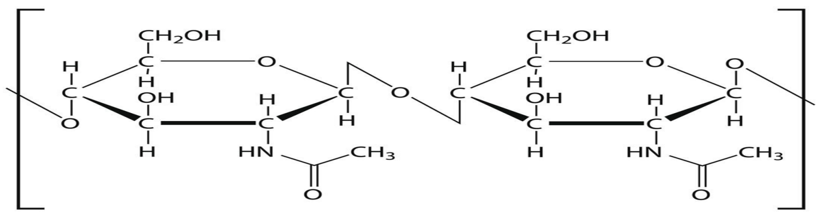

Fig. 1. Chemical structure of chitin. (Source: WEB-4, 2007).

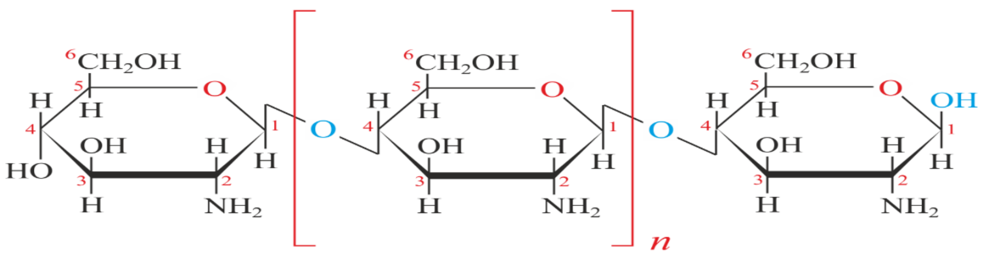

Fig. 2. Structure of chitosan

Chitosan

Chitosan was first reported by Roughet in 1859, who obtained the acid soluble fraction of chitin during boiling in a concentrated potassium hydroxide solution. It occurs naturally in some fungi but its content is much lesser than that of chitin. Chitosan is chemically defined as a copolymer consisting of two residues 2 acetomido-2deoxy β-D glucopyranose.

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 the chitin shells of shrimp and other crustaceans with an alkaline substance, like sodium hydroxide. Chitosan widely used in vastly diverse, ranging from waste management to food processing, medicine, and biotechnology (Kalult, 2008). In agriculture, the use of chitosan has been established to improve the yield of rice and orchid production. Chitosan can be utilized in a large number of industrial applications. Among main features include biocompatibility, biodegradability, antibacterial, chelating properties and non-toxicity (Kim, 2010).

Chitosan consumption are innumerous e.g. refutation of digestive function, fat absorption preventing its absorption by the body reduction of sugar and cholesterol levels in the body (Mathur *et al.*, 1990). Chitosan reduces LDL cholesterol levels without significantly affecting HDL cholesterol levels and others essential nutrients. The indigestibility in the upper gastrointestinal tract, high viscidity, polymeric nature and low affinity for alter in the lower gastrointestinal tract are factors responsible for the hypocholestrolermic effect of a fibrous diet. Chitosan meets most of criteria and has cleared the problems, bile acids and free fatty acid in solution with low PH through ionic bonds resulting from the aminic groups (Damian *et al.*, 2005). Chitosan is an excellent film forming material chitosan films has selective permeability to gasses (Co_2 and O_2) and good mechanical properties (Domard and Domard, 2001).

Chitosans are used in dietary supplements, water treatment, food preservation, agriculture, cosmetics, pulp & paper and medical applications (Sanford, 2002). There has been a large increase in chitosan research during the past decade. This is due to its biocompability, biodegradability, non-toxicity, and other unique properties such as film forming ability, chelation and adsorption properties and antimicrobial activity (Kumar, 2000).

Chitosan is a natural polysaccharide comprising of copolymers of glucosamine and *N*-acetyl glucosamine, and can be obtained by the partial deacetylation of chitin. Chitosan has been widely used in vastly diverse fields, ranging from waste management to food processing, medicine and biotechnology. These products were characterized by their biological activity as antimicrobial and antifungal properties (Limam *et al.,* 2011).

Application of chitin:

Chitin have immense applications in various fields such as food industry, cosmetics, agriculture, water treatment, biomedicine, textile, biotechnology, paper industry, wound healing agents etc. Chitin is used in toothpaste, mouthwashes and chewing gum. They freshen the breath and prevent the formation of plaque and tooth decay. The deacidifying ability of chitin is utilized in coffee industry and to clarify the beverages such as wine, beer and fruits juices. In paper industry, chitin helps in recycling paper (Bhavani and Dutta, 1999). In textile industry, chitin used in printing and finishing preparations.

Agriculture

Chitin is a good inducer of plant defense mechanisms for controlling diseases. It has also been assessed as a fertilizer that can improve overall crop yields. In agriculture, chitin treated seeds (wheat) were found to have growth accelerating and growth enhancing effects.

Industrial

Chitin is used in industry in many processes, examples of the potential uses of chemically modified chitin in food processing include the formation of edible films and as an additive to thicken and stabilize foods. Processes to size and strengthen paper employ chitin and chitosan. In food industry, microcrystalline chitin is good emulsifying property, superior thickening and gelling agent. It also used as a dietary fibre in baked foods.

Medical

The interest in chitin originates from then study of the behavior and chemical characteristics of lysozyme, an enzyme present in the human body fluids it dissolves certain bacteria by cleaving the chitinous material of the cell wall. A wide variety of medical applications for chitin and chitin deravatives have been reported over the last three decade. It has been suggested that chitosan may be used inhibit fibroplasias in wound healing and to promote tissue growth and differentiation in tissue culture (Datta *et al.,* 2004).

Application of chitosan

Tissue engineering

Tissue engineering is the development and manipulation of laboratory-grown cells, tissues or organs that would replace or support the function of defective or injured parts of the body. The special attention on chitosan has been paid for the repair of articular cartilage. Microporous chitosan/calcium phosphate composite scaffolds have been synthsized and characterized for tissue engineering. They reported that chitosan provides a scaffold form and calcium phosphates encourage osteoblast attachment which strengthens the scaffold (Zhang and Zhang, 2001)

Wound healing process

Chitin and Chitosan show good effect on wound dressing/wound healing process have the abilities to enhance the wound healing process.the repeating mono-subunit, which is present in chitin and chitosan, N-acetyl glucosamine (NAG),is an important component of dermal tissue and necessary for scar tissue repair. Chitin and chitosan effectively support cell growth by their high positive surface and their surface leads to thrombosis.

Gene therapy

Several literature survey show that chitosan is a suitable material for efficient non-viral gene therapy (Jayakumar *et al,.* 2010). Besides many good characteristics, chitosan has growth-inhibition effect on tumor cells. The ligand-targated approach is expected to deliver drugs to tumor tissues selectively with high efficiency. Although *in vivo* studies of targated chitosan nanoparticles are currently limited, results from *in vitro* studies have demonstrated their promise for applications in cancer treatment and diagnosis (Hang, 2010).

Chitosan film as food packing item

As chitosan shows antimicrobial activity so its film has shown great promise for their applicaton in food preservation. The antimicrobial activity limits or prevents microbial growth by extending the interval period and reducing the growth rate or decreasing live counts of microorganisms (Han, 2000) which support the chitosan film for its potentiality in the packaging of food items and food preservation.

Development of Artificial Kidney

The design of artificial kidney systems has made possible separative hemodialysis and the sustaining life of chronic kidney failure patients. Chitosan membrane has been proposed as an artificial kidney membrane because of their suitable permeability and high tensile strength. The most important part of artificial kidney in the semi permeable membrane and so far, made from commercial regenerated cellulose and cuprophone. Since the primary action of the cellulose membrane is that a sieve, there little selectivity in the separation of two closely elated molecules. A series of membrane prepared from chitin and chitoson improved dialysis properties. One of the most serious problem 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 dialysed only at great risk. most chance, hence there are the most challenging problems still to be resolved in the development of membrane which are inherently blood compatible from there point of view chitosan is haemostatic that is cause clots.

Chitosan in waste water treatment

Chitin and chitosan mixtures were found to remove arsenic from contaminated drinking water. Chitosan molecule has the ability to interact with bacterial surface and in asorbed on the surface of the cells and stack on the microbial surface and forming impervious layer around the cell leading to block the channel.

Application of chitosan and chitosan as a nanoparticle in waste water treatment

Water containing unwanted substances which adversely affect its quality and thus making it unsuitable for use is termed as waste water. Waste water is generated from various sources such as residential areas, commercial/industrial properties, agricultural etc. composition of waste water varies widely and depending upon the sources from which it generates, common constituents of wastewater are pathogenic and nonpathogenic micro organisms. The most important pathogenic organisms responsible for water borne diseases in India are bacteria viz., *E. coli, Shigella flexinari and Vibrio cholera.* Organic substances such as excreta, plant materials, food protein and inorganic substances like metal particles, ammonia along with gases when left untreated these constituents may pose threat to living beings and the environment, which make it essential to threat waste water before disposal various physical, chemical and biological treatment process are used for waste water treatment. Metals which are discharged into natural water as increased concentration from sewage, industrial effluent or mining operation can have serve toxicological effects on human and aquatic ecosystem heavy metals As, Cr, Pb, Hg, Cu, Zn, Ni are toxic for plants and human beings. These metals even in traces amount, interfere with or inactivate enzymes of living cells. Therefore, their discharge into environment should be minimized and controlled carefully.

Chitosan as a nanoparticle

Synthesized nanoparticles of naturally occurring chitosan have many potentials in low cost water disinfection system. The antibacterial properties of chitosan nanoparticle have been explained by various mechanism one theory possess increase in membrane permeability and eventual rupture and leakage of intracellular components when the positively charged chitosan particle react with negatively charged cell membrane as the chief antimicrobial mechanism. Another mechanism proposes chitosan penetrate cell membrane walls and binds with DNA and thus inhibit RNA synthesis in cell.

Base material for stem cell culture

Chitosan is a natural biomaterial with a structural similarity to hyaluronic acid of extra-cellular matrix. Though the osteogenic property of chitosan is well established in tissue engineering application, the exact mechanism is not yet understood. They utilize chitosan to modify tissue culture plates to understand its effect on adhesion and osteoblast differentiation of bone marrow derived human mesenchymal stem cells. The two major objectives are to evaluate the potential of chitosan for tissue culture plate modification and to understand the mechanism of osteogenesis by chitosan in terms of gene expression and mineral matrix deposition. These results will pay way to develop chitosan-based culture plates and biomimetic scaffolds for various cell cultures and bone tissue engineering application.

Harmful effects of chitin and chitosan

Gavhane *et al* (2013) reported wide biomedical applications of chitin and chitosan, however, he also highlighted some limitations such as allergy and constipation. Furhermore people with intestinal malasorption syndroms should not use chitosan. Its adverse effects on the growth of children and on the outcome of pregnancy were also reported. However, application of chitin and chitosan have faced some limitation with high viscosity and low solubility at neutral pH (Kim & Dewapriya, 2014)

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Table 1. Utilizatiaon of chitosan in different industries and mode of action

Industry	**Mode of application**	**Reference**
Cosmetics	It is function as a moisturizer, cream, pack material, lotions, nail enamel, nail laequers, foundations, eye shadow, and lipstick.	Arnaz *et al.*, 2018
Water engineering	Chitosan used as flocculating agents. It also acts as chelating and heavy metals trapper. Chitosan was effective in removing petroleum products from wastewater.	Pontius, 2016
Paper industry	Chitosan involved in manufacture of paper which is resistant to moisture	Habibie *et al.*, 2016
Agriculture	Chitosan helps in significant reduction/ suppression of fungal pathogens.	Sharp, 2013
Burn treatment	Chitosan is used for burn treatment. Chitosan can form tough, water-absorbent, biocompatible film.	Baxter *et al.*, 2013
Wound healing/Wound dressing	Chitosan has been found to have an effective on wound healing/ wound dressing process. Regenerated chitin fibers, non-woven mats, sponges and film exhibit an increase wound healing by 30%.	Patrulea *et al.*, 2015
Drug delivery system	Chitin /chitosan are still utilized in the pharmaceutical field. Compounds having a molecular weight lower than 2900 pass through membrane derived from chitosan.	Ali and Ahmed, 2017
Bone filling material	In addition, an interesting application is composite bone filling material, which form a self -hardening paste for tissue regeneration in treatment of periodontal bony defects	Levengood and Zhang, 2014
Anticancer drug	Chitosan have been claimed as anticancer drugs	Babu and Ramesh, 2017