

APPLICATIONS OF CHITOSAN IN DENTISTRY- A REVIEW ARTICLE

Dr. Sameer Chauhan¹, Dr. Sneha Das², Dr. Fawaz Abdul Hamid Baig³, Dr. Syed Shah Hussain Qadri⁴, Dr. Radhika. D⁵, Dr. Himanshi Modi⁶

¹Assistant Professor, Department of Prosthodontics and Crown & Bridge, K. M Shah Dental College and Hospital, Sumandeep Vidyapeeth, Waghodia, Vadodara, Gujarat, INDIA. csameer309@gmail.com

²MDS, Consultant Prosthodontist, Hyderabad, Telangana. snehadab9@gmail.com

³Assistant professor. Dept of Oral and Maxillofacial surgery, King Khalid University College of Dentistry, Abha, KSA. fbik@kku.edu.sa

⁴Consultant, Department of Conservative Dentistry and Endodontics, CLOVE Dental, Hyderabad, Telangana, India. dr.sshqadri@gmail.com

⁵MDS, Consultant Prosthodontist & Implantologist, Observership at Familia Dental, Carlsbad, New Mexico State, USA. radhikad3011@gmail.com

⁶PG Student, Department of Periodontology, Pb. Government Dental College, Amritsar, Punjab. himanshi.modi08@gmail.com

DOI: 10.47750/pnr.2022.13.S10.157

Abstract

Chitosan is a biopolymer that has a large wound management application and biological properties, helping the organisms with fast healing, stimulates the cell proliferation including bacteriostatic and fungistatic particularly useful for wound treatment and as a support material to tissue engineering. The possibilities of application of chitosan are so huge and fascinating as well as not quite discovered. Properties of chitosan like biocompatibility, anti-inflammatory and others could give promising results in periodontal care or wound healing after teeth extractions. The aim of this work is to review possible applications of chitosan in dentistry area.

Keywords: Chitosan; Biomedical; Bioengineering materials; Biodegradability; Selective Permeability; Polyelectrolyte action; Natural polysaccharide.

Introduction

Biomaterials are those non-living materials used in the medical, biomedical and other fields, aiming to interact with the biological system.¹ Many of these materials, such as chitosan, are used as effective alternatives for the replacement of tissues, including bone tissue, since they do not present risks of disease transmission or immune rejection, as well as unlimited availability and low cost.² Recently, several researches have been carried out aiming at new materials capable of being associated with other substances that promote bone formation, especially biopolymers, in particular chitosan, which presents great potential in the repair of bone defects, in relation to the limitations of other biomaterials.³ One of the most important fields of applications of natural compounds it is medicine. Such materials would have some advantages over synthetic ones. Materials derived from the nature, have been shown to yield faster healing with less incompatibility in human beings. The new materials which are used should help to reduce the operation time and improve patient recovery. The development of reconstructive surgery, cardiac surgery, transplantation and dentistry would not have been possible without progress in the field of material science, chemistry and technology polymers for biomedical and bioengineering materials. One of the new and promising biomaterials being used in dentistry is chitosan.⁴ Chitosan and its derivatives have excellent biocompatibility, non-toxicity to human beings, biodegradability, reactivity of the deacetylated amino groups, selective permeability, polyelectrolyte action, antimicrobial activity, ability to form gel, film and sponge, absorptive capacity, anti-inflammatory and wound healing.⁵ One of the most important properties of chitosan is high bioactivity, that makes this material very interesting to develop new biomaterials for application in dentistry area. The use of biopolymers in the treatment of diseased tissues was started in the area of dentistry. The scientific and technological advances in the area of biomaterials and medical devices have allowed a considerable evolution in this area, in particular, focusing on new biomacromolecules and biocompatible materials for clinical use.⁶

BIOLOGICAL AND CHEMICAL PROPERTIES

Chitosan is a straight chain cationic polysaccharide (deacetylated polysaccharide), usually refers to a cationic copolymer composed of 2-amino-2-deoxyglucose (60-100%) and 2-acetyl-amino-2-deoxyglucose-D-glucoside (0-50%), which exists naturally or is obtained by deacetylation of chitin.^{7,8} Chitin is found mainly in the exoskeletons of crustaceans, but also in some fungi.⁹ In 1859, Rouget treated chitin with hot potassium hydroxide solution, resulting in the discovery of chitosan, which also laid the foundation for modern chitosan production.¹⁰ Chitosan can be biodegraded to non-toxic residue by lysozyme or chitinase, and it hydrolyzes glucosamine-glucosamine, glucosamine-N-acetyl-glucosamine, and N-acetyl-glucosamine bonds, so it has good biodegradability.¹¹ Secondly, acetylation increases the interaction between chitosan and cells by increasing the number of positive charges, thus improving the biocompatibility. It has been found to have no antigenic response and even has anti-inflammatory properties. The hemostatic effect of chitosan is also a major feature, mainly because it can induce platelet adhesion and aggregation, and activate endogenous blood coagulation.¹² The chitosan can also control bleeding by adsorbing plasma and red blood cell coagulation. Because the chitosan has biodegradability, biocompatibility, hydrophilic, antimicrobial properties, biological activity and other properties, and have different forms of processing (solution, blend, sponge, film, gel, paste, tablet, microspheres and micro particles, etc.), it has many biomedical applications, including effective wound healing, tissue regeneration, dosing, bone regeneration, anti-infection and so on.¹³ Since it comes from natural and renewable resources, not only it is an economical natural biopolymer, but also cost effective.

Applications of chitosan in dentistry

Chitosan, a versatile hydrophilic polysaccharide derived from chitin, has a broad antimicrobial spectrum to which gram-negative, gram-positive bacteria and fungi are highly susceptible. Chitosan is mainly used as antimicrobial and antibacterial agent in dentistry.

Table 1- Chitosan application in dentistry area

Dental Specialties	Chitosan Applications
Preventive dentistry	-Component of daily mouth wash
	-Component of toothpaste against dental plaque
	-Component of toothpaste against erosion/abrasion
	-Mucoadhesive cariostatic substance delivery systems
Conservative dentistry	-Direct pulp capping
	-Antibacterial against <i>S. mutans</i>
	-Component of toothpaste against erosion/abrasion included demineralised dentine matrix
	-Indirect pulp capping
Endodontics	-Antibacterial against <i>E. faecalis</i> using new photo sensitizer
	-Sustained release of calcium ions from the calcium hydroxide in the root canal system
	-Improving stability of dentin collagen
	-Removal of smear layer after root canal instrumentation
	-Inhibition of biofilm by incorporation with zinc-oxide eugenol-based sealer
	-Regulation of stem cell differentiation from apical papilla
	-Ingredient of triple antibiotic intracanal paste against <i>Candida albicans</i> and <i>E. faecalis</i>
Oral surgery	-Guided bone regeneration
	Facilitate early bony consolidation in distraction osteogenesis

	Bone regeneration at dental implant defects
	-Titanium coating
	-Hemostasis of oral surgery wounds
	-Bone tissue engineering in oral reconstruction
	-New bone substitute material
	-Repairing TMJ disc-Guided periodontal tissue regeneration
Periodontology	-Guided periodontal tissue regeneration
	-Antioxidant delivery system
	-Epithelial attachment re growth
	-Antibacterial and plaque-reducing action
	-Treatment of periodontitis
	-Advanced scaffolds in periodontal tissue engineering
	-Antimicrobial photodynamic therapy against P. gingivalis
	-Periodontal ligament cells delivery system
Prosthetic dentistry	-Modification of glass ionomer restoratives
	-Antibacterial activity of composite
	-Antibacterial activity of dental adhesive
	-Modification of lithium disilicate glass ceramic cementation Procedure
Orthodontics	-Preventing against demineralization around orthodontic brackets

Antimicrobial activity of chitosan

Applications of the antimicrobial activity of chitosans are currently being investigated in food packaging, textile and cosmetic industries, and in biomedical applications, including dentistry. The adherence of oral bacteria on the tooth surface leads to plaque formation. It is believed that the adhesion between the bacteria and the tooth surface is due to electrostatic and hydrophobic interactions. Positively charged amine groups of chitosan derivatives can actively play against these interactions and prevent the plaque formation.¹⁴ The antimicrobial effects of chitosan depend on its degree of de-acetylation and molecular weight. Chitosans are polycationic in nature with active amino and hydroxyl functional groups. Chitosans adsorb well to salivary pellicles and create a positively charged and more hydrophobic pellicle surface. The positively charged amino groups in chitosan interact with negatively charged microbial cell surfaces and which results in the loss of barrier function of the microbial cell wall and the leakage of proteinaceous and other intracellular material. The positive charge of chitosan-treated pellicles helps in the decreasing the viability of *S. sanguinis* attached to saliva coated enamel treated with chitosan. Chlorohexidine with chitosan combination has more effect on reduction in cell viability than chlorhexidine alone.¹⁵ Sano et al (2002) demonstrated the effect of increased hydrophobicity of salivary pellicles after chitosan adsorption and its influence on reduction in adhesion of *Streptococcus sobrinus* to saliva-coated hydroxyapatite disks, which was minimal for chitosans with a molecular weight of 5–6 kDa and a degree of acetylation of 50–60%. They also have demonstrated that the low-molecular-weight chitosans inhibited the initial adhesion of oral bacteria to human tooth surfaces at a level comparable to that of a 50 mg l-1 (50 ppm) chlorhexidine solution. Busscher et al (2008) demonstrated the application of chitosan in oral health care as a promising antimicrobial agent. They evaluated the effects of a chitosan on bacterial adhesion and growth on chitosan-treated pellicles. Chitosan caused a reduction in bacterial adhesion and was responsible for bacterial death upon contact.¹⁶

Chitosan in Dentifrices

Dentifrices are agents used along with a toothbrush to cleanse and polish natural teeth. Dentifrices should have maximum cleansing efficiency with minimum tooth abrasion. Dentifrices perform three important functions such as: 1. They assist the toothbrush to mechanically the teeth. 2. They polish teeth to provide increased light reflectance and superior esthetic appearance.

3. Finally, they act as vehicles for the delivery of therapeutic agents that provide known benefits. Therapeutic agents include fluorides, tartar control agents, desensitizing agents, peroxides, and bicarbonates. The high polish as an added benefit enables teeth to resist accumulation of microorganisms and stains better than rougher surface. Chlorhexidine gluconate solution is most commonly used mouth rinse for the prevention of plaque formation and development of gingivitis since it has good antimicrobial activity against the microbes responsible for oral infections. However, the side effects associated with CH are sensitivity changes in tongue, poor taste, taste disturbance, extrinsic tooth staining, pain, and the content of alcohol. So, there is a necessity to develop a novel material that fulfils the requirements of oral health care products. Researchers have explored the applications of chitosan in dentifrices. Chitosan possesses good antimicrobial properties, acts as a good gelling agent, and does not require any preservatives. Mohire et al (2010) developed chitosan based polyherbal toothpastes with enhanced performance in oral care as chitosan inhibits the growth of *Streptococcus mutans* and *Porphyromonas gingivalis*; microorganisms responsible for caries and gingivitis, respectively. These polyherbal tooth pastes are composed with chitosan, eugenol and *Pterocarpus marsupium* aqueous extract, *Stevia rebaudiana* aqueous extract, *Glycyrrhiza glabra* aqueous extract. Chitosan based polyherbal tooth pastes proved to be a promising to be a potential oral hygiene product, which inhibited the growth of microorganisms responsible for caries and gingivitis and also potentiates the effectiveness of active ingredients of toothpaste for antimicrobial and anti-inflammatory activities.

Chitosan based adhesives

Several materials have been attempted to improve the antimicrobial properties of dental adhesives, including methacryloxy dodecyl bromide, inorganic agents, methacryloxy ethyl cetyl dimethyl ammonium chloride and chlorhexidine, with varying degrees of success. Antibacterial activity of a self etching primer was improved by the incorporation of CH. However, incorporation of chlorhexidine with higher concentrations has the negative effect on the bond strength of adhesive to dentin. Elsaka et al (2012) evaluated the antibacterial activity and bond strength of single bond adhesives modified with various concentrations of chitosan. Adhesives with the lower concentrations of chitosan were proved to be more effective against *S. Mutans*. However, greater the concentration of chitosan has negative effects on microtensile bond strength, degree of conversion and pH. The viscosity of the adhesive resin is more as the concentration of chitosan increases that prevents the infiltration of resin in to the demineralised dentin.

Chitosan as implant surface modifier

The role of surface topography has been the interesting area of investigation in implant dentistry for several years. Several types of implant surface textures are currently available for clinical use. Some of these have the ability to enhance and direct the growth of bone and achieve osseointegration when implanted in osseous sites. Various surface characterization methods of titanium implants were discussed in the literature; including mechanical, chemical, electrochemical, vacuum, thermal and laser treatments. Biomimetic deposition such as calcium phosphate and/or carbonate apatite coatings form more complex and porous structure over the implant surfaces. Electrodeposition of Chitosan in combination with calcium phosphate on the Ti6Al4V implants significantly improved the biocompatibility with no adverse affects on the other properties of implants. It has been reported that electrolytically deposited calcium phosphate was initially octacalcium phosphate, which later transferred into carbonate apatite. This is because of the presence of chitosan that influences calcium phosphate formation and crystallization, with the result that octacalcium phosphate is inhibited to transfer into carbonate apatite and crystallinity is decreased. Increase in the concentration of chitosan has the negative affects on both the coating thickness and surface roughness.¹⁷

Chitosan as dentin collagen

Various chemicals such as EDTA, NaOCl, and MTAD are used during non-surgical root canal treatment to clean and seal the root canals. These chemicals may affect the structural integrity of root dentin. Treatment with EDTA results in demineralization of dentin with exposed collagen fibrils that contributes to interfacial nanoleakage at the dentin-sealer interface. In addition, there is a reduction in the mechanical strength of dentin when exposed to NaOCl.¹⁸ Other factors those influence the structural integrity of root dentin are bacterial enzymes and host-derived matrix metalloproteinases (MMPs). Recently, more attention has been given on crosslinking of collagen and neutralization of MMPs to stabilize dentin collagen.¹⁹ Alternatively,

photodynamic crosslinking has been reported to induce rapid and stable covalent crosslinking of collagen by exposing photosensitizers such as rose Bengal to an appropriate wavelength of light (540 nm). In addition to crosslinking, reinforcement of the collagen matrix can be achieved by incorporating biopolymers such as chitosan that can be crosslinked with collagen fibrils. Incorporation of chitosan improves the biological and mechanical properties of collagen constructs significantly. More recently, the effect of carboxy methyl cellulose on structural integrity of dentin was evaluated and it was proved that there is a significant improvement in the chemical stability, tensile strength and toughness of dentin collagen by chemically/photodynamically crosslinking collagen matrix with carboxy methyl cellulose chitosan.^{20,21}

As dental scaffold material

An organic scaffold is used to provide a surface on which cells may adhere, grow, and spatially organize. Biocompatibility is the first and foremost important characteristic of scaffold to prevent adverse tissue reactions. The synthetic polymers such as poly(lactic) acid (PLA) and poly(glycolic) acid (PGA) are most commonly used in tissue engineering. More recently, Chitosan is considered as scaffold material because of its good biocompatibility and degradability via naturally occurring enzymes, it has been used for numerous dental tissue engineering applications.²²

Conclusion

Chitosan is a biocompatible biopolymer, is currently being used for various applications in dentistry due to its various biological properties. It is capable of activating host defences to prevent infection and accelerate wound healing as well as repairing the tissues. Research is continuing on new derivatives of chitosan in order to provide a better form for application to the site of effect apart from the antimicrobial activities.

REFERENCES

1. Williams KR, Blayney AW (1987) Tissue response of several polymeric materials implanted in the rat middle ear. *Biomaterials* 8(4): 254-258.
2. Hall EE, Meffert RM, Hermann JS, Mellonig JT, Cochran DL (1999) Comparison of bioactive glass to demineralized freeze-dried bone allograft in the treatment of intrabony defects around implants in the canine mandible. *J Periodontol* 70(5): 526-535.
3. Park JS, Choi SH, Moon IS, Cho KS, Chai JK, et al. (2003) Eight-week histological analysis on the effect of chitosan on surgically created one-wall intrabony defects in beagle dogs. *J Clin Periodontol* 30(5): 443-453.
4. Ezoddini Ardakani F, Navab Azam A, Soghra Y, Fatehi F, Rouhi G (2011) Effects of chitosan on dental bone repair. *Health* 3(4): 200-205.
5. Souza Gadelha de Crvalho MM, Montenegro Stamford TC, Pereira dos Santos E, Tenorio P, Sampaio F (2011) Chitosan as an oral antimicrobial agent. Science against microbial pathogens: communicating current research and technological advances pp. 542-550.
6. Ji QX, Zhong DY, Lu R, Zhang WQ, Deng J, et al. (2009) In vitro evaluation of the biomedical properties of chitosan and quaternized chitosan for dental applications. *Carbohydr Res* 344(11): 1297-1302.
7. Sano H, Shibasaki K-i, Matsukubo T, Takaesu Y. Effect of chitosan rinsing on reduction of dental plaque formation. *Bull Tokyo Dent Coll.* 2003;44(1):9-16. Aguilar A, Zein N, Harmouch E, Hafdi B, Bornert F, Offner D, et al. Application of Chitosan in Bone and Dental Engineering. *Molecules.* 2019;24(16):3009.
8. Morin-Crini N, Lichtfouse E, Torri G, Crini G. Applications of chitosan in food, pharmaceuticals, medicine, cosmetics, agriculture, textiles, pulp and paper, biotechnology, and environmental chemistry. *Environ. Chem. Lett.* 2019;17(4):1667-92.
9. Crini G. Historical review on chitin and chitosan biopolymers. *Environ. Chem. Lett.* 2019;17(4):1623-43.
10. Park SI, Daeschel MA, Zhao Y. Functional properties of antimicrobial lysozyme-chitosan composite films. *J. Food Sci.* 2004;69(8):215-21.
11. Xia WS, Liu P, Liu J. Advance in chitosan hydrolysis by non-specific cellulases. *Bioresour. Technol.* 2008;99(15):6751-62.
12. Rao SB, Sharma CP. Use of chitosan as a biomaterial: Studies on its safety and hemostatic potential. *J. Biomed. Mater. Res.* 1997;34(1):21-8.
13. Fakhri E, Eslami H, Maroufi P, Pakdel F, Taghizadeh S, Ganbarov K, et al. Chitosan biomaterials application in dentistry. *Int. J. Biol. Macromol.* 2020;162(2):956-74.
14. Senel S, McClure SJ. Potential applications of chitosan in veterinary medicine *Advanced Drug Delivery Reviews*, 2004; 56:1467-1480.
15. Kenawy ER, Worley SD, Broughton R. The chemistry and application of antimicrobial polymers: a state-of-the-art-review. *Biomacromolecules* 2007; 8: 1359-1384.
16. Van Der Mei HC, Engels E, De Vries J, Dijkstra RJB, Busscher HJ. Chitosan adsorption to salivary pellicles. *Eur J Oral Sci* 2007; 115: 303-307.
17. Helander IM, Nurmiaho LEL., Ahvenainen R, Rhoades J, Roller S. Chitosan disrupts the barrier properties of the outer membranes of Gram negative bacteria. *Int J Food Microbiol* 2001; 71: 235-244.
18. Rabea EI, Badawy MET, Stevens CV, Smaghe G, Steurbaut W. Chitosan as antimicrobial agent: applications and mode of action. *Biomacromolecules* 2003; 4: 1457-1465.
19. Decker EM, Ohle Cvon, Weiger R, Wiech I, Brex M. A synergistic chlorhexidine/chitosan combination for improved antiplaque strategies. *J Periodontol Res* 2005; 40: 373-377.
20. Sano H, Shibasaki K, Matsukubo T, Takaesu Y. Effect of molecular mass and degree of deacetylation of chitosan on adsorption of *Streptococcus sobrinus*

6715 to saliva treated hydroxyapatite. Bull Tokyo Dent Coll 2002; 43: 75–82.

21. Sano H, Shibasaki K, Matsukubo T, Takaesu Y. Comparison of the activity of four chitosan derivatives in reducing initial adherence of oral bacteria onto tooth surfaces. Bull Tokyo Dent Coll 2001; 42: 243–249.
22. Busscher HJ, Engels E, Dijkstra RJB, van der Mei HC. Influence of a chitosan on oral bacterial adhesion and growth in vitro. Eur J Oral Sci 2008; 116: 493–495.