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Characterization of cubosomes loaded with water insoluble drug SN38

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【Purpose】SN38, a very potent anticancer drug, has low water solubility 7 μg/mL and is prone to hydrolysis under physiological conditions rendering it biologically inactive. To overcome these problems, we tried to prepare cubosomes due to their sophisticated lipid bilayer-based inner structure.

【Method】Mixtures, with various ratios, of phytantriol (cubic phase forming amphiphile), didodecyldimethylammonium bromide (DDAB, co-lipid), SN38 and Poloxamer 407 (steric stabilizer) were homogeneously mixed and then probe-sonicated. Inner structure was characterized using small angle X-ray scattering. Particle size and zeta potential were measured using dynamic and electrophoretic light scattering, respectively. Drug concentration was determined by reversed-phase HPLC. Gel filtration was used to confirm encapsulation efficiency (EE). Drug stability test was carried out at 25°C in a PBS medium.

【Results and Discussion】Inner structures of all cubosomes were of the cubic space group *Pn3m*. Empty cubosomes had a median diameter of 93 nm, zeta potential of 3.93 mV and a polydipersity index (PDI) value of 0.054, indicating a monodispersion. SN38-loaded cubosomes had a median diameter of 120 nm and a zeta potential value of 8.38 mV and a PDI value of 0.18 which also can be considered as a monodispersion, for freshly prepared formulations. Loading SN38 into cubosome made it possible to increase its solubility up to 110 μg/mL, which is almost 16-fold of the free drug water solubility. EE was found to be 93.7%. Encapsulated SN38 was stable as only 10% was hydrolyzed into the inactive form after 24 h, whereas more than 90% of the free drug was hydrolyzed within 3 h. After 24 h period at 25°C in a PBS medium, median diameter was still less than 150 nm, which is within the range of passive targeting for future *in vivo* anticancer application.