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Application of Chitosan Biomaterials in Dentistry—A Narrative Review

Nidhish Krishna[1] Nikita Lolayekar[1]

[1] Department of Pediatric and Preventive Dentistry, A B Shetty Memorial Institute of Dental Sciences, Nitte (Deemed-to-be-University), Mangalore, Karnataka, India

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Address for correspondence Nidhish Krishna R., BDS, Department of Pediatric and Preventive Dentistry, A B Shetty Memorial Institute of Dental Sciences, Nitte (Deemed-to-be-University), Mangalore 575018, Karnataka, India (e-mail: nidhish.20dped05@student.nitte.edu.in).

Abstract

Chitosan is a versatile natural biomaterial that has been researched for a range of bio-dental applications. It possesses various desirable qualities such as biocompatibility, hydrophilicity, biodegradability, and a broad antibacterial range (covering Gram-negative and Gram-positive bacteria as well as fungi). Moreover, the molecular structure contains reactive functional groups, which provide numerous reaction sites and possibilities for the formation of electrochemical interactions at the cellular and molecular levels. Chitosan's unique features have attracted material scientists from all over the world to explore its applications in dentistry. The objective of this review is to highlight the creation of new chitosan biomaterials and as to how it is a vital component for the improvement and modification of existing dental materials being used.

Keywords
- biomaterials
- dentistry
- chitosan

Introduction

The intricacy of anatomical structures in the oral cavity as well as the constant communication with the external environment leads to microbial colonization, production of dental plaque, and its outcome leads to various diseases related to the oral cavity. Massive efforts have been made to treat and prevent infectious diseases, as well as to restore normalcy.[1] In recent years, the concept of biomaterials has been widely promoted, resulting in significant advances in the design and application of safe and functional materials. Biomaterials are natural, synthetic, or semisynthetic substances that are intended to be implanted into biological ecosystems.[2,3]

One such material is chitosan, which is a biodegradable and biocompatible natural polysaccharide, that has a wide range of applications in the field of dentistry due to its functional versatility and ease of access. Chitosan and its derivatives can be used as dental adhesives, barrier membranes, bone replacement, tissue regeneration, and antibacterial agents in the treatment of oral diseases.

They can be transformed using chemical or enzymatic techniques to produce a variety of derivatives and forms that are nontoxic and biocompatible, such as gels, micro-/nano-particles, fibers, sponges, and films, depending on the field of use.

Because of its particular composition and properties, chitosan can thus be a potential source for the production of diverse dental materials.

Methodology

A thorough search was undertaken in literature which was available in the English language from 1992 to 2021, which constituted review articles, original research, as well as case reports. The search was performed in Google Scholar, Science Direct, and National Library of Medicine's PubMed database. Also, searches in hard copies of available journal were performed manually using chitosan, dental applications of chitosan, and biomaterials as keywords.

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Chemical Structure of Chitin and Chitosan

Chitin is an aminated polysaccharide produced by a variety of invertebrate animals. Chitin, also known as poly (-(14)-N-acetyl-D-glucosamine, is a significant natural polysaccharide that was first discovered in 1884. It is a key component of arthropod exoskeletons, which comprise insects and crustaceans. Some microorganisms, such as bacteria, fungus, protozoa, and algae species, have also been reported to contain chitin.[4]

The majority of chitin production is devoted to the creation of chitosan, a deacetylated derivative and its chemical properties have an impact on the molecule's functional capabilities. Chitosan's polycationic nature also allows it to interact with a wide range of compounds. This, together with its structural capabilities and biocompatibility, makes chitosan a promising candidate for the development of functional materials in a wide range of sectors.[5]

Application of Chitosan Biomaterials in Dentistry

Chitosan, because of its unique qualities and compatibility to merge with other materials,[6] has turned out to be a suitable material for bio-dental applications. Chitosan-based materials have been extensively researched for a wide range of dental applications.[7]

Preventive Dentistry

Chitosan-Containing Mouthwash

Chitosan mouthwash inhibits the proliferation of *Streptococcus mutans* by interfering with bacterial adhesion and biofilm formation, as well as *Lactobacillus brevis*.[8] It has analgesic, anti-inflammatory properties, reduced toxicity, and higher antibacterial efficacy than commercial mouthwashes with or without alcohol.

The cationic nature of chitosan-containing toothpastes, together with their low pH and tendency to bind to structures with negative zeta potentials such as enamel and salivary pellicles, leads to the formation of a protective multilayer organic matrix.

Chitosan-containing toothpaste was shown to be efficient in penetrating thick, mature biofilm layers, lowering the plaque index by 70.47% and the bacterial load by 85.29%.[9]

Chitosan for Enamel Remineralization

Chitosan has the potential to attach to the negatively charged surfaces like tooth enamel because of the free amino groups in the protonated structure.

The chitin-bioglass complex and hydrogels have been found to promote mineral deposition and affect the surface and subsurface microhardness of erosive or carious enamel lesions.[10]

Chitosan-Based Varnish

The mineral components from the enamel are reported to be inhibited by propolis-based chitosan varnish which slows down the process of demineralization. In a study by Zhang et al, when chitosan and propolis were mixed, they had a synergistic effect that promoted antibacterial activity.[11]

Restorative Dentistry

Adhesion and Dentin Bonding

Chitosan coated with methacrylic acid (Chit-MA70) has been evaluated as a primer for a "etch-and-rinse" adhesive system using human teeth, and it has significant bonding strength.[12]

Restorative Materials

Chitosan can be used as an alternative restorative material when blended with dental composite and glass ionomer. Methacrylate-modified chitosan was discovered to have antibacterial activities against *Streptococcus mutans*, inhibiting the production of biofilms.

Microshear bond strength of chitosan-modified glass ionomer cement (GIC) was shown to be substantially higher than that of standard GIC and demonstrated increased compressive and flexural strength, as well as higher antibacterial activity.[13,14]

Endodontic Therapy

Root Canal Irrigant

Chitosan can be used in endodontic procedures because of its broad-spectrum antibacterial capabilities, high chelating capacity in acidic conditions, and stimulates dentin remineralization. Suzuki et al concluded that the antibacterial impact and elimination of the smear layer took only 5 minutes, and was significantly greater than 10% citric acid and chitosan-citrate solution was found to be a potential root canal irrigant.[15]

Intracanal Medicament

Calcium hydroxide in combination with chitosan formulation demonstrated the most sustained release of calcium ions while maintaining a high alkaline pH for up to 30 days. It can thus be used in long-term dressings for root canal treatment.[16]

Direct Pulp Capping

Subhi et al investigated the cellular effects of gypsum-based chitosan material (Gp-CT) as a pulp capping agent in comparison to Dycal and discovered that cell viability was much greater in pulp stem cells treated with (Gp-CT) than in pulp stem cells treated with Dycal and when calcium phosphate carboxymethyl-chitosan composite (CaP-CMCS) was used as a pulp capping material, pulp stem cells were shown to differentiate into odontoblastic cells.

CaP-CMCS composite showed quick gelation, improved mechanical properties, biological compatibility, and odontogenic potential, achieving the first critical components of a potentially regenerative pulp capping agent that is rapidly curing, stable, and biocompatible.[17]

Dental Pulp Regeneration

In regenerative endodontic treatment scaffolds are vital for transporting active molecules and cells into the root canal and are the most significant factor in determining regenerative endodontic therapy outcome.

The usage of a chitosan-based cellularized fibrin hydrogel as a scaffold can help limit endodontic bacteria growth. Incorporating chitosan into a fibrin hydrogel can aid in the formation of dental pulp tissue without affecting the viability, shape, or proliferation of dental pulp cells in the collagen matrix.[18]

Pulpotomy

Chitosan is a powerful hemostatic agent. It forms a cross-linked clot barrier by interacting directly with red blood cells and thrombocytes. Chitosan promotes wound healing by increasing the release of platelet-derived growth factor-AB and transforming growth factor-1. Chitosan-containing hydrogels have been found to stimulate odontogenic development of dental pulp stem cells (DPSCs).[19] As a result of these advantages, chitosan can be used as a medication for pulpotomy. In primary molars, Kothari et al examined the effectiveness of chitosan and formocresol as pulpotomy medicaments. It was observed that the clinical success rate was 96.6% in both the groups, whereas the radiographic success rate in chitosan was 96.6%, however, in formocresol it was 89.6%.[20]

Pulpectomy Medicament

Imani et al conducted an in vitro study to assess the antibacterial effects of chitosan, formocresol, and camphor monochlorophenol (CMCP) as pulpectomy medicaments on Enterococcus *faecalis*, *Staphylococcus aureus*, and *Streptococcus mutans*, the results showed that the antibacterial efficacies of the materials (indicated by colony reduction) were significantly different. Chitosan's antibacterial effectiveness was comparable to that of formocresol or CMCP in both stages (after 1 or 7 days of therapy). As a result, it was determined that chitosan is antibacterial and can be utilized as a medicament in pulpectomy of infected primary teeth.[21]

Stem Cell-Based Regenerative Therapeutics

Stem cell-based transplantation strategies that use embryonic stem cells and, more recently, adult dental stem cells to induce pluripotent stem cells in tooth regeneration show promise in the field of dentistry and have the potential to transform the approach in treating diseases and alleviating oral conditions.[19] Significant progress has led to the utilization of chitosan as a carrier for chitosan-mediated stem cell repair. Yang et al used DPSCs that were cultivated on a collagen–chitosan complex and were able to produce a dentine–pulp complex.[22]

Drug Delivery and Periodontal Therapy

Chitosan-based delivery systems can be in the form of micro-nanoparticles, fibers, membrane, and gels.[7] Methods utilizing a local delivery system can combat inflammation and infection and also promote tissue regeneration.

Chitosan Gels

Chitosan-based gels with viscosities ranging from 1 to 4% can be injected into periodontal pockets and utilized as drug carriers to transfer active drugs such as statins, doxycycline, or other antibiotics/antiseptics such as tetracycline to disease sites, hence aiding periodontal healing.[19]

Nanoparticles

Chitosan nano-microparticles can be utilized to transport therapeutic compounds, such as anti-inflammatory medications, and release them in a continuous way.[7]

Meanwhile, investigators discovered that self-assembled chitosan/phospholipid nanoparticles surpass the drug hydrophobicity limitation on the carrier structure and stability of the encapsulation in the face of enzyme attack from the environment is improved.

Magnetic targeting chitosan nanoparticles were organized as imaging agents for photodynamic therapy and it was noted that it exhibited a significant photodynamic effectiveness on SW480 carcinoma cells both in vitro and in vivo at concentrations of 0 to100 µm.[23]

Fibers, Films, and Microspheres

Implantable film of chitosan-based matrix delivery technology is commonly used as an intrapocket carrier, particularly in interproximal pockets.[24]

Khajuria et al developed a chitosan-based film loaded with risedronate/zinc-hydroxyapatite (CRZHF) for periodontitis therapy that has a high mucoadhesive strength and flexibility and it exhibited acceptable stability in the periodontal pocket for approximately 11 days, as well as a continuous release of risedronate at a high concentration.[25]

Patients with periodontitis may benefit from the use of chitosan-based films loaded with local anesthetics as it achieved sustained anesthesia and relieved pain.[26]

Chitosan microspheres containing clindamycin, tetracycline, doxycycline, fluoroquinolone antibiotics, and chlorhexidine have been developed to transport medications to periodontal pockets.[7]

Li et al developed an antimicrobial peptide-loaded poly (lactic-co-glycolic acid)/chitosan composite microsphere for sustained peptide release against the oral and periodontal bacteria *Fusobacterium nucleatum* using electrospraying and combined crosslinking-emulsion procedures. However, a variety of parameters impact the release properties of chitosan microspheres, including chitosan molecular weight and concentration, drug content, and crosslinking density.[27]

Guided Tissue Regeneration

Chitosan collagen membrane for guided tissue regeneration (GTR) significantly reduced infrabony and furcation anomalies while decreasing probing pocket depth, increasing clinical attachment at furcation locations, facilitated tissue repair, and had an osteoinducing effect.[28]

Chitosan membrane can be coupled with bone morphogenetic protein to treat buccal gingival recession and aids bone and gum regeneration. Due to its unique bioproperties, chitosan collagen membrane is an efficient barrier for GTR and guided bone regeneration treatments, making it an excellent membrane for periodontal regeneration.[7]

Implant Dentistry

Chitosan-Coated Titanium Dental Implants

Chitosan is a feasible biocompatible and bioactive coating for orthopaedic and craniofacial implant devices that can promote bone growth and osseointegration and prevent infections with better wound healing.

Chitosan is an efficient bioactive coating for dental implants due to its capacity to suppress *Porphyromonas gingivalis* bacterial adherence and increased fibroblast-cell adhesion.

Titanium implants coated with chitosan have improved mechanical strength and longevity, has more osteoblast cell development and attachment than uncoated titanium.[29]

Oral Surgery

Bone Regeneration

Matinfar et al[30] combined chitosan and carboxymethyl cellulose with reinforced triphasic calcium phosphate fibers demonstrating that three-dimensional-printed chitosan scaffolds have good osteogenic capabilities.

Chitosan can be used with biomimetic calcium phosphate (Bio-CPC) in bone transplant procedures. In vitro results showed that Bio-CPC-reinforced chitosan can increase odontoblast development and differentiation while also improving bone strength and characteristics.[19]

Wound Dressing

Chitosan dressing is a hemostatic agent that can dramatically minimize postextraction bleeding while also improving pain control in patients who are taking oral antithrombotic drugs.

Chitosan-based dental dressing has become increasingly popular in dental surgery. It has been shown in clinical trials to be safe and effective for hemostasis in patients who received oral antithrombotic therapy, reduced the duration of bleeding, discomfort, and improved surgical wound healing rate and prognosis.[31]

Sinha et al reported that the average hemostatic time was 1.5 minutes and showed increased platelet adhesion and aggregation, as well as platelet growth factor release.[32]

Temporomandibular Joint Disc Repair

Chitosan can also be utilized to treat temporomandibular joint (TMJ) disorders, disc displacement, and degeneration. Cell seeding, proliferation, chondrogenic induction, cell survival, and extracellular matrix deposition were all enhanced by the fibrin-chitosan scaffold. TMJ-synovium generated mesenchymal stem cells in combination with a fibrin-chitosan hybrid scaffold have been shown to mend TMJ disc perforation, increase fibrocartilage regeneration, and improve TMJ disc reparative potential.[33]

Prosthodontics

Chitosan can be used as a dental adhesive for acrylic denture bases to eliminate *Candida albicans* fungal infections. When compared with lower molecular weight chitosan and carboxymethylcellulose, high molecular weight chitosan has the best antifungal activity against most Candida species and completely inhibited *Candida albicans* adhesion to acrylic denture bases while having no toxic effect on gingival fibroblast viability and proliferation. It has sufficient retention to be used as a denture adhesive.[34]

Chitosan's antifungal effect suggests that it produces a permeable film at the contact which serves two purposes: direct inhibition of fungal growth and activation of multiple defense systems. Accumulation of chitinases, synthesis of proteinase inhibitors, lignification, and stimulation of callous formation are some of the defense mechanisms.[35] Pena proposed that apoptosis-like mechanism is a part of chitosan's fungicidal activity and the efflux of nucleotides and metabolic pathway substrates results in the inhibition of the main metabolic pathways, respiration, and fermentation, depriving the cells of their main energy sources.[26]

Conclusion

Chitosan is a biopolymer that has been widely researched for its unique features and applications. In terms of therapeutic success and outcome, the increased use of chitosan in a variety of dental applications seems promising.

Although its qualities have been thoroughly investigated, there are still some concerns to be addressed, such as the fact that extracted chitosan can vary in structure and molecular weight from low to high, resulting in inconsistent physiochemical characteristics and variability.

It has a lot more potential in terms of biological applications in the future. However, there is a scarcity of clinical evidence on the use of chitosan-based polymers in dental applications. More research, particularly in vivo investigations and clinical trials, is required to move chitosan-based materials from research to clinical usage.

Conflict of Interest
None declared.

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