Mollusk Glue Inspired Mucoadhesives for Biomedical Applications

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Abstract:

Chitosan (CH), partially N-deacetylated chitin, is a biodegradable and biocompatible polymer that has shown great potential in drug delivery and tissue engineering applications. Although bioadhesive, CH has limited mucoadhesion in wet conditions due to weak interactions with biological surfaces. DOPA (3,4-dihydroxy-L-phenylalanine), a catechol-containing molecule naturally present in marine mussel foot proteins, has been shown to increase the mucoadhesion of several polymers. We report here a simple and bioinspired approach to enhance CH mucoadhesion in wet conditions by preparing mixed hydrogels including CH and different catechol-containing compounds, namely DOPA, hydrocaffeic acid (HCA), and dopamine (DA). We characterized the hydrogels for their swelling, release kinetics of the catechol compounds, and mucoadhesive strength to rabbit small intestine. The swelling of the hydrogels was pH dependent with maximum swelling at pH 1. The hydrogel swelling was higher in the presence of the DOPA and DA but lower in the presence of HCA. HCA/CH hydrogel also showed the slowest catechol release, most likely due to electrostatic interactions between CH and HCA. Lower hydrogel swelling and slower HCA release resulted in increased mucoadhesion: HCA/CH showed more than 2-fold enhancement of mucoadhesion to rabbit small intestine compared to CH alone. Since it is known that catechol compounds can be oxidized, we analyzed the oxidation of DOPA, HCA, and DA at different pH values and its effect on mucoadhesion. We found that oxidation occurring before contact with the intestinal mucosa did not improve mucoadhesion, while oxidation occurring during the contact further increased the mucoadhesion of HCA/CH hydrogels. These results show that mucoadhesion of CH hydrogels can be increased with a simple bioinspired approach, which has the potential to be applied to other polymers since it does not require any chemical modification.

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