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A cell-penetrating peptide conjugated carboxymethyl- β -cyclodextrin to improve intestinal absorption of insulin

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Abstract

In this study, a cell-penetrating peptide conjugate, R8-carboxymethyl- β -cyclodextrin (R8-CM- β -CD), was synthesized, and then we prepared the supramolecular complex (insulin/R8-CM- β -CD). The physicochemical properties of the complex were characterized. The supramolecular complex could facilitate the uptake of insulin, meanwhile, induce a significantly higher internalization of insulin. Interestingly, the transportation efficiency of insulin/R8-CM- β -CD across the Caco-2 cell monolayer was about 3 times greater than that of insulin/CM- β -CD. Further studies on the mechanism in increasing uptake efficiency showed that R8-CM- β -CD was internalized via different styles of endocytosis and could inhibit P-glycoprotein (P-gp) efflux pumps. Importantly, the formulation of insulin/R8-CM- β -CD showed the highest increase in the permeability of insulin and the best biological response in diabetic rats of all the treatments. In addition, no sign of toxicity was observed after administrations of R8-CM- β -CD. These results demonstrated that R8-CM- β -CD was a promising carrier for use in protein drug delivery.

Keywords

cell-penetrating peptide, cyclodextrin, mechanism, absorption efficiency, insulin.

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