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インスリン持続放出システムとしてのシクロデキストリンポリシュードロタキサンハイドロゲルの有用性評価

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【Purpose】The development of injectable hydrogels for protein delivery is a major challenge. A delivery formulation where gelation and drug loading can be achieved simultaneously taking place in an aqueous environment and without covalent crosslinking would be attractive. In this study, we examined *in vitro* and *in vivo* evaluations of α- and γ-cyclodextrin (CyD) polypseudorotaxane supramolecular hydrogels for insulin delivery as a sustained release system.

【Methods】The supramolecular structure of insulin hydrogels was confirmed with ^{1}H-NMR, X-ray diffraction, differential scanning calorimetry (DSC) and scanning electron microscopy (SEM). *In vitro* release of insulin from polypseudorotaxane supramolecular hydrogels was measured by the modified dispersed amount method and quantitative analysis was performed by HPLC. Serum insulin and glucose levels after subcutaneous administration of insulin CyD hydrogels to rats were determined by enzyme immunoassay and mutarotase-glucose oxidase method, respectively.

【Results and discussion】Insulin CyD hydrogels were prepared by inclusion complexation between high molecular weight polyethylene glycol (PEG) and CyDs. The polypseudorotaxanes were performed by inserting one PEG chain in the α-CyD cavity and two PEG chains in the γ-CyD cavity. The *in vitro* release study showed that the release rate of insulin from the supramolecular hydrogels decreased in the order of γ-CyD hydrogel > α-CyD hydrogel. This decrease was controlled by the addition of CyDs to the medium. The serum insulin level after subcutaneous administration of γ-CyD hydrogel to rats was significantly prolonged, which was clearly reflected in the prolonged hypoglycemic effect. These results suggested that γ-CyD polypseudorotaxane supramolecular hydrogel will have the potential application as a sustained delivery system for insulin.