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In vivo evaluation of pre-activated α-cyclodextrins as a mucoadhesive intra-vesical drug delivery system

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The study was designed to synthesize and characterize pre-activated α-cyclodextrin (α-CD) derivatives as mucus adhering excipients for intra-vesical drug delivery. Sodium periodate (NaIO4) was used to oxidize α-CD and subsequently cysteamine was covalently attached to carbonyl groups of oxidized α-CD via reductive amination to produce thiolated α-CD. L-cysteine-2-mercaptonicotinic acid conjugate (Cys-MNA) was covalently attached to carbonyl groups of oxidized α-CD to produce pre-activated α-CD having enhance stability against oxidation at higher pH. Thiolated and pre-activated α-CD derivatives were quantitatively assayed for the attached thiol groups and MNA groups, respectively. Cell viability and tolerability was evaluated via Resazurin assay and via red blood cells (RBC) lysis assay, respectively. Mucoadhesive properties were evaluated on porcine bladder mucosa. Trimethoprim (TMP) was encapsulated into thiolated and pre-activated α-CD derivatives and the dissolution behavior was evaluated *in vitro*. Thiol groups attached to thiolated α-CD derivatives α-CD-SH_{780} and α-CD-SH_{1426} were 780±68 µmol/g and 1426±66 µmol/g, respectively. For the entirely pre-activated α-CD derivatives, α-CD-MNA_{3609} and α-CD-MNA_{4285} number of attached MNA groups were 3609±19 µmol/g and 4285±43 µmol/g, respectively. Thiolated and pre-activated derivatives of α-CD did not show adverse effects to cells determined via Resazurin and RBC lysis assays. Mucoadhesion on porcine bladder mucosa was significantly improved for thiolated and pre-activated α-CD derivatives. Thiolated α-CD-SH_{1426} showed 15-fold and pre-activated α-CD-MNA_{4285} showed 25-fold improved mucoadhesion compared to unmodified α-CD. Further, pre-activated α-CD-MNA_{4285} showed 2-fold enhanced dissolution of encapsulated TMP compared to free TMP over 3h. The study shows that pre-activated α-CD could be an excipient of the choice for the formulations of mucoadhesive intra-vesical drug delivery systems.

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