27J-pm03S

SN38 封入キューボソームの一層コーティング

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【Purpose】SN38, a potent anticancer drug, has low water solubility 7 μg/mL. Previously, we prepared cubosomes with a high drug loading to overcome its problem. In order to reduce the particle size and increase drug loading furthermore, we applied a new concept of one layer coating.

【Method】Phytantriol (cubic phase forming amphiphile), didodecyldimethyl ammonium bromide (DDAB) (additive), SN38 and Pluronic F127® or F108® (steric stabilizers) were homogeneously mixed and probe-sonicated. After that, the coat, a PEGylated non-ionic surfactant (IGEPAL® CO-I720 (I720)), was added to cubosome formulation at different ratios and the mixture was vortexed. To establish the effect of their adhesion on the cubosome surface, we compared the polydispersity index using dynamic light scattering (DLS) and zeta and surface potentials using electrophoretic light scattering. Inner structures were characterized using small angle X-ray scattering. Drug loading was determined by HPLC. Shelf-life stability tests were carried out at 25°C in a PBS medium, then measured by DLS.

【Results and Discussion】Addition of I720 caused a phase conversion of the DDAB-cubosome from the primitive cubic lattice ($Pn\bar{3}m$) to the body-centered cubic one ($Im\bar{3}m$), raising surface potential by 10 mV. Adding I720 decreased the mean particle size from 165 to 142 nm. Furthermore, it significantly increased drug loading, 138 μg/mL against 127 μg/mL for the non-coated DDAB-cubosome. Coated DDAB-cubosomes maintained the low particle size over a week showing good stability as well as the non-coated ones. We conclude we could successfully coat cubosomes with a one layer coat that increased the drug loading, decreased particle size and maintained it over the storage conditions.