

Chitosan A Boon or a Bane to the Future of Dentistry

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Abstract:

Background: The article aims at giving knowledge about an ecofriendly, biodegradable and most of all a biocompatible material- "Chitosan". It is obtained by the deacetylation of chitin which is a byproduct of shell fishes that go waste. Many researches are being done to explore the use of this versatile material. Recently dental material researchers have shifted their focus to a more ecofriendly and biocompatible material that can be put to use in dentistry. This is where the role of chitosan becomes important. As it has proven properties like biocompatibility and antibacterial property, makes it a center of focus in the medical and dental field in this era which focuses more on materials that are more organic and thereby reduce the pollution and harm that we cause to mother nature.

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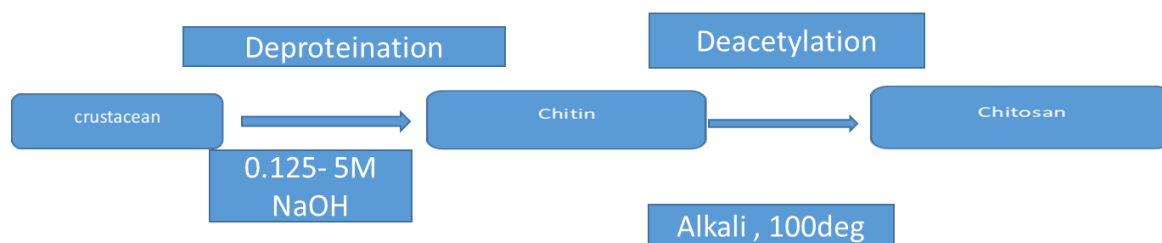
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I. Introduction

Chitosan is a natural polysaccharide, which has attracted attention in dental research in the recent years. Chitosan is a natural polysaccharide, coming from the deacetylation of chitin, which is obtained from the shells of crabs and shrimp.¹ This polysaccharide has a molecular weight ranging from 1,000,000 to 3,000,000 and properties of biocompatibility, biodegradability, bioadhesion and atoxicity to the human body.² It has a high chelating ability for various metal ions in acidic conditions and has been applied widely for the removal or recovery of metal ions in different industrial areas. Chitin, after cellulose, is the most abundant substance in nature, which makes its use very interesting from the ecological point of view as well as economically viable.³

II. Production of Chitosan

The discovery of chitosan was in 1859 by Rouget when the chitin was subjected to a treatment with hot potassium hydroxide solution. In the period of 1894, Gilson confirmed the presence of glucosamine in chitin and in the same period was named chitosan by Hopper-Seyler.^{4,5} Chitin is a straight homopolymer consisting of (1,4)-linked N-acetyl glucosamine units found in the exoskeleton of crustaceans such as crabs and shrimp. Chitosan is prepared by hydrolysis of acetamide groups of chitin. This is normally conducted by severe alkaline hydrolysis treatment due to the resistance of such groups imposed by the trans arrangement of the C2-C3 substituents in the sugar ring.^{6,7} Thermal treatments of chitin under strong aqueous alkali are usually needed to give partially deacetylated chitin (DA lower than 30%), regarded as chitosan 8. Usually, sodium or potassium hydroxides are used at a concentration of 30-50% w/v at high temperature (100°C). There are two major different methods of preparing chitosan from chitin with varying degree of acetylation are known. They include; the heterogeneous deacetylation of solid chitin and the homogeneous deacetylation of pre-swollen chitin under vacuum (by reducing pressure) in an aqueous medium. Heterogeneous deacetylation is the preferred industrial treatment, in which the process involves preferential reaction in the amorphous regions of the polymer, leaving almost intact the intractable crystalline native regions in the parent chitin. On the other hand, homogeneous modification is conducted by use of moderately concentrated alkali (13% w/w) acting on pre-swollen chitin to improve the interaction with the alkali and left to react at 25-40°C for 12-24 hours.⁷ Chitosan can be blended with various components in the liquid form and shaped into various physical forms such as resins, microspheres, hydrogels, membranes and fibers. The selection of one particular physical form depends mainly on the system configuration to be used for particular applications.⁸ Chitosan is soluble in dilute acids, such as acetic acid, formic acid, lactic acid, as well as inorganic acids, after prolonged agitation. However, the solubility is dependent on several parameters, such as the degree of deacetylation, molar mass, concentration of acid and biopolymer and ionic strength.⁹



III. Properties of Chitosan

Antibacterial Property

The exact mechanism of antibacterial activity is yet to be fully understood. It is known that chitosan's antimicrobial activity is influenced by a number of factors that act in an orderly and independent fashion. The most prevalent proposed antibacterial activity of chitosan is by binding to the negatively charged bacterial cell wall causing disruption of the cell, thus altering the membrane permeability, followed by attachment to DNA causing inhibition of DNA replication and subsequently cell death.¹⁰

Another possible mechanism is that chitosan acts as a chelating agent that electively binds to trace metal elements causing toxin production and inhibiting microbial growth (Divya et al. 2017).¹¹

Chelating property

Chitosan possesses high chelating capacity for various metal ions (including Ni²⁺, Zn²⁺, Ca²⁺, Co²⁺, Fe²⁺, Mg²⁺ and Cu²⁺) in acid conditions, and it has been widely applied for the removal or recovery of metal ions in different industries.¹² Metal ions that combine with cell wall molecules of microorganism are crucial for stability of the cell wall. Chitosan-mediated chelation of such metal ions has often been implicated as a possible mode of antimicrobial action.¹³ Not only does chelation play a part in acid condition, it is also able to combine divalent metal ions in neutral condition. Additionally, via chelating capacity, chitosan metal complex is prepared and exerts strong antimicrobial activity.¹⁴

IV. Uses in Dentistry

Bone Scaffold and bone Regeneration

Chitosan which is a natural polymer and evokes minimal foreign body reaction and fibrous encapsulation. Unlike many synthetic polymers, chitosan has a hydrophilic surface that promotes cell adhesion and proliferation and its degradation products are non-toxic. Chitosan is an especially attractive as a bone scaffold material as it supports the attachment and proliferation of bone-forming osteoblast cells as well as formation of mineralized bone matrix in vitro.¹⁵ studies have shown that modified chitosan scaffolds exhibit osteoconductivity in vivo in surgically created bone defects.¹⁶ these can be used to create 3-dimensional scaffolds with different pore structures for use in bone tissue engineering. It can also be combined with a variety of materials including ceramics and polymers to yield composite scaffolds with superior mechanical and biological properties.¹⁷ Mathews et al., proposed that chitosan can increase mineralization by upregulating the associated genes as a mechanism for the osteogenesis of this substance.¹⁸ From study conducted by Fatemeh et al it was reported that chitosan increases the activity of osteoblasts and helps bone formation and accelerated socket wound healing compared to control group.¹⁹

Anticariogenic potential

Researchers demonstrated that this polysaccharide has antimicrobial action in a great variety of microorganisms, included gram-positive bacteria and various species of yeast.²⁰ The antimicrobial action mechanism of the chitosan is not yet fully elucidated, being several mechanisms are suggested by the literature. Some authors suggested the amino groups of the chitosan when in contact with physiological fluids are protonated and bind to anionic groups of the microorganisms, resulting in the agglutination of the microbial cells, and growth inhibition.²¹ Another postulate is the interaction between the positive load of the chitosan and the negative load of the microbial cell wall, because it causes the rupture and loss of important intracellular constituent of the microorganism life. Chitosan with low molecular weight penetrates in the cell and is linked to the microorganism DNA inhibiting the transcription and consequently the translation, whereas the chitosan of high molecular weight acts as a chelate agent, binding to the cell membrane.²² Experiments were performed in the Microbiology Laboratory-Nucleus of Research in Environmental Sciences- UNICAP (Recife, PE, Brazil) The mechanisms of chitosan from crabs and fungi to inhibit the tooth colonization by *S. mutans*, *S. sanguis*, *S. mitis* and *S. oralis* were evaluated through the adherence test of chitosan to dental and bacteria surface. Chitosan from crabs and fungi, in all concentration tested, decreased the adsorption of *Streptococcus* strains to dental

enamel, reduced the bacteria cell wall hydrophobicity and decreased the glucan production by bacteria. enamel in the presence of chitosan from crabs and fungi, in all concentrations studied. Chitosan demonstrated best performance at the concentration of 2mg/mL for *S. mutans* and of 3mg/mL for *S. sanguis*, *S. mitis* and *S. oralis*.²³

Direct pulp Capping

Study done by Widyasari reported a greater number of odontoblast like cell differentiation with chitosa when compared to calcium hydroxide. There was a significant difference in between the number of odontoblast cells in the 7th and the 14th day in the chitosan group. chitosan as direct pulp capping material has a 88.957% degree of deacetylation which has a high percentage of acetyl groups that are more active so that chitosan could stimulate the differentiation of odontoblast-like cells. The degree of deacetylation of chitosan, could also affect the biological character of chitosan, including biodegradation of chitosan caused by lysozyme enzyme produced by inflammatory cells and macrophages neutrophil.

Guided tissue regeneration

GTR with chitosan is in the animal phase study however it shows promising results for future use. Yeo et al. demonstrated the regenerative effects of the chitosan nonwoven membranes in one-wall intrabony defects in beagle dogs. . Compared with Biomesh membranes, which are bioabsorbable membranes made by polylactic acid, polyglycolic acid, and lactide/glycolide copolymer and are clinically used nowadays, the results showed that chitosan membranes induced more amount of new cementum and bone and that cementoblasts and osteoblasts were densely arranged along the new bone surface in the chitosan group. Moreover, the PDL observed in the chitosan group presented more regular pattern and a denser fiber arrangement than those in the surgical control group.²⁴ Park et al. also studied the effect of compound chitosan membranes in surgically created one-wall intrabony defects in beagle dogs. The membranes were made by immersing collagen sponge in the chitosan solution, and chitosan covered the surfaces of collagen sponge and formed membranes, so it was the chitosan that played the role of excluding unwanted tissues and guiding regeneration, whereas collagen just worked as a carrier.²⁵

Smear layer Removal

It has a high chelating ability for various metal ions in acidic conditions and has been applied widely for the removal or recovery of metal ions in different industrial areas. The same principle is being exploited for its ability to remove smear layer.¹ Various theories have been put forward for chelation mechanism of chitosan to dental structure. The first is the bridge model theory, which states that two or more amino groups of a chain of chitosan bind to the same metal ion. The second theory states that only one amino group of the chitosan is involved in the binding.²⁶ Chitosan polymer is composed of several units of dimer of chitin which has got nitrogen atoms with free pairs of electrons which lead to ionic interaction between the metal and the chelating agent. In an acid medium, this forms an ionic form which results in the amino groups being protonated which is responsible for attraction to other molecules and results in adsorption. The process of formation of complexes between chitosan and metal ions occurs as a result of ion exchange, adsorption, and chelation. The prevalent conditions such as the pH of the solution, the chemical structure of chitosan, and the type of ions determine the type of interaction which takes place. A study done by Pimenta et al showed that application of the 0.2% of chitosan solution for 3 to 5 min was the most viable combination for use on the root dentin.²⁷

V. Conclusion

Chitosan is a new biomaterial which was introduced into the field of dentistry recently. At present its use in dentistry is still in the research phase. It has quite a lot of hurdles to cover until it reaches its clinical trials. However due to the inherent properties of this material and the results from numerous in- vitro studies show that this material will be a boon to the future of dentistry.

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