Novel Calcium Phosphate and Calcium Fluoride Nanocomposites with Antibacterial and Low-Shrinkage-Stress Capabilities to Inhibit Dental Caries

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INTRODUCTION

- Methacrylate-based dental composites are the most widely used materials in dentistry to restore defective tooth structures.
- The major etiological factors for resin composite failure are recurrent caries and tooth fracture, primarily due to the lack of bioactivity and the development of polymerization shrinkage stress, respectively, at the tooth-restoration interface.
- There are strategies to reduce shrinkage stresses include changing the resin matrix's chemistry by the use of resin systems with a unique polymerization behavior, such as ether-based triethylene glycol divinylbenzyl ether.
- Recently, a low-shrinkage-stress resin (UV) was developed via mixing urethane dimethacrylate (UDMA) and ether-based triethylene glycol divinylbenzyl ether (TEG-DVBE), which resulted in reducing polymerization stresses.
- From a clinical point of view, nanoparticles of amorphous calcium phosphate (NACP) and calcium fluoride ($nCaF_2$) may contribute to reducing the initial formation of recurrent caries by releasing calcium, phosphate, and fluoride ions.
- This approach in conjunction with antibacterial effect of dimethylaminododecyl methacrylate (DMADDM) may be advantageous to reduce the rates of secondary caries lesion formation around the resin composite margin.
- **Aim:** The aim of this study was to develop a novel bioactive nanocomposite to inhibit dental caries, and to investigate the antibacterial function and cytotoxicity of the low-shrinkage-stress nanocomposite containing DMADDM, NACP, and $nCaF_2$.

MATERIALS AND METHODS

- DMADDM was synthesized via a modified Menschutkin reaction. NACP and $nCaF_2$ were made using a spray-drying technique. Novel low-shrinkage-stress was formulated using 55.8% urethane dimethacrylate (UDMA) and 44.2% of ether-based triethylene glycol divinylbenzyl ether (TEG-DVBE) (all mass %) at filler:matrix mass ratio of 35:65. Then, the following resin composite were developed:

(1) Heliomolar commercial control composite (denoted "Commercial control");
(2) Experimental control resin composite: 35% UV + 65% glass (denoted as "Experimental control");
(3) 35% UV + 20% NACP + 45% glass (denoted as "UV+NACP");
(4) 32% UV + 3% DMADDM + 20% NACP + 45% glass (denoted as "UV+NACP+DMADDM");
(5) 35% UV + 20% $nCaF_2$ + 45% glass (denoted as "UV+$nCaF_2$");
(6) 32% UV + 3% DMADDM + 20% $nCaF_2$ + 45% glass (denoted as "UV+$nCaF_2$+DMADDM").

- The mechanical and physical properties were assessed via flexural strength and modulus of elasticity.
- To assess the antibacterial properties, 48-h *Streptococcus mutans* (*S. mutans*) biofilms were grown over the resin composite surface and the colony-forming units (CFUs), metabolic activity, and lactic acid production by biofilms were assessed.
- The cytotoxicity was investigated against human gingival fibroblasts (HGFs) and dental pulp stem cells (DPSC).

RESULTS

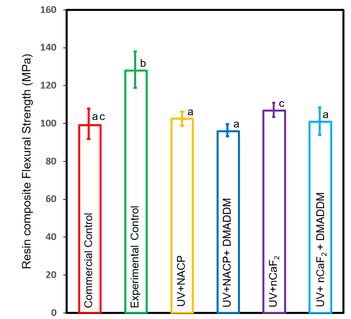

Figure 1. The incorporation of 3% DMADDM with 20% of NACP or $nCaF_2$ resulted in comparable flexural strength values to the commercial control. ($P > 0.05$)

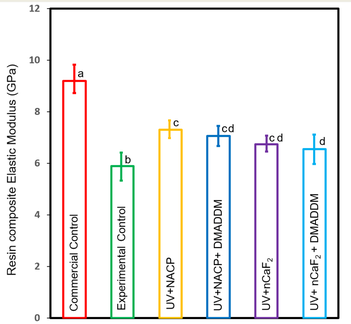

Figure 2. The incorporation of 20% of NACP or $nCaF_2$ with or without DMADDM resulted in an increase of elastic modulus values to the experimental control. ($P < 0.05$)

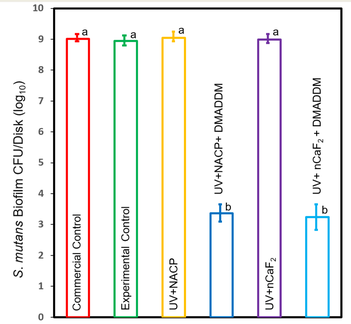

Figure 3. The incorporation of DMADDM into a novel resin composite containing NACP or $nCaF_2$ significantly reduced CFUs count for *S. mutans* compared to the commercial control. ($P < 0.05$)

RESULTS

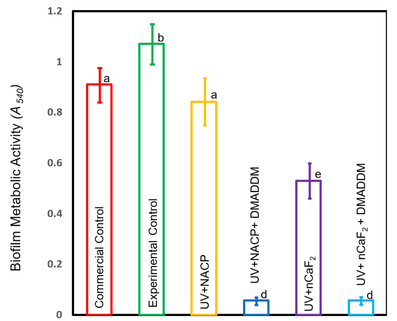

Figure 4. Metabolic activity of biofilm MTT "(mean ± SD; n = 6)". The incorporation of DMADDM in low-shrinkage-stress resin composite containing NACP or $nCaF_2$ reduced the metabolic activity of *S. mutans* compared with experimental and commercial control ($p < 0.05$)

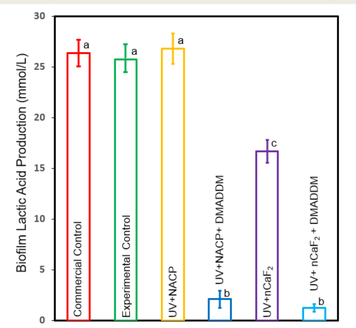

Figure 5. Lactic acid production by biofilms on resin composites (mean ± SD; n = 6). The low-shrinkage-stress resin composite with DMADDM significantly reduced lactic acid production compared to other groups ($p < 0.05$).

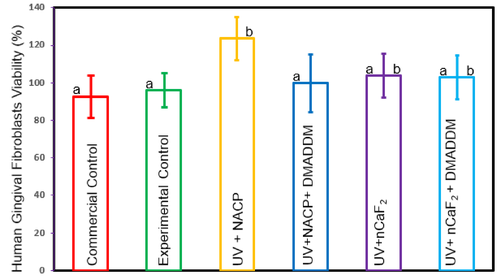

Figure 6. The viability of Human gingival fibroblast toward the newly developed low-shrinkage-stress resin composite (mean ± SD; n= 3x3).

RESULTS

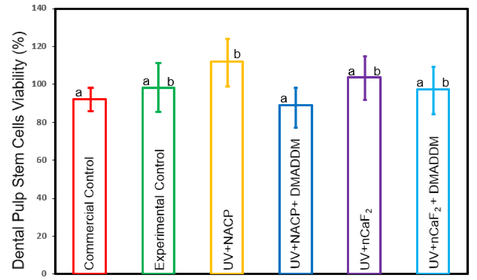

Figure 7. The viability of dental pulp stem cells toward the newly developed low-shrinkage-stress resin composite (mean ± SD; n= 3x3). The UV+NACP group exhibited a significant increase in viability compared to the commercial control ($p < 0.05$). However, all other novel resin composite groups showed comparable viability to commercial control ($p > 0.05$).

DISCUSSION & CONCLUSION

- A novel bioactive and low-shrinkage-stress nanocomposite was developed that possessed excellent mechanical and biocompatible properties, while reducing biofilm CFU and lactic acid production by orders of magnitude.
- The incorporation of 3% DMADDM with NACP or $nCaF_2$ demonstrated higher antibacterial activity without compromising the mechanical properties.
- The suggested contact-killing mechanism for DMADDM is based on ionic interaction with the bacterial membrane.
- NACP and $nCaF_2$ fillers may reduce the risk of minerals loss by neutralizing the pH inside the oral cavity.
- All the groups tested were defined as non-cytotoxic to HGFs and DPSC in accordance with ISO recommendations with viability higher than 75%.
- Developing a bioactive low-shrinkage-stress resin composite that could help in minimizing the formation of the gap at the tooth-restoration interface might help in increasing the survival rate of resin composite and reduce the onset of recurrent caries.
- Preclinical studies are required to investigate the effectiveness of these formulations against biofilm models with high clinical relevance to evaluate the applicability and the antibacterial activities of this material.

ACKNOWLEDGEMENT

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