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Bottom-up preparation and structural study of monodispersed lipid particles with internal structure[1] HOJUN KIM, ALANA ALFECHE, CECILIA LEAL, University of Illinois at Urbana-Champaign — Lipid based nanoparticles having internal bicontinuous cubic phases, also known as cubosomes, are becoming increasingly interesting drug delivery platforms. Compared to the liposomes, they offer an augmented surface area for drug encapsulation. However, this simple argument is insufficient to explain the cellular delivery performance of cubosomes compared to other lipid-based nanoparticles. One could argue that their topology facilitates membrane fusion and endosomal escape but at the moment the exact mechanism of cubosome cellular internalization and endosomal escape is still unknown. This is partially because the practical use of cubosomes has been limited due to hurdles of uncontrollable size and shape distributions. The conventional top-down preparation methods (sonication/homogenization) yield large and polydisperse particles. In this presentation we introduce a new system based on microfluidic devices to prepare small (200 nm) and monodisperse cubosomes with a quality not possible using conventional methods. With this approach, we successfully prepared spherical and monodisperse cubosomes (PDI: 0.01) with and without drug loading. To characterize the cubosomes and the formation mechanisms, we utilize Small Angle X-ray Scattering (SAXS) and Cryogenic TEM.

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