

Chitosan Nanoparticles In Endodontics: A Comprehensive Review

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ABSTRACT

Background: Nanotechnology has found extensive applications in various fields of dentistry, including restorative dentistry, due to its significant improvements and promising potential in enhancing the clinical efficacy of restorative materials and procedures. Nanoparticles exhibit antimicrobial, antifungal, and antiviral properties, making them effective in disrupting bacterial cell walls, increasing cell membrane permeability, generating reactive oxygen species, and interfering with DNA replication through the controlled release of ions. Nanomaterials in dentistry have been categorized and classified according to their use in different disciplines of dentistry, mainly based on their shape, composition, and function. These categories include Conventional NPs, Unconventional NPs, Nanomaterials based on carbon nanotubes (CNTs), and Metallic and non-metallic nanomaterials. Chitosan, a versatile natural biomaterial, is emerging as a key ingredient in the development of dental materials. It is renowned for its biocompatibility, hydrophilicity, biodegradability, and broad antibacterial spectrum, which includes Gram-negative and Gram-positive bacteria as well as fungi. Additionally, chitosan aids in restoring the mechanical integrity of the diseased dentinal matrix and promotes tissue regeneration. Its applications in restorative and endodontic therapy are diverse, encompassing enamel remineralization, glass ionomer cement (GIC) enhancement, dentin bonding and adhesion, pulpotomy, direct pulp capping, intracanal irrigants and medicaments, and pulp regeneration. This review aims to explore the various applications of chitosan in conservative dentistry and endodontics, highlighting its potential benefits and the scope of its use.

Keywords: Chitosan, nanoparticles, endodontics.

INTRODUCTION

Recent advancements in dentistry have introduced new materials that are both safe and efficient. Nanoparticles (NPs) are used to increase antibacterial and remineralization capabilities as inorganic and organic NPs. Inorganic NPs include silver, zinc oxide, titanium oxide, and gold, while organic NPs include silica, quaternary ammonium salt monomers, and chitosan NPs. Furthermore, nanofillers are used to enhance the process of remineralization, which includes metals, nano-hydroxyapatite, nano-amorphous calcium phosphate (ACP), dicalcium phosphate NPs, casein

phosphopeptide-ACP (CPP-ACP), and calcium fluoride NPs.

Chitosan, a macromolecule composed of repeated D-glucosamine units, is derived from the deacetylation of chitin, making it the second most abundant biopolymer after cellulose. Chitin was first isolated by French professor Henri Braconnot in 1811. In 1859, C. Rouget discovered that boiling chitin with hot potassium hydroxide solution resulted in deacetylation, forming an acid-soluble substance later named chitosan by Hoppe Seiler. In 1994, Ohya and colleagues developed chitosan

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nanoparticles through emulsifying and crosslinking techniques.

Chitosan nanoparticles are commonly synthesized using methods such as ionotropic gelation, polyelectrolyte complexation, microemulsion, emulsification solvent diffusion, and reverse micellar methods. The preferred method, heterogeneous deacetylation, involves treating chitin with a hot NaOH solution, resulting in the selective reaction in amorphous regions of the polymer. This process yields free hydroxyl groups and primary amino groups, imparting a positive charge to chitosan and enabling its interaction with negatively charged surfaces. When chitosan interacts with anions, it forms beads large enough to limit drug delivery. Effective nanoparticles range in size between 10 nm and 100 nm.

Applications

1. **Smear Layer Removal:** Chitosan's chelating properties effectively remove the inorganic portion of the smear layer by forming complexes with metal ions and removing dentin calcium ions. Studies have shown that chitosan-EDTA (1:1) is a potent root canal irrigant that performs dual roles in root canal disinfection and smear layer removal. When in contact with the dentin surface, chitosan induces remineralization of demineralized dentin through its covalent interaction with dentin collagen, attracting calcium ions and facilitating the formation of a calcium-phosphate layer. Chitosan also improves dentinal surface degradation by collagenase and shows higher micro-hardness and lower surface roughness compared to EDTA.
2. **Haemostasis, Pulpotomy, and Pulpectomy:** Chitosan is utilized to arrest bleeding. Celox, a hemostatic agent containing chitosan, binds to negatively charged erythrocytes and forms a cross-linked clot barrier. In pulpotomy, chitosan diluted with sterile saline is applied to the pulp chamber to achieve hemostasis, promoting the formation of reparative dentin and hard tissue, making it suitable for pulpotomy procedures. Chitosan's antibacterial effectiveness compared to formocresol has shown that chitosan is highly antibacterial and can be utilized as a

medicament in pulpectomy of infected primary teeth.

3. **Direct Pulp Capping:** Gypsum-based chitosan material (Gp-CT) has shown higher cell viability in pulp stem cells compared to Dycal. The calcium phosphate carboxymethyl-chitosan composite (CaP-CMCS) has demonstrated quick gelation, improved mechanical properties, biological compatibility, and odontogenic potential, making it a promising regenerative pulp capping agent. Chitosan nanoparticles may leach out of the sealer mass, providing diffusible antibacterial properties while inhibiting the surface adherence of *E. faecalis*.
4. **Enamel Regeneration:** Biomimetic production of enamel-mirroring material is regarded as the future of preventive dentistry. Studies indicate that organic amelogenin delivery using chitosan restorative formulations can aid enamel regeneration by inducing apatite nucleation. Chitosan-based hydrogels serve as carriers for amelogenin, supporting dental pulp cell collection, promoting crystal growth, and mineral deposition.
5. **Dentin Remineralization:** The nanometric scale of nanomaterials allows penetration into the dentin tubules and collagen fiber network, producing sustained drug release and full effectiveness. Chitosan has also been used for improving dentin bonding, as it effectively inactivates MMPs and kills bacteria on dentin through its cationic properties, reducing collagen degradation and enhancing bonding durability. Modified chitosan by quaternary ammonium salt, N,N,N-Trimethyl chitosan (TMC), has better solubility and stronger cationic properties under neutral conditions than ordinary chitosan, enabling easier application and increased biological effects. Phosphorylated chitosan acts as an analogue, inducing homogeneous nucleation. Carboxymethyl chitosan/amorphous calcium phosphate (CMC/ACP) nano-complexes infiltrate collagen fibrils, facilitating dentin remineralization.

6. **Restorative Materials:** Chitosan nanoparticles combined with GIC enhance the release of cell signaling peptides and growth factors, improving flexural strength and fluoride release rates. This combination is beneficial for vital pulp therapy and exhibits significant antibacterial properties. Chitosan-based composites (CBCs) have potential for developing long-lasting mechanical characteristics, appropriate contact duration, and sustained release profile, while retaining a strong affinity with the oral mucosa.
7. **Intracanal Medication and Sealers:** A combination of 2% chlorhexidine gel and chitosan exhibits strong antimicrobial effects against *C. albicans* and *E. faecalis*. Incorporating chitosan nanoparticles into zinc-oxide eugenol (ZOE) sealers enhances antibacterial efficacy.
8. **Chitosan-Based Adhesives and Varnish:** Chitosan has been incorporated into bioadhesive polymers and dentine replacement materials. It effectively increases the resistance of dental restorations when used in "etch and rinse" adhesive systems, showing higher shear bond strength and reduced collagen destruction. The mineral components from the enamel, when inhibited by propolis-based chitosan varnish, slow down the process of demineralization. When chitosan and propolis were mixed, they had a synergistic effect that promoted antibacterial activity.
9. **Pulp Regeneration:** Advances in stem cell research have facilitated the use of chitosan as a carrier for stem cell repair, particularly in the regeneration of the dentine-pulp complex. Mobilized dental pulp stem cells, such as SHEDs and SCAP, have shown potential in forming odontoblastic cells for endodontic regeneration. A nanofibrous architecture enhances the adsorption of the cell adhesion protein compared to a smooth-walled architecture scaffold. The nanofibrous architecture scaffold is similar to the physical architecture of natural collagen fibers, providing a favorable extracellular matrix-like environment for the attachment and proliferation of human DPSCs. Nanofibers used

for the seeding of regenerative cells act as a scaffold, resulting in a porous 3D surface that promotes the attachment of cells.

Limitations

Chitosan's low solubility in neutral and alkaline pH environments poses a challenge. Its mucoadhesive and permeation-enhancing properties are strongest in the duodenal area but can be modified with derivatives. The toxicological profile of chitosan derivatives is still under investigation, with limited clinical data available despite promising results in animal models.

CONCLUSION

Chitosan is a promising biomaterial for dental applications, ranging from restorative dentistry to tissue-engineered scaffolds for complex healing processes. Despite rigorous investigations, issues such as variability in extracted chitosan's structure and molecular weight remain. Ensuring reproducibility of the correct molecular weight is a challenge. Nevertheless, chitosan's potential in various fields of dentistry is vast, necessitating further research to translate chitosan-based materials from laboratory to clinical applications.

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