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Chitosan in Dentistry

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Abstract

To elaborate on the uses of chitosan in various field of dentistry. Along with its properties and mechanism of action.Chitosan is a linear polysaccharide composed of randomly distributed β-(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucasamine. Chitosan is a sugar that is obtained from the hard outer skeleton of shellfish, including crab, lobster, and shrimps. It has a number of commercial and possible biomedical uses (1). In medicine, it may be useful in bandages to reduce bleeding and as an antibacterial agent; it can also be used to help deliver drugs through the skin, hemodialysis, cholesterol control, calcium absorption, bilirubin absorption, and hypertension control(2).

INTRODUCTION

Chitosan is a linear polysaccharide composed of randomly distributed β-(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucasamine. Chitosan is a sugar that is obtained from the hard outer skeleton of shellfish, including crab, lobster, and shrimps. It has a number of commercial and possible biomedical uses (1). In medicine, it may be useful in bandages to reduce bleeding and as an antibacterial agent; it can also be used to help deliver drugs through the skin, hemodialysis, cholesterol control, calcium absorption, bilirubin absorption, and hypertension control (2).

Applications of Chitosan in Dentistry

Chitosan is widely used in dental medicine due to it's broad spectrum of biological activities:

- Chitosan is used as antiplaque agent hence used in toothpaste, mouthwash, and chewing gum.
- Chitosan binds to the outer surface of bacteria by electrostatic forces, it provides

an antibacterial activity against various pathogenic bacteria hence used as irrigant and medicament in endodontics.

- Chitosan is used as chelating agent in endodontics.
- Chitosan is used as a restorative material with composite, GIC, and as hydrogel
- Chitosan stimulates the wound healing process.
- Chitosan is used for bone regeneration and bone repair.

1. Chitosan in Endodontics

A. Antibacterial and antifungal mechanism of chitosan

Chitin and chitosan have been investigated as an antimicrobial material against a wide range of target organisms like algae, bacteria, yeasts and fungi in experiments involving in vivo and in vitro interactions with chitosan in different forms. Recent data in literature has the tendency to characterize chitosan as bacteriostatic rather than bactericidal. The antimicrobial activity of chitosan has been observed with a wide variety of microorganisms including fungi, viruses and some bacteria (Hirano & Nagano, 1989; Chirkov, 2002; Rabea et al., 2003). It was found that the antimicrobial activity of chitosan is influenced by intrinsic factors as well as environmental conditions: Physicochemical properties of chitosan: type of chitosan, molecular weight (MW), degree of deacetylation (DDA), chemical modification, environamental conditions : pH, temperature, salt concentration, nutrient composition models have been proposed, the most acceptable being the interaction between positively charged chitin/chitosan molecules and negatively charged microbial cell membranes. In this model the interaction is mediated by the electrostatic forces between the protonated NH+3 groups and the negative residues, presumably by competing with Ca2+ for electronegative sites on the membrane surface.

Chitosan is a versatile material with proved antimicrobial activity. Three antibacterial mechanisms have been proposed:

- The ionic surface interaction resulting in cell wall leakage;
- The inhibition of the mRNA and protein synthesis via the penetration of chitosan into the nuclei of the microorganisms;
- The formation of an external barrier, chelating metals and provoking the suppression of essential nutrients to microbial growth. It is likely that all events occur simultaneously but at different intensities.

Antifungal Property

The antimicrobial activity of chitosan has been observed with a wide variety of microorganisms including fungi, viruses and some bacteria (Hirano & Nagano, 1989; Chirkov, 2002; Rabea et al., 2003) . Similarly to bacteria the chitosan activity against fungus is assumed to be fungistatic rather than fungicidal with a potential to communicate regulatory changes in both the host and fungus. Generally chitosan has been reported as being very effective in inhibiting spore germination, germ tube elongation

As an antimicrobial irrigation solution in endodontics

It has been shown to cease the growth of E. faecalis and S.Aureus.

It has been proved to be as effective as NaOCl, without the side effects of NaOCl.

Hence it is a safer alternative and equally effective.

B. Chitosan is Used as Chelating Agent in Endodontics.

Currently, the combined use of EDTA and sodium hypochlorite is the most widely used by endodontists to remove the smear layer from root canals. However, the search for more biocompatible solutions than EDTA to minimize the aggression to the periapical tissues has increased over the years.

The use of chitosan at 0.2% concentration was checked in which the comparison between the substance prepared with different concentrations and action times on dentin showed that application of the 0.2% concentration for 5 min was the most viable combination for use on the root dentin. The similar chelating effect of 0.2% chitosan compared to the other tested solutions, allied to its advantageous properties already and low concentration, indicate that this chelating solution should be preferred for dentin decalcification.

C. Removal of Smear Layer

15% EDTA, 0.2% chitosan and 10% citric acid had similar smear layer removal capacity with a significant difference ($P < 0.05$) from 1% acetic acid 15% EDTA, 0.2% chitosan and 10% citric acid effectively removed smear layer from the middle and apical thirds of the root canal. 15% EDTA and 0.2% chitosan were associated with the greatest effect on root dentin demineralization, followed by 10% citric acid and 1% acetic acid. In the absence of dentin, after 10 seconds of contact with the bacterial suspension, 6% NaOCl showed the lowest bacterial count; the difference to the negative control was significant. After 30 seconds, 6% NaOCl displayed 0 colony-forming units per milliliter, whereas 1% NaOCl and QMiX showed reduced number of colonies in comparison with the negative control. After 1 minute, both concentrations of NaOCl presented no bacterial growth and QMiX reduced the number of colonies, but EDTA and CHX had bacterial counts similar to the negative control. Dentin had a significant inhibitory effect on 6% NaOCl (10 seconds), 1% NaOCl (10 seconds and 1 minute), and QMiX (10 seconds and 1 minute). After 6 hours, both concentrations of NaOCl, QMiX, and CHX killed all bacteria, regardless of the presence of dentin. Raman analysis revealed chemical changes and shifts in Amide bands with the modification of dentin collagen-matrix. The use of riboflavin and chitosan/riboflavin formulations to modify dentin-collagen matrix, with the defined ratios, stabilizes the collagen fibrillar network and enhances resin infiltration and hybrid layer formation. These preliminary results are encouraging for subsequent consideration of chitosan/riboflavin modification in adhesive dentistry. the present *in vitro* results demonstrated that there were no significant differences among 0.2% chitosan, 15% EDTA and 10% citric acid solutions in the reduction of root dentin microhardness. Distilled water, which was used as a control, did not alter the microhardness.

2 Chitosan is Used as Antiplaque Agent

Chitosan has been used as a chemical agent for mouthwashes that provide clinical benefit for plaque control [(1,2,3)]. It is non toxic, biocompatible, biodegradable, and has an extended retention time in the oral mucosa along with its antimicrobial property. Studies have shown that the molecular chitosan prevents the adsorption of Streptococcous Mutans onto hydroxyapatite crystals [(4,5,6)]. Chitosan has a synergistic antiplaque effect with chlorhexidine. It can be used in the form of toothpaste and chewing gum.

The chitosan solution reduced the plaque index and the vitality of the plaque flora significantly when compared to DW, but this was less than the reductions found with the positive control of 0.1% chlorhexidine solution. The water-soluble reduced chitosan exhibited potent antibacterial effect on *S. mutans*, and displayed a significant antibacterial and plaque-reducing action during the 4-day plaque regrowth.

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3 Chitosan Stimulates The Wound Healing Process.

Chitosan and chitin in vivo have wound healing enhancing properties. Numerous reports describe the stimultory effects of chitosan on tissue reactions involved in wound healing. Chitosan has widely been used as an effective agent in various medical fields and dentistry in particular (Chandy & Sharma, 1990; Shigemasa et al., 1995; Kas, 1997; Illum, 1998; Hirano, 1999; Muzzarelli et al., 1999). Chitosan has many useful and advantageous biological properties in the application as a wound dressing:

- Biocompatibility
- Biodegradability
- Haemostatic activity
- Protection from bacterial infections
- Provision of a moist and healing environment
- Low toxicity

Chitosan Usage in Dentistry.

In the dental medicine, reserach is focused on gel development to allowed an easy application on open wounds in oral cavity. The clinical therapeutic approach to the problems of periodontitis has shown a variety of pathways. Biocompatible materials like chitosan and its modifications were used for the reduction of the periodontal pockets in the surgical interventions. Chitosan ascorbate, obtained by mixing chitosan with ascorbic acid and sodium ascorbate, was produced in gel, suitable for the treatment of periodontitis (Muzzarelli et al., 1989). Chitosan was progresively reabsorbed by the host, with a good clinical recovery, tested in 52 patients. In vivo, the tooth mobility and tooth pocket depths were significantly reduced. Bumgardner et al. (2003) used chitosan as bioactive coating to improve osseointegration of orthopaedic and cranifacial implant devices. Coating material was made from 91.2 % deacetylated chitosan (MW: 200,000 Da), which was chemical linked to titanium coupons. The bonded coatings exhibited minimal degradation within 8 weeks in cell cultures. They supported increased osteoblastic cell attachment and proliferation as compared to uncoated titanium controls. A relation between high grade of deacetylation and low degration of polymers was demonstrated.

4. Chitosan Use In Bone Regeneration And Repair

Chitosan has been shown to be one of the most promising biomaterials for orthopedic and dental applications. Due to its interesting characteristics, chitosan is considered as a suitable alternative for bone graft. Chitosan improves bone regeneration in dental bone loss.

A studies pertaining to this has been done by: Fatemeh Ezoddini- Ardakani, Alireza Navab Azam, Soghra Yassaei,Farhad Fatehi, Gholamreza Rouhi showing that the effects on bone repairing.

Chitosan is used for bone engineering, The combination of biocompatible polymers and bioresorbable ceramic materials can mimic the natural function of bone. CTS with HAp composites are found to be potential bone implant materials with good osteoconductive, osteoinductive and osteogenic properties. The addition of CNT to improve the mechanical properties of CTS and ceramic (HAp) composite would surely support and stimulate the function of natural bone. The development of research on the efficacy of CTS composite will open great possibilities for future bone tissue engineering.

5. Chitosan Is Used As A Restorative Material

A Chitosan as a Dual Function Restorative Materials.

Chitosan-H, chitosan-H-propolis, chitosan-H-propolis-nystatin has been shown to increase the dentine bond strength. it acts as a bio-adhesive. Nystatin acts as an antioxidant property. The release of both nystatin and propolis confer the added benefit of dual action of a functional therapeutic delivery when comparing the newly designed chitosan-based hydrogel restorative materials to commercially available nystatin alone.

The added benefits of their unique functionality involve increased dentin adhesive bond strengths (after 24 h and after 6 months) and positive influence on the nystatin release. Nystatin was a model therapeutic agent, evaluating the concept of using functional materials as carriers for pro-drugs as well as displaying a certain degree of defence mechanism for free radical damage of the novel functional drug delivery. Overall, there was an insignificant relapse in the shear bond strength after 6 months.

B. Chitosan-Fluroaluminosilicate Resin Modified Glass Ionomer Cements.

This material has shown to promote cell proliferation and function is required for regenerative pulp therapy. Resin modified glass ionomer cement (RMGIC), a broadly used liner or restorative material, can cause apoptosis to pulp cells mainly due to HEMA (2-hydroxyethyl methacrylate), the released residual monomer. Recent studies found that chitosan and albumin could promote release of protein in GIC while translationally controlled tumor protein (TCTP) has an anti-apoptotic activity against HEMA. RMGIC supplemented with TCTP had less cytotoxicity than RMGIC and can protect cells from apoptosis better than RMGIC supplemented with TCTP.

C. Chitosan Based Gels as Functional Restorative Biomaterials (In Vitro)

Studies on a dual restorative material containing chitosan and other additives shows that the release of naproxen confers the added benefit of synergistic action of a functional therapeutic delivery when comparing the newly designed chitosan-based hydrogel restorative materials to the commercially available products alone. Neither the release of naproxen or the antioxidant stability was affected by storage over a 6-month period. The hydrogel formulations have a uniform distribution of drug content, homogenous texture and yellow colour (SEM study). All chitosan dentin treated hydrogels gave significantly higher shear bond values than dentin treated or not treated with phosphoric acid. The added benefits of the chitosan treated hydrogels involved a positive influence on the naproxen release as well as increased dentin bond strength as well as demonstrating good antimicrobial properties and enhanced antioxidant stability. The therapeutic polymer approach described here has a potential to provide clinical benefit, through the use of “designer” adhesive restorative materials with the desired properties.

D. Chitosan as A Hydrogel in Polymer Cross Linking.

Use of the natural polymer, chitosan, as the scaffold material in hydrogels has been highly pursued thanks to the polymer's biocompatibility, low toxicity, and biodegradability. The advanced development of chitosan hydrogels has led to new drug delivery systems that release their payloads under varying environmental stimuli.

6. Chitosan Nanoparticles

The applications of chitosan nanoparticles are:

- As antibacterial agents, gene delivery vectors and carriers for protein release and drugs
- Used as a potential adjuvant for vaccines such as influenza, hepatitis B and piglet paratyphoid vaccine
- Used as a novel nasal delivery system for vaccines. These nanoparticles improve antigen uptake by mucosal lymphoid tissues and induce strong immune responses against antigens.
- Chitosan has also been proved to prevent infection in wounds and quicken the wound-healing process by enhancing the growth of skin cells.
- Chitosan nanoparticles can be used for preservative purposes while packaging foods and in dentistry to eliminate caries.
- It can also be used as an additive in antimicrobial textiles for producing clothes for healthcare and other professionals.
- Chitosan nanoparticles show effective antimicrobial activity against Staphylococcus saprophyticus and Escherichia coli.
- These materials can also be used as a wound-healing material for the prevention of opportunistic infection and for enabling wound healing.

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