## Development of bioactive dental nanomaterials for anticaries therapy

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## ABSTRACT

Dental caries is a multifactorial disease in which the fermentation of sugars from daily diet by bacteria from the biofilm (dental plaque) leads to localised demineralisation of tooth surfaces, which may ultimately result in cavity formation. Restorative dental materials such as resin composites and adhesive systems are in contact with tooth and can be the ideal vehicle for delivering anticaries agents. Based on nanotechnology, nanoparticles of silver (NAg) and nanoparticles of amorphous calcium phosphate (NACP) were introduced into restorative materials to achieve antimicrobial and remineralizing properties, respectivately. Another strategy to combat caries lesions around restorations is the incorporation of antibacterial monomers in the dental material composition. The antibacterial, remineralizing and mechanical properties of these new materials indicate that novel nano-sized agents can fight bacteria and reduce the demineralization in restored tooth cavities.

Keywords: dental materials, nanoparticles, nanotechnology, dental caries.

Statement of purpose: Resin-based composite and adhesive systems are popular direct restorative options in dentistry. These restorations can fail mainly due to secondary caries and restorative material fracture. Secondary caries is caries developed adjacent to restorations at the restoration-tooth structure interface. It is the main cause for restoration failure and replacement. The development of direct-filling restorative dental materials with antibacterial and remineralizing properties is a promising approach to addressing the caries problem. Tremendous efforts have been made in developing approaches that not only show high antibacterial efficacy, but also maintain the load-bearing properties of dental materials. Nanotechnology is a promising approach to developing the next generation of dental materials, to not only replace the missing tooth volume as traditional restorations, but also inhibit oral biofilms and remineralize tooth caries. Based on this approach, nanoparticles of silver (NAg) were introduced into restorative dental materials to achieve antimicrobial properties. The use of antimicrobial polymers also offers promise for enhancing the efficacy of antibacterial dental materials. Antibacterial monomers can be copolymerized with the dental resin matrix and hence be immobilized in the composite and not released or lost overtime. Another strategy to combat caries lesions around restorations, also based on nanotechnology, is to drive the shift of demineralization to remineralization via calcium (Ca) or phosphate (P) ion release from nanoparticles of amorphous calcium phosphate (NACP). Here we report the development of dental materials including primer and adhesives containing the above cited agents.

**Materials and methods:** A set of antibacterial (0.1% NAg; 5% DMADDM (dimethylaminododecyl methacrylate) and remineralizing agents (20% NACP) were syntetized and incorported in dental primer and adhesive. Bacteria viability was assessed using a dental plaque microcosm biofilm model with human saliva as inoculum to measure metabolic activity, lactic acid production, and colony-forming unit (CFU) counts for total microorganisms, total streptococci, and mutans streptococci after biofilm growth on 9 mm resin disks. Mechanical properties were measured by shear bond testing to evaluate the bonding strenght of the new materials to human dentin.

**Results:** Dental primer and adhesive containing nano-sized antibacterial and remineralizing agents of 0.05% NAg, and adhesive containing NAg and NACP (0-40%) were able to inhibit biofilms and lactic acid without compromising the mechanical properties (Fig. 1) (Melo et al. J Biomed Mater Res B Appl Biomater 2013; 101(4):620-9). Bonding agents containing antibacterial DMADDM and remineralizer NACP also presented suitable mechanical properties (Chen C., et al. Dent Mater. 2014;30(8):891-901). The new DMADDM could be incorporated into the NACP dental adhesive to impart a strong antibacterial activity without compromising the mechanical properties(Fig. 2).



**Fig. 1.** Dentin shear bond strength. (A) Primer containing 0.05% NAg, and (B) adhesive containing NAg and NACP (0-40%). (adapted from Cheng et al., 2013 and Melo et al., 2013 with permission).



Fig. 2. Antibacterial activity of primer and adhesive containing DMADDM and NACP. CFU counts for total microorganisms were greatly decreased, compared to control (p < 0.01). (adapted from Chen et al., 2014 with permission).

**Conclusion:** It can be concluded that NAg, NACP and DMADDM incorporated in restorative materials are promising to kill caries-associated bacteria and inhibit the demineralization along the tooth-restoration margins. The novel method of combining antibacterial agents (NAg and DMADDM) with remineralizing agent (NACP) may enable new strategies for caries control by reduction of cariogenic bacteria and remineralizing tooth lesions around the restorations.

## References

[1] Cheng L, Zhang K, Melo MAS, Weir MD, Zhou X, Xu HHK. Anti-biofilm dentin primer with quaternary ammonium and silver nanoparticles. J Dental Res 2012; 91(6): 598-604.

[2] Melo MA, Cheng L, Weir MD, Hsia RC, Rodrigues LK, Xu HH. Novel dental adhesive containing antibacterial agents and calcium phosphate nanoparticles. J Biomed Mater Res B Appl Biomater 2013; 101(4):620-9.

[3] Chen C, Weir MD, Cheng L, Lin NJ, Lin-Gibson S, Chow LC, Zhou X, Xu HH. Antibacterial activity and ion release of bonding agent containing amorphous calcium phosphate nanoparticles. Dent Mater. 2014 Aug;30(8):891-901.