Chitins: Chitin and its Derivatives

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Background

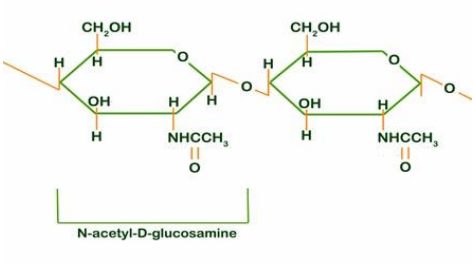
The growth of chitin and chitosan market has created good demand for the exoskeleton of shellfish through the world by the shrimp processing industry. Chitins is a relatively recent term used to collectively refer chitin and its derivatives such as chitosan and chitosan oligomers. Chitin was first isolated by Braconnot in 1811 from mushroom and was named 'fungine'. Subsequently, an identical material was isolated from insects in 1821 by Odier and named it as "chitine". He was the first person to observe remarkable similarity between cellulose and chitin. In 1859 chitosan, Rouget discovered a partial deacetylated chitin by boiling chitin in concentrated potassium hydroxide. It was finally named chitosan by Hoppe-Seiler (1894) but most information available today has been obtained since 1950. The book "The Integument of Arthropods" by Richards (1951) gave thrust on chitin while Tracey (1957) reviewed the structure and detection and quality analysis of chitin. Jeuniaux (1963) published a book on chitin and its enzymatic breakdown and in 1964 BrimaCombe and Webber wrote a monogram on chitin. In 1967, Rudall first addressed the concept of chitin-protein complex which opened the door for additional work on the subject. A bibliography on chitin and its derivatives was published by Pariser and Boch (1972).

Chitin

Chitin is the most abundant organic compound next to cellulose in the earth. Chitin represents 14-27% and 13-15% of the dry weight of shrimp and crab processing waste, respectively. Chitin is present as chitin-protein complex along with minerals mainly calcium carbonate. So the process of chitin production consists of deproteinisation with dilute alkali and demineralization with dilute acids. Chitin on deacetylation gives chitosan and on hydrolysis with concentrated HCl gives glucosamine hydrochloride. CIFT has developed technology for production of chitin, chitosan and glucosamine hydrochloride from prawn shell waste.

Structure of chitin

Chitin occurs in three polymorphic forms which differ in the arrangement of molecular chain within the crystal cell. The α- chitin is the tightly compacted most crystalline polymorphic form where the chains are arranged in an anti-parallel fashion, β- chitin is the form where the chains are parallel and γ- chitin is the form where the chains are "up" to everyone "down" (Muzzrelli, 1977a). Deacetylation of chitin with strong alkali yields chitosan, polymer of β- (1-4)-D glucosamine (Fig.2).



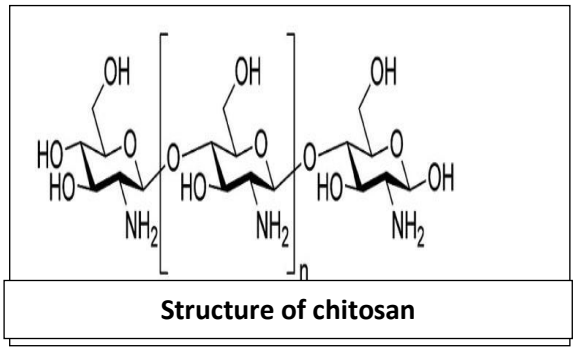
Structure of chitin

Carboxymethyl chitin

Carboxy methyl chitin is another high value derivative of chitin. It has successfully proved its use in the field of cosmetics as moisturizer, skin smoothener and a cleaner for face skin conditioning it is used for the preparation of food products also.

Chitosan

Chitosan is prepared by deacetylation of chitin. Chitosan is almost colorless, light in weight and soluble in dilute organic acids. Its uses are hindered due to its insoluble nature in water, alkali and organic solvents. It gives viscous solution when dissolved in dilute organic acids such as formic acid, acetic acid, citric acid etc. Pure chitosan is not hydrolyzed by lysozyme while chitin or partiallydeacetylated chitin is hydrolyzed. For hydrolysis to occur it is important that at least 6 contiguous acetamido side groups should be present in the substrate. The probability of having 6 contiguous residues with the necessary acetamido side groups decreases as the deacetylation increases. The molecular weight of chitosan derived from intrinsic viscosities of chitin from crab and shrimp generally falls in the range of 150-400 KDa. Depending on the extent of deacetylation chitin contains 5 to 8 % nitrogen, which in chitosan is in the form of primary aliphatic amino group. Chitosan undergoes the reactions typical of amines, of which N-acylation and schiff reactions are the most important. Chitosan derivatives are easily obtained under mild conditions and can be considered as substituted glucans. The properties of chitin and chitosan vary considerably depending on the source and production process. The quality requirements of chitosan and its derivatives vary with the end use.

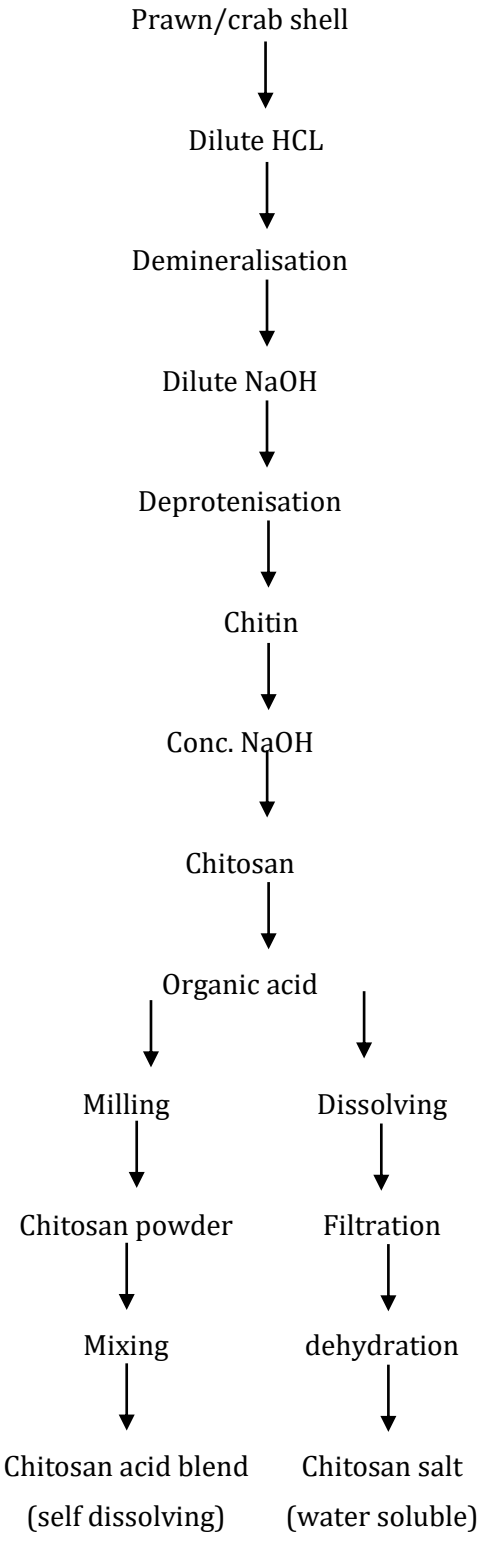


Structure of chitosan

Preparation of chitosan from prawn/crab shells

Chitin represents 14-27% and 13-15% of the dry weight of shrimp and crab processing waste respectively. Dry prawn waste contains 23% and dry squilla contains 15% chitin. Chitin is present as chitin protein complex along with minerals mainly calcium

carbonate. So the process of chitin production consists of deproteinisation with dilute alkali and demineralization with dilute acids. The chitin thus obtained is deacetylated to chitosan using conc. alkali.



Advantages of chitosan

Chitosan is soluble at acidic pH and becomes insoluble at pH above 6.5. Chitosan is a versatile polymer and interest in chitosan is because of its variety of useful forms that are commercially available or can be made available. Since chitosan is non-toxic and can be administered orally, it has mainly been studied as an oral delivery system in the form of tablets or particles (microspheres, beads, etc.). Its muco-adhesive and permeation enhancement properties have been used for transdermal and sustained gastrointestinal drug delivery. Its biodegradability and tissue compatibility make it a suitable compound for implantable delivery devices.

Applications of chitosan

Chitosan with its unique-combination of biological, physical and chemical properties is widely used in a variety of applications in both the industrial and medical fields. These properties produce a novel, versatile-biopolymer that can be tailor-made to suit a specific application with the required modes of function.Chitosan is used in dental and surgical appliances as a haemostatic agent, wound healing, biodegradable films as a replacement for artificial skins for removing toxic heavy metals, wine clarification, industrial effluent treatment, agriculture, photography, cosmetic applications and textiles and as an immobilizing agent for enzyme.The five international conferences on chitin and chitosan (1977, 1982, 1985, 1988 and 1991) have thrown light on various applications in different fields. These applications can be classified under the following heads.

1. Clarification and purification
2. Chromatography
3. Paper and textiles for photography
4. Food and nutrition
5. Medical and pharmaceuticals
6. Agriculture

Agriculture

Many products are marketed based on chitosan for plant protection, growth promotion, seed coating etc. But these applications have not put in to large scale adoption so far. The shelf life of vegetables and fruits also can be extended with the application of chitosan coating. With the growing awareness of the adverse effects of hazardous chemicals in agriculture and popularization of organic farming, chitosan products will find use. Antivirus, antibacterial, nematocidal, insecticidal and pesticidal properties of chitin and chitosan have to be taken to the field by researchers to ensure safety of agriculture products.

Medical and pharmaceuticals

The cholesterol lowering and weight management properties of chitosan has received much attention in recent years. Oral administration of chitin is generally recognized as safe (Harrison 2002). Sugano *et al* (1978) were the first to report the cholesterol lowering effect of chitosan and the report suggests that a diet containing 5% chitosan reduced liver cholesterol to half or more in cholesterol fed rats. In similar studies reduction of both liver and serum cholesterol in rats fed on diets containing 1% chitosan and 0.1% bile salts was observed. Chitin has also shown to reduce plasma cholesterol in cholesterol fed boiler chicken with diet containing 1.5 to 3% chitin. Thus the ability of reducing cholesterol in animals is well established (Razdan and Paterson,

1996).When adult males were fed on chitosan containing biscuits for 2weeks (3g/day for week1, 6g/day for week 2) experienced a significant decrease of 6% in total cholesterol. The reports of animal studies and human trials provide convincing evidence that chitosan is effective in lowering total and LDL cholesterol. Chitosan is also effective in lowering serum cholesterol and hypertension in human with restricted diet and is being used as food supplement in persons suffering from obesity.

Chitosan with its unique-combination of biological, physical and chemical properties is widely used in a variety of applications in both the industrial and medical fields. These properties produce a novel, versatile-biopolymer that can be tailor-made to suit a specific application with the required modes of function. Since chitosan is non-toxic and can be administered orally, it has mainly been studied as an oral delivery system in the form of tablets or particles (microspheres, beads, etc.). Its muco-adhesive and permeation enhancement properties have been used for transdermal and sustained gastrointestinal drug delivery. Its biodegradability and tissue compatibility make it a suitable compound for implantable delivery devices. Despite the outstanding scientific progress being made in terms of the application of chitosan in drug delivery systems, chitosan-based drug delivery products have not yet been launched in the market. Clinical trials involving chitosan-based drug delivery systems are underway for a wide-range of pharmaceutical formulations and some products may be expected in future. With a wide range of potential applications in medicine and pharmaceutics, there is tremendous scope for future research on chitosan and its derivatives. Chitosan certainly seems to be a carrier material of the 21st century in drug delivery devices.

Chitosan derivatives

Chitosan is not soluble in water but is soluble in dilute acid solutions like 1 % acetic acid. This has limited its applications in water soluble environments like human health and plant protection. Hence, the free amino and hydroxyl groups can be derivatized with new molecules to improve the functional properties of Chitosan.

Advantages of Chitosan derivatives

1. They are biodegradable and biocompatible
2. They are non-toxic and water soluble
3. They can be modified to impart special properties

Important derivatives

1. N-Trimethylene Chloride Chitosan: N-Trimethylene chloride Chitosan (TMC) is a quaternary derivative of Chitosan and it has a superior aqueous solubility, intestinal permeability as well as higher absorption over a wide pH range.
2. Chitosan Esters: Esters of chitosan with glutamate, succinate and phthalate have a differential solubility profile. These esteric forms are insoluble in acidic condition and provide sustained release of drugs in basic condition.
3. Chitosan Conjugates: Chitosan can be conjugated with a bioactive excepients for delivery of active ingredients such as Calcitonin. Chitosan conjugates such as 5-methylpyrrolidinone chitosan, chitosan-4-thiobutylamidine conjugate have exhibited enhanced absorption as well as mucoadhesives properties.
4. Carboxymethyl chitosan (CM-Chitosan): CM-Chitosan is prepared by reacting monochloroacetic acid with Chitosan. The derivative is soluble in water and gives

viscous solutions. An unique property of CMC is that it is more thermo-stable compared to the similar structural polymer carboxymethyl cellulose.

Major Applications

1. Controlled release and drug delivery
2. Scaffolds for biomedical applications like stents, organs
3. Tissue engineering, wound healing and regenerative medicine
4. Food supplements and natural preservatives
5. Anti-viral and anti-tumor applications
6. Bio-composite materials with functional properties

Glucosamine hydrochloride

Glucosamine is chemically glucose in which a hydroxyl group on the second carbon atom is substituted with an amino group. It crystalizes as glucosamine hydrochloride during purification under acidic conditions. It is one of the amino sugars used by biological systems for bringing modification to the functions of proteins (Ronda and Zynudheen, 2014).

Health claims of Glucosamine

Although glucosamine was discovered long back, the interest in nutraceutical use received great attention since last two decades.

- ***To treat joint pain***

  The rationale in using glucosamine for arthritis is that it is absorbed by the body and distributed to all organs. In the joint and synovial fluid this glucosamine will stimulate the synthesis of proteoglycans that help in repair of damaged cartilage. Although many clinical trials have shown benefits, the evidence is not equivocal. There are more than 100 generic preparations of glucosamine alone or in combination in the market.

- ***As stomach antacid***

  Research in mice has shown that, glucosamine is having good acid neutralization and peptic ulcer healing properties. Peptic ulcers is a major problem affecting adult human beings and oral administration of glucosamine will relieve pain associated with it and also helps in synthesis of gastric mucosa to repair the ulcer.

- ***Anti-aging property***

  Latest research has claimed that glucosamine supplementation mimics low calorie diet in rats and increased the life span compared to control animals. Calorie restriction was proven in animals to improve the life span in laboratory studies. Although the mechanism of action of glucosamine is not clear in this case, it was shown to reduce the amount of glucose metabolized through the glycolytic pathway thus mimics low calorie diet.

- ***Wound healing***

  Hyaluronic acid is highly hydrated and provides strength and elasticity to the skin. By binding and retaining some moisture in a wound re-epithelialization can proceed more quickly. This water-binding effect is also important for cosmetic uses of

glucosamine. It can increase the skin's content of hyaluronic acid to increase moisturization, leading to enhanced skin barrier properties and reduced dryness

- ***Cosmetics***

  Glucosamine has also been reported to have potential to inhibit skin melanin production. Glucosamine has been shown to inhibit glycosylation, the addition of polysaccharide units to proteins in in-vitro melanocyte cell culture. Glycosylation is a required step in the conversion of certain inactive pro-enzymes to their active forms. Active tyrosinase, a key enzyme in the pathway for melanin production, is glycosylated. Thus, glucosamine inhibits the production of melanin in melanocytes.

Suggested readings

1. Tracey, M. V. (1957) Rev. Pure Applied Chemistry. 7: 1-14
2. Pariser, E.R. and Boch, S. (1972). Derivatives – An annotated Bibliography of selected publications from 1965 to 1971. 142-146. MIT Cambridge, Mass.
3. Domard, A., Jeuniaux, C., Muzzarelli, R., Roberts, G. 1996. Advances in chitin science. Jacquez ANDRE Publisher, France

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