Development of Topical Medicaments to Promote Caries Arrest

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Introduction

Silver Diamine Fluoride (SDF) is an efficacious caries-arresting medicament (CAM) used as an interim measure to stabilize carious lesions, however, its use results in a permanent dark discoloration of teeth, limiting patient acceptance (1).

Drug-silica co-assembled particles (DSPs), which exhibit sustained release of antimicrobial drug octenidine dihydrochloride (OCT), have demonstrated effectiveness at preventing biofilm formation when incorporated in dental restorative materials (2).

OCT is a cationic surfactant with an antimicrobial spectrum of activity similar to that of chlorhexidine and no known drug resistance (3) .

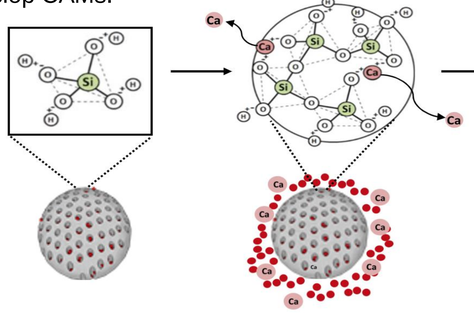
While DSPs could serve as drug depots for the development of CAMs owing to their high drug content, their drug release profile must be modulated, since CAMs are applied to areas with a pre-existing biofilm; and biofilm disruption necessitates a higher drug concentration relative to that needed to prevent its formation.

Objectives:

(1) Develop novel quick-release DSPs (modified-DSPs) by incorporating network-modifying ions into their silica construct
(2) Evaluate the biofilm-disruption efficacy of these modified-DSPs using in-vitro models.

Hypothesis

Drug release from DSPs can be modulated through changes in its silica network i.e. incorporation of network-modifying ions such as calcium and phosphorus into their silica structure. Modified-DSPs with accelerated drug release could be utilized to develop CAMs.



Removal of network-modifying ions from the silica construct of the modified-DSPs will accelerate the dissolution of silica from the walls around the pores of the particles, leading to an increased drug exposure and consequently increased drug release from the degrading pores relative to diffusion mediated drug release from intact pores.

Fig 1: Schematic representation of mechanism of accelerated drug release from modified-DSPs

Methods & Results

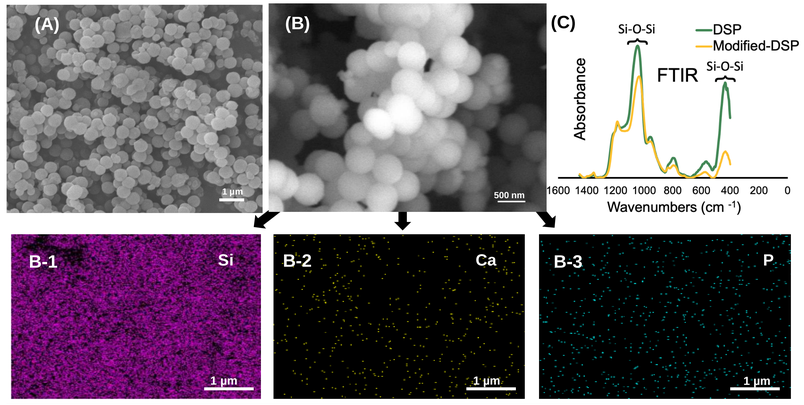


Fig 2: (A) SEM image of modified-DSPs (B1-3) SEM EDX showing the incorporation of network-modifying ions into modified-DSPs (C) FTIR spectra of DSPs & modified-DSPs. Reduction in the intensity of peaks around wavelength 1088 and 466 cm^{-1} in the modified-DSP spectra denotes increased disorganisation and decreased polymerisation within the silica network due to the incorporation of the network-modifying ions.

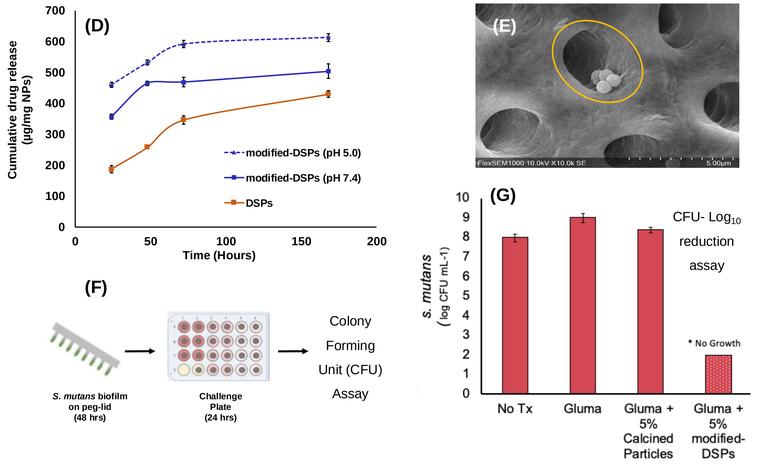
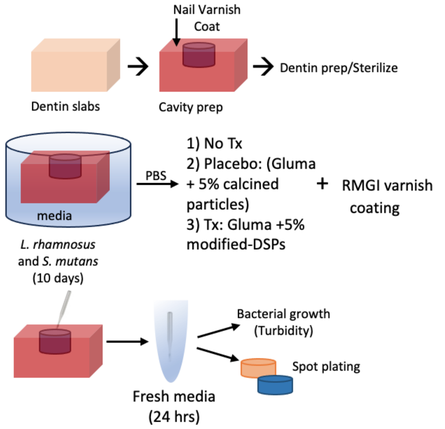
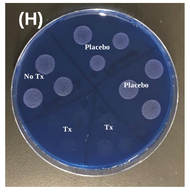


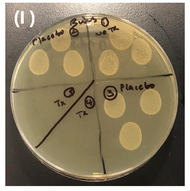
Fig 3: (D) Drug release kinetics of modified-DSPs demonstrating accelerated drug release and pH-responsiveness. (E) CAMs were formulated by incorporating modified-DSPs into Gluma (Kulzer) and applied to dentin slabs. SEM image showing the delivery of modified-DSPs into dentinal tubules using CAM formulation. (F and G) Assessment of antimicrobial efficacy of the CAM formulation using single species biofilm. Results demonstrate a 6-log reduction in bacterial growth using CAM formulation relative to negative controls.

Methods & Results





Mitis Salivarius: *S. mutans*



MRS agar : *L. rhamnosus*

Fig 4: Assessment of antimicrobial efficacy of the CAM treatment formulation using dentin slabs and dual-species biofilm. Results demonstrated that dentin slabs were completely disinfected by CAM formulations, whereas control specimens yielded bacterial growth. Growth of *S. mutans* and *L. rhamnosus* was confirmed by spot plating the media in selective agars (H and I).

Conclusions

Introduction of network-modifying ions into the silica construct of DSPs can accelerate drug release.

Modified-DSPs demonstrate potent antimicrobial/antibiofilm effects and can be further developed as CAMs with esthetic outcomes.

References

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Funding

Alpha Omega Research Grant, CAPD travel and research award, Harron Scholarship, Mock Scholarship, Dr. W. Bruce and Susan Malloch Fellowship, Canadian Institutes of Health Research [MOP 115113, PJT-165957], Canada Foundation for Innovation John R. Evans Leaders Fund (CFI_JELF) [project #35378] , Ministry of Research and Innovation (MRI), Ontario Research Fund (ORF) [ORF-35378], University of Toronto Connaught Innovation Award