Chitin and chitosan: Chemistry, properties and applications

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Chitin and chitosan are considerably versatile and promising biomaterials. The deacetylated chitin derivative, chitosan is more useful and interesting bioactive polymer. Despite its biodegradability, it has many reactive amino side groups, which offer possibilities of chemical modifications, formation of a large variety of useful derivatives that are commercially available or can be made available via graft reactions and ionic interactions. This study looks at the contemporary research in chitin and chitosan towards applications in various industrial and biomedical fields.

Keywords: Chitin, Biodegradability, Chitosan, Biomaterials

Introduction

Chitin is the second most ubiquitous natural polysaccharide after cellulose on earth and is composed of β(1→4)-linked 2-acetamido-2-deoxy-β-D-glucose¹ (N-acetylglucosamine) (Figure 1). 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 (−NHCOC₂H₅) at the C-2 positions. Similarly the principle derivative of chitin, chitosan is a linear polymer of α (1→4)-linked 2-amino-2-deoxy-β-D-glucopyranose and is easily derived by N-deacetylation, to a varying extent that is characterized by the degree of deacetylation, and is consequently a copolymer of N-acetylglucosamine and glucosamine (Figure 2). Chitin is estimated to be produced annually almost as much as cellulose. It has become of 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.

![Figure 1 — Structure of chitin](image1)

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 carotenoid 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 lagoons. 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 its utility.

![Figure 2 — Partially deacetylated chitin](image2)

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Chitin and chitosan the naturally abundant and renewable polymers have excellent properties such as, biodegradability, bio-compatibility, non-toxicity, and adsorption. The reaction of chitosan is considerably more versatile than cellulose due to the presence of -NH₂ groups. Various efforts have been made to prepare functional derivatives of chitosan by chemical modifications, graft reactions, ionic interactions, and only few of them are found to dissolve in conventional organic solvents. Chitosan is only soluble in aqueous solutions of some acids, and some selective N-alkylidinations and N-acylation have also been attempted. Although several water-soluble or highly swelling derivatives are obtained, it is difficult to develop the solubility in common organic solvents by these methods. Modification of the chemical structure of chitin and chitosan to improve the solubility in conventional organic solvents has been reviewed by many authors. On the other hand, only a few reviews have been reported on biomedical applications of chitin/chitosan, and no comprehensive review has yet been published covering the entire range of applications. The present review covers the literature from 1993 to 2003 dealing with properties, processing, and applications in various industrial and biomedical fields.

**Chitin and Chitosan Processing**

Chitin and chitosan are natural resources waiting for a market. They were waste products of the crabbing and shrimp canning industry. The US Department of Commerce reported in 1973 that they were over 1.50,000 Mt of chitin produced as processing waste from shellfish, krill, clams, oysters, squid, and fungi. Commercially chitin and chitosan are of great importance owing to their relatively high percentage of nitrogen (6.89 per cent) compared to synthetically substituted cellulose. The crustacean shells mainly involves the removal of proteins and the dissolution of calcium carbonate that is present in crab shells in high concentrations. The resulting chitin is deacetylated in 40 per cent sodium hydroxide at 120 °C for 1-3 h. This treatment produces 70 per cent deacetylated chitosan.

The following four steps in chronological order of the process are needed to produce chitosan from crustacean shells: (i) Deproteinization, (ii) Demineralization (Unpublished data, one of the authors, Pradeep Kumar Dutta investigated a new method of demineralization of crustacean shells and claimed better property than the existing process), (iii) Decolouration, and (iv) Deacetylation.

![Chitin and Chitosan Processing Diagram](image)

Crustacean shells → Size reduction → Protein separation → (NaOH) → Washing Demineralization (HCl) → Washing and Dewatering → Decolouration → Chitin → Deacetylation (NaOH) → Washing and Dewatering → Chitosan

**Properties of Chitin and Chitosan**

Most of the naturally occurring polysaccharides e.g., cellulose, dextrin, pectin, alginic acid, agar, agarose, and carragenas are natural and acidic in nature, whereas chitin and chitosan are examples of highly basic polysaccharides. Their properties include solubility in various media, solution, viscosity, polyelectrolyte behavior, polyoxysalt formation, ability to form films, metal chelations, optical, and structural characteristics.

Although the β(1→4)-anhydroglucosidic bond of chitin is also present in cellulose the characteristic properties of chitin/chitosan are not shared by cellulose. Chitin is highly hydrophobic and is insoluble in water and most organic solvents. It is soluble in hexafluoroisopropanol, hexafluoroacetone, and chloroalcohols in conjunction with aqueous solutions of mineral acids and dimethylacetamide (DMAc) containing 5 per cent lithium chloride (LiCl). Recently the dissolution of chitosan in N-methyl morpholine-N-oxide (NMMO)/H₂O has been reported by Dutta et al. The hydrolysis of chitin with concentrated acids under drastic conditions produces relatively the pure amino sugar, D-glucosamine.

Depending on the extent of deacetylation, chitin contains 5 to 8 per cent (w/v) nitrogen, which is mostly in the form of primary aliphatic amino groups as found in chitosan. Chitosan undergoes the reactions typical of amines, of which N-acylation and Schiff reactions are the most important. Chitosan glucans are easily obtained under mild conditions but it is difficult to obtain cellulose glucans.
$N$-acylation with acid anhydrides or acyl halides introduces amido groups at the chitosan nitrogen. Acetic anhydride affords fully acetylated chitins. Linear aliphatic $N$-acyl groups higher than propionyl permit rapid acetylation of the hydroxyl groups in chitosan\textsuperscript{5,6}. Highly benzoylated chitin is soluble in benzyl alcohol, dimethyl sulphoxide (DMSO), formic acid, and dichloroacetic acid. The $N$-hexanoyl, $N$-decanoyl and $N$-dodecanoyl derivatives have been obtained in methanesulphonic acid\textsuperscript{1}.

Chitosan forms aldimines and ketimines with aldehydes and ketones, respectively, at room temperature. Reaction with ketoacids followed by reduction with sodium borohydride produces glucans carrying proteic and non-proteic amino acid groups. $N$-carboxy-methyl chitosan is obtained from glyoxylic acid. Examples of non-proteic amino acid glucans derived from chitosan are the $N$-carboxybenzyl chitosans obtained from $o$- and $p$-phthalaldehydic acids\textsuperscript{22}.

Chitosan and simple aldehydes produce $N$-alkyl chitosan upon hydrogenation. The presence of the more or less bulky substituent weakens the hydrogen bonds of chitosan; therefore, $N$-alkyl chitosans swell in water inspite of the hydrophobicity of alkyl chains. They retain the film forming property of chitosan\textsuperscript{1,3}. Chitosan is more versatile in comparison to chitin due to the presence of amino groups at the C-2 positions.

**Chemical Properties of Chitosan**

The chemical properties of chitosan are as follows:

- Linear polyamine,
- Reactive amino groups,
- Reactive hydroxyl groups available,
- Chelates many transitional metal ions.

**Biological Properties of Chitosan**

Following are the biological properties of chitosan:

- Biocompatible
  - Natural polymer,
  - Biodegradable to normal body constituents,
  - Safe and non-toxic,
  - (the research in chitinase is noteworthy in this respect).
- Binds to mammalian and microbial cells aggressively,
- Regenerative effect on connective gum tissue,
- Accelerates the formation of osteoblast responsible for bone formation,
- Hemostatic,
- Fungistatic,
- Spermicidal,
- Antitumor,
- Anticholesteremic,
- Accelerates bone formation,
- Central nervous system depressant,
- Immunoadjuvant.

**Derivatives of Chitin and Chitosan**

Chitosan may be readily derivatized by utilizing the reactivity of the primary amino group and the primary and secondary hydroxyl groups. Glycol chitin, a partially $o$-hydroxyethylated chitin was the first derivative of practical importance\textsuperscript{4,23}.

Derivatives of chitin may be classified into two categories; in each case, the $N$-acetyl groups are removed, and the exposed amino function then reacts either with acyl chlorides or anhydrides to give the group $\text{NHCOR}$ or is modified by reductive amination to $\text{NHCH}_2\text{COOH}$ of greatest potential importance are derivatives of both types formed by reaction with bi- or polyfunctional reagents, thus carrying sites for further chemical reaction\textsuperscript{24,25}. In practice, such reactions are carried out on native chitin or on incompletely deacetylated chitin, chitosan, so that the resulting polymer contains three types of monomeric units.

These polyampholytes are particularly effective in removing metal cations from dilute solutions. Chitosan itself chelates metal ions, especially those of transition metals, and also finds application as a matrix for immobilization of enzymes\textsuperscript{26}. Special attention has been given to the chemical modification of chitin, since it has the greatest potential to be fully exploited. Reactions with pure chitin have been carried out mostly in the solid state owing to the lack of solubility in ordinary solvents. A 50 per cent deacetylated chitin has been found to be soluble in water\textsuperscript{1,17}. This water-soluble form of chitin is a useful starting material for its smooth modifications, through various reactions in solution phase. Some of the very recently reported chitosan derivatives are enumerated as follows:
(i) N-phthalamoylation of Chitosan

Owing to its poor solubility in some limited organic solvents, it needs some chemical modifications. N-phthalamoylation of chitosan was expected to be effective for solubilization since it affixes a bulky group to the rigid backbone and breaks hydrogen atoms on the amino groups to prevent hydrogen bonding. Fully deacetylated chitosan was treated with phthalic anhydride in DMF to give N-phthalamoyl-chitosan. It was readily soluble in polar organic solvents. Further reactions had been carried out using this new derivative to improve the solubility of chitosan. Those are given below for better understanding.

![Chemical structure](image)

All these derivatives are soluble in common polar organic solvents.

(ii) Dendronized Chitosan-sialic Acid Hybrids

To improve water-solubility, Sashiwa et al. have successfully synthesized dendronized chitosan-sialic acid hybrids by using gallic acid as focal point and tri(ethylene glycol) as spacer arm. The water solubility of these novel derivatives was further improved by N-succinylation of the remaining amine functionality.

(iii) Methylthiocarbamoyl and Phenylthiocarbamoyl Chitosans

Recently, Baba et al. have synthesized methylthiocarbamoyl and phenylthiocarbamoyl chitosan derivatives to examine the selectivity toward metal ions from aqueous ammonium nitrate solution.

![Chemical structure](image)

(iv) Lactic/glycolic Acid-chitosan Hydrogels

The synthesis of chitosan hydrogels was carried out by Qu et al. by direct grafting of D,L-lactic and/or glycolic acid onto chitosan in the absence of catalysts. They demonstrated that a stronger interaction existed between water and chitosan chains after grafting lactic and/or glycolic acid. The side chains could aggregate and form physical crosslinking, which results in pH-sensitive chitosan hydrogels. These hydrogels are considered potentially useful for biomedical applications such as, wound dressings and drug delivery systems, since both polyester side chains and chitosan are biocompatible and biodegradable.

(v) CdS Quantum dots (QDs) Chitosan Biocomposite

Derivatives with CdS QDs improved aqueous solubility and stability of chitosan. They also influenced the thermal decomposition of chitosan. In the presence of this thermal decomposition of chitosan was shifted to 50 °C. An efficient procedure for the preparation of CdS QDs chitosan biocomposite is achieved by mixing chitosan with Cd(Ac)\(_2\) and subsequently dissolving in 1 per cent HAc aqueous solution, followed by the treatment with CdS and thus smooth, flat, yellow CdS QDs chitosan composite films were obtained.

(vi) Chitosan-gadopentetic Acid Complex Nanoparticles for Cancer Therapy

The potential of gadolinium neutron capture therapy has been reported in the recent past. In 1999, Tokumitsu et al. have reported that chitosan-gadopentetic acid complex nanoparticles could be used for gadolinium neutron capture therapy (Gd-NCT). It is a cancer therapy that utilizes protons and neutrons and electrons emitted \textit{in vivo} as a result of the nuclear neutron capture reaction with administered gadolinium-157, a non-radio element. Tokumitsu et al. have demonstrated that Gd-NCT using novel gadolinium-loaded nanoparticles are potentially highly suitable for intratumoral injection into solid tumor.

(vii) Nanocomposite from Natural Polysaccharide (Chitin/chitosan)

Although chitin and chitosan are useful biomass polymers, their applications are limited. An outstanding concept would bring a revolution by mixing natural polymers with man made polymers (synthetic polymers). Institute for Marine Resource and Environment, Japan studied mechano-chemical preparation of a novel composite under a dry and solid state. They synthesized a new type of polysaccharide composite by ball-milling a polysaccharide with synthetic polymer. The thermal
behaviour and molecular motion of the synthetic polymer in the composite are entirely different from those of original one. These results suggest strong interactions between a polysaccharides and synthetic polymer and thus compatibilization of the polysaccharides and synthetic polymer. The authors' laboratory synthesized chitosan-polyactic acid based nanocomposites under mild conditions for smart drug release (Unpublished results).

Applications of Chitin and Chitosan

The interest in chitin originates from the study of the behaviour 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 walls. A wide variety of medical applications for chitin and chitin derivatives have been reported over the last three decades. It has been suggested that chitosan may be used to inhibit fibroplasia in wound healing and to promote tissue growth and differentiation in tissue culture.

The poor solubility of chitin is the major limiting factor in its utilization and investigation of its properties and structure. Despite these limitations, various applications of chitin and modified chitins have been reported in the literature, e.g., as raw material for man-made fibres. Fibres made of chitin and chitosan are useful as absorbable sutures and wound-dressing materials. These chitin sutures resist attack in bile, urine and pancreatic juice, which are difficult with other absorbable sutures. It has been claimed that wound dressings made of chitin and chitosan fibres accelerate the healing of wounds by about 75 per cent. Apart from their applications in the medical field, chitin and chitosan fibers have potential applications in wastewater treatment, where the removal of heavy metal ions by chitosan through chelation has received much attention. Their use in the apparel industry, with a much larger scope, could be a long-term possibility.

Industrial Applications of Chitosan

Due to its physical and chemical properties, chitosan is being used in a vast array of widely different products and applications, ranging from pharmaceutical and cosmetic products to water treatment and plant protection. In different applications, different properties of chitosan are required. These properties change with, e.g., degree of acetylation and molecular weight as well.

Cosmetics

Usually organic acids are used as good solvents for cosmetic applications. A natural aminopoly-saccharide, chitosan can be encompassed in the class of hydrocolloids. However, unlike the most of other hydrocolloids which are polyanions chitosan is the only natural cationic gum that becomes viscous on being neutralized with acid. It facilitates its interaction with common integuments (skin covers) and hair. Chitin and chitosan are fungicidal and fungistatic in nature. Chitosan is compatible with lots of biologically active components incorporated in cosmetic products composition. Chitosan or chitosan-derivative nanocomposites in the range of 1-10 μm, as well as microcapsules including various hydrophobic substances find a wide application in cosmetics. It may be noted that substances absorbing the harmful UV radiation or different dyes can be easily covalently linked to chitosan aminogroups. Compositions based on chitosan and other hydrocolloids containing anti-oxidants, anti-allergic, and anti-inflammatory substances of vegetable origin, new types of depilatory and means for curling and doing the hair are being worked out by the workers of Sonat Co., USA. Chitin, chitosan and their derivatives offer uses in three areas of cosmetics: hair care, skin care, and oral care.

Chitosan and hair are complementary to each other owing to carry opposite electrical charges: chitosan positive and hair negative. A clear solution that contains chitosan forms a clear, elastic film on hair, thereby increasing its softness, smoothness, and mechanical strength. The material can also form a gel when added to mixtures of alcohol and water. Chitosan can be used in shampoos, rinses, permanent wave agents, hair colorants, styling lotions, hair sprays, and hair tonics. Several derivatives of chitosan and chitin have potential applications in hair care. They include glyceryl chitosan, an adduct of an oligomer of hydrolyzed chitosan, n-hydroxypropyl chitosan, quaternary hydroxypropyl-substituted chitosan, polyoxyalkylene chitosan, chitosan oligosaccharides, chitin sulphate, and carboxymethyl chitin. Some derivatives of chitosan can form foam and create emulsifying action and chitin powder can be used directly in shampoo.
products are so high that they cannot penetrate the skin. Thus, e.g., chitosan can function as a moisturizer for skin. Because of its lower costs, it might compete with hyaluronic acid in this application. Both chitosan and chitin are already found in creams, pack material, lotions, nail enamel, nail lacquers, foundation, eye shadow, lipstick, cleansing materials, and bath agents. Chitosan acylated with an organic diacid anhydride, and fine particles of chitin or chitosan are used for skin care.

Both, chitin and chitosan, can be used in toothpaste, mouthwashes and chewing gum. They freshen the breath and prevent the formation of plaque and tooth decay. Salts of chitosan, added to toothpaste, mask the unpleasant taste of silicon oxide and bind powders so that they maintain their granular shapes. Chitin can also be applied as a dental filler material and both chitin and chitosan absorb candida like thicans, a fungus that sticks to teeth, making them candidates to clean false teeth.

The other applications of chitosan are described elsewhere and few of these are summarized:

**Water Engineering**

Due to its polycationic nature, chitosan can be used as flocculating agent. It can also act as chelating agent, and heavy metals trapper. Weltrowski et al. used chitosan N-benzyl sulphonate derivatives as sorbents for removal of metal ions in acidic medium. In 1999, Bhavani and Dutta reported the removal of colour from dyehouse effluents using chitosan as an adsorbent. Considerable amounts of world production of chitin and chitosan and derivatives are used in wastewater treatment. Chitosan molecules agglomerate largely anionic wastes in solution to form precipitates and floe, hence it act as a flocculent for recycling of food processing waste. Chitosan can compete effectively with synthetic resins in the capture of heavy metals from processing water. Chitin has been used to decontaminate plutonium containing wastewater, and water containing methyl-mercury acetate, a significant pollutant of wastewater from acetaldehyde production. Application of chitosan/chitin mixture was found to remove arsenic from contaminated drinking water. Chitosan has also been found effective in the removal of petroleum and petroleum products from wastewater. The deacidifying ability of chitin is utilized in coffee industry and to clarify the beverages such as wine, beer, and fruit juices. Regenerated chitin, chitosan, and other chitinuous membranes could be widely used for such processes as osmosis, reverse osmosis, micro-filtration, desalination, dialysis, and haemodialysis. Beds of flaked chitosan can also be used for purification of potable water.

**Paper Industry**

Biodegradable chitin and chitosan can strengthen recycled paper and increase the environmental friendliness of packaging and other products. Chitosan is already involved in the manufacture of paper because chitosan molecules greatly resemble those of cellulose the main constituent of plant walls. It also saves chemical additives and increases output. Lastly the paper produced with chitosan has a smoother surface and is more resistant to moisture. Among other things, chitosan is of great value in the production of toilet paper and for wrapping paper and cardboard. Hydroxymethyl chitin and other water soluble derivatives are useful end derivatives in paper making. It can be used as a biodegradable packaging material for food wrap and other products.

**Textile Industry**

Derivatives of chitin have been produced and used to impart antistatic and soil repellent characteristics to the textiles. In textile industry, chitin can be used in printing and finishing preparations, while the chitosan is able to remove dyes from dye processing effluents. Besides these, chitin and chitosan both have made remarkable contribution to medical related textile sutures, threads, and fibres.

**Food Processing**

Use of chitosan in food industry is well known because it is not toxic for warm-blooded animals. Microcrystalline chitin (MCC) shows good emulsifying properties, superior thickening, and gelling agent for stabilizing foods. It is also used as a dietary fibre in baked foods. The use of MCC solved some of the problems such as, flavour, colour, and shelf-life, posed by other sources of fibre. It could be of special importance for manufacturing protein-fortified bread, even without such ingredients as emulsifiers and shortenings. Chitin and chitosan act as solid support for the entrapment of whole microbial, animal, or plant cell immobilization. Chitin has been used in immobilization of enzymes. It can be used as a non-absorbable carrier for highly concentrated food ingredients, e.g., (Food dyes and nutrients). In India, incorporation of chitin in poultry feed at a level of 0.5
per cent decrease the food consumption ratio and increases body weight by 12 per cent in comparison with birds fed a chitin free diet. Similarly, nutritional studies in the US have shown that chicks fed on a diet containing dried whey and chitin, utilized whey more efficiently and gained more weight than those fed similar but chitin free diet. Trials also showed that small amounts of chitin added to the diets of chicks and calves enabled the animals to digest milk lactose through increased growth of specific intestinal bacteria. These bacteria impede the growth of other types of organisms and generate the enzyme required for lactose digestion. This property may be of immense importance, since certain groups of human and many animals have lactose intolerance. There is no complete study on the metabolism of chitin and chitosan in the human body, therefore, the use of these polymers in food processing industries still needs to be further explored.

Agriculture

Chitin treated seeds (wheat) were found to have growth accelerating and growth enhancing effects. Chitinous additions to the potting mixtures/soil resulted in significant reduction in root knot worm infestations and suppression of fungal pathogens.

Photography

In colour photography, chitosan has been used as a fixing agent for the acid dyes in gelatin and also acts as an aid to improve diffusion, an important step in developing photographs.

Chromatographic Separations

Chitin and chitosan find wide varieties of applications in chromatographic separations. The presence of free –NH₂ groups, primary –OH groups and secondary –OH groups in chitosan makes it as an useful chromatographic support. Use of chitosan in thin layer chromatography for separation of nucleic acids have also been reported. Rhee et al. have used chitin and chitosan as sorbent material to solid phase extraction of phenol and chlorophenols by using High-Performance Liquid Chromatography (HPLC).

Solid State Batteries

Due to insolubility of chitosan in water, it cannot take part alone in fabrication of solid state proton-conducting polymer batteries. Therefore, chitosan is dissolved in acetic acid to produce ionic conductivity. The conductivity is due to the existence of proton in the acetic acid solution. The transport of these protons is considered to occur through many microvoids in polymer. Small dielectric constants from piezoelectric studies attributed the presence of many microvoids in this polymer structure. The choice of a more suitable electrode material may produce a better battery system.

Chitosan Gel for LED and NLO Applications

Recently, dyes containing chitosan gels have been used as potential components in lasers and other light-emitting devices (LEDs). The process, called doping, utilizes dyes such as, porphyrin compounds that resemble the heme groups in blood. Research on porphyrins and other dyes, such as, fluorinated coumarin and rhodamine B for transparent thin films, nickel porphyrins to investigate any new properties of films are on the line. One of the authors (PKD) at the laboratory the chitosan containing azomethine chromophore as a pendant group for NLO applications has been reported (Unpublished results).

Biomedical Applications of Chitosan

The design of artificial kidney systems has made possible repetitive hemodialysis 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 semipermeable 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 dialysed 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.

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 many potential advantages of tissue engineering include the development or revolution of current technology in total hip, knee, cartilage, tendon, and vascular replacement. Many of these practices at present involve implantation either an autologous or synthetic graft in place of the damaged area. Within the body the implant must satisfy requirements relative to biocompatibility as well as functional and mechanical stability. Many materials can react compatibly with the body. But unfortunately, they cannot meet the long-term mechanical, geometrical, and functional requirements of the body. Therefore, tissue engineering technology has been developed to construct artificial tissues that can mimic the natural ones by combining with modulated cells with different types of scaffolding materials, including natural and synthetic polymers. Among these material polylactide (PLA), polyglycolide (PGA) and their copolymer, polylactide-co-glycolide (PLGA) have received much attention because of their biodegradability and biocompatibility, these are suitable candidates for tissue engineering. Chitosan and its some derivatives have been studied for use in several biomedical applications including wound dressings, drug delivery systems, and space filling implants. But little, in comparison to these, has been done to explore use of chitosan within the tissue engineering paradigm. Chitosan has been found to have an acceleratory effect on the tissue engineering processes owing to its polycationic nature. This enhances the cells attraction to this polymer. It has been found that degree of cell attachment also depends on the per cent of deacetylation of the chitosan.

In 2000, Prasitsilp et al. showed how degree of deacetylation affected in vitro cellular responses to chitosan from two different sources, shrimp and cuttle fish. They examined four chitosan substrates, two from each source, differing by about 10 per cent in deacetylation and ranging between 76 and 90 per cent deacetylation. Results indicated that cells are more readily attached to more highly deacetylated chitosans from both sources.

In 2003, Wang et al. have developed a novel method (thermally induced phase separation method) to prepare polyglycolic acid (PGA)-chitosan hybrid matrices using solvents of low toxicity (DMSO and acetic acid). The matrices with the weight ratio of PGA to chitosan being 7:3 and 3:7 were called the P/C-1 (containing 70 wt per cent PGA) and P/C-2 (containing 30 wt per cent PGA) matrices, respectively. They cultured fibroblast cells in DMEM supplemented with 10 per cent FBS. These were seeded onto chitosan and PGA-chitosan hybrid matrices at a density of 1.5 x 10^6 cells/cm². Results indicated that the cell adhesion and proliferation was better on the P/C-1 matrix than that on the chitosan and P/C-2 matrices. The P/C-1 hybrid matrix was characterized by large pore size, good mechanical properties and degradability. The success of seeding cells in this matrix demonstrated the potential of the matrix as new biomaterial for tissue engineering.

In a study to modify PLA surface due to its special activity chitosan was used by Zhu et al. They showed that chitosan/heparin (CS/Hp) complex was easily immobilized onto the PLA surface, and the bioactivity could be given to PLA surface. This surface of PLA/CS/Hp should be in favour of living cells. They cultured L929 fibroblast cells in an incubator fitted with water-jacket at 37 °C. The incubator was equilibrated with 5 per cent CO₂ and was kept at approximately 99 per cent relative humidity. These cells were routinely grown in DMEM medium containing 10 per cent FBS and 1 per cent antibiotic-antimycotic in a 75 cm² cell culture flask. Finally, they found that number of L929 fibroblasts attached on PLA/CS/Hp complex was maximum and PLA surface modified with chitosan had more adhesion cells compared with that of unmodified PLA.

Recently, many efforts have been made on chitosan for using it as scaffolding material in tissue engineering. In 2001, Jarry et al. demonstrated that chitosan can be easily processed into porous scaffolds, films and beads. Kast et al. showed that chitosan-thioglycolic acid (chitosan-TGA) conjugate is a promising candidate as scaffolding material in tissue engineering.

Attempts have been made by Madihally and Matthew to develop procedures for synthesizing many porous chitosan scaffolds for the applications toward several types of engineered tissues. In these procedures, first of all, chitosan solutions with concentrations of 1, 2 or 3 wt per cent were prepared by direct dissolution in 0.2 M acetic acid. Bulk chitosan scaffolds were prepared by freezing and lyophilizing chitosan solutions in pre-cooled, flat bottomed glass tubes. Planar scaffolds were prepared.
by freezing 25-50 mL chitosan solution in 10 cm diam polystyrene petri dishes. Thereafter, they were lyophilized. Tubular scaffolds were formed by freezing a chitosan solution in the annular space between concentric silicone or PTFE tubes. Chitosan solution of 1 or 2 wt per cent concentration was administered into the annular space and the whole assembly was frozen by direct contact with dry ice (−78°C). The outer tube was then removed and the assembly was lyophilized.

Microporous chitosan/calcium phosphate composite scaffolds have been synthesized and characterized for tissue engineering by Zhang and Zhang. They showed that the role of chitosan was to provide a scaffold form, on the other hand, calcium phosphates’ bioactivity presumably encourages osteoblast attachment and strengthens the scaffold. The composite scaffold was found to be stronger, bioactive and biodegradable. The effect of this towards osteoblast cell attachment depends on the ration of chitosan to the two types calcium phosphates (β-tricalcium phosphate and calcium phosphate inverted glass).

The special attention on chitosan has been paid for the repair of articular cartilage. Articular cartilage is particularly vulnerable to injury trama, disease or congenital abnormalities because of its avascular, alymphatic and aneural nature. Once damaged, it has little capacity for intrinsic repair. Although many repair techniques have been attempted over the past four decades, but none has succeeded to regenerate long-lasting hyaline cartilage tissue to replace defected or damaged cartilage. Recently, preliminary studies on chitosan-GAG composite and its biologically interaction with articular chondrocytes showed promising results. Chitosan and its derivatives are being extensively used for bone tissue engineering and central nervous system also.

Wound Healing/Wound Dressing

Chitosan has been found to have an acceleratory 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.

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.

Artificial Skin

The effect of treatment with chitosan and saline solution on healing and fibroplasia of wounds made by calpel 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-scal damage, plastic skin surgery are being made by the use of chitosan.

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.
Drug Delivery Systems

The applicability of natural polysaccharides such as, agar, konjac, 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.

Conclusions

It is chitin and chitosan which can readily be derivatized by utilizing the reactivity of the primary amino group and the primary and secondary hydroxyl groups to find applications in diversified areas. In this review, an attempt has been made to increase the understanding of the importance and characteristics of the chitin and chitosan by describing various aspects, including the chemical properties, biological properties, processing, and applications. In view of this, this study will attract the attention of entrepreneurs, industrialists, academicians, and environmentalists.

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