

# A pH-Sensitive Delivery System for the Prevention of Dental Caries Using Salivary Protein

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## Abstract

Dental caries remains one of the most common chronic diseases worldwide. In previous studies, salivary proteins (e.g. histatin 3, statherin) have demonstrated biological functions including the inhibition of crystal growth, antibacterial activities, which are directly related to tooth homeostasis and prevention of dental caries. However, proteins are susceptible to the high proteolytic activities in the oral environment. Therefore, pH-sensitive chitosan nanoparticles (CNs) have been proposed as potential carriers to protect proteins against enzymatic degradation at physiological salivary pH, in addition to swell selectively at lower pH conditions to facilitate the release of the encapsulated proteins, as major oral complications occur under acidic conditions (e.g. dental caries and dental erosion). Four different types of chitosan polymers were investigated and the optimal CNs formulation was selected, the chosen formulation had a good batch to batch reproducibility with an average hydrodynamic diameter of  $144 \pm 6$  nm, a polydispersity index of  $0.15 \pm 0.04$ , and a zeta potential of  $18 \pm 4$  mV at the final pH of 6.2. Histatin 3 encapsulation and release profiles were characterized by cationic polyacrylamide gel electrophoresis. The CNs successfully encapsulated histatin 3 at 2%, 5% and 10% w/w loading ratios, they also selectively released histatin 3 under acidic conditions. Through protein degradation study in whole saliva supernatant, histatin 3 encapsulated inside the delivery system demonstrated a prolonged survival time compared to the free histatin 3. The results of this study have demonstrated the pH-responsive property and the protection offered by CNs.