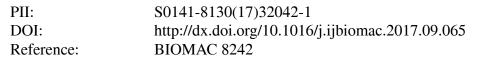
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ACCEPTED MANUSCRIPT

A novel controlled drug delivery system based on alginate hydrogel/chitosan micelle composites

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Abstract

In this study, we present a novel cross-linked unimolecular micelle based on chitosan. For controlling drug delivery *via* oral administration, emodin (EMO) encapsulated micelles were loaded into sodium alginate hydrogel matrix to construct the pH-sensitive hydrogel/micelle composites. The optimized formulation of micelle that consists of 8.06 % CaCl₂, 1.71 % chitosan and 26.52 % β -GP was obtained by the combination of Box-Behnken experimental design and response surface methodology. The morphological analysis showed that the micelles exhibited a smaller diameter of about 80 nm in aqueous solution, but dilated to 100-200 nm in hydrogel owing to the formation of polyelectrolyte complexes. The physical characteristics in simulated digestive fluids were investigated, demonstrating that the ratio of hydrogel to micelle distinctly affected swelling, degradation and *in vitro* drug release behaviors. The hydrogel/micelle (1:1) exhibited a sustained-release profile, while hydrogel/micelle (3:1) exhibited a colon-specific profile. Their corresponding release mechanisms revealed that the release of drug from these two formulations followed a complex process, in which several mechanisms

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