Development of a Dentotropic Enzyme-Based Antimicrobial System for Caries Prevention and Treatment

Laura Weber, Dhruvkumar Soni, and Dong Wang

Department of Pharmaceutical Sciences, Lozier Center for Pharmacy Sciences Education and Center for Drug Discovery, University of Nebraska Medical Center, Omaha, NE 68198-6025, USA

Maintenance of effective local concentrations of antimicrobials on the tooth surface is critical for management of cariogenic bacteria in the oral cavity. Through the development of an enzyme-based antimicrobial system, local retention of the antimicrobial hydrogen peroxide (H_2O_2) on the tooth surface can be achieved for extended periods of time without affecting the normal oral microbiome. Glucose oxidase (GO) catalyzes the oxidation of glucose to H_2O_2 and gluconic acid. A GO-containing liposome with a pyrophosphate (PPi)-modified cholesterol (Chol) component has been formulated. Through the chelation of the PPi moiety with hydroxyapatite (HA, the main component of dental enamel), GO-containing liposomes can be immobilized on the tooth surface for several hours and produce hydrogen peroxide in the presence of glucose (from food or beverage consumption). A novel PPi-Chol moiety has been designed and synthesized. The GO-containing dentotropic liposome has been found to selectively bind to HA particles as evidenced by fluorescence microscopy studies of both binding and non-binding liposomes loaded with Alexa Fluor 488-conjugated GO. By visualization of the relative fluorescence intensities, higher binding is apparent with the PPi liposomes versus the non-binding and free GO controls. Furthermore, the liposomes are able to retain the enzyme activity over the course of 8 hours while bound to HA. It is expected that studies of the prevention and treatment of biofilms of *S. mutans*, the main oral cariogenic bacteria, will show antimicrobial effectiveness in a simulated oral environment. This novel enzyme-based antimicrobial system can thus selectively bind to and be retained on HA while retaining enzymatic activity. With positive data from the bacteria assays, it may be able to be used independently or be incorporated into regular dentifrice formulations to provide better prevention and treatment of dental caries.