Lipid-liquid crystalline nanoparticles in drug delivery system

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Hydrated lipids exhibit polymorphism, thereby forming a variety of lyotropic liquid crystalline phases with distinct 3D liquid-crystalline structures such as lamellar, hexagonal or cubic phases. Bicontinuous lipidic cubic phases (LCPs) exhibit a combination of material properties that makes them highly interesting for various biomaterial applications: they are non-toxic, biodegradable, optically transparent, thermodynamically stable in excess water, and can incorporate active molecules of virtually any polarity. An interesting property of cubic phase is also their ability to disperse into nanoparticles called “cubosomes”. Cubosomes are less viscous and they can stably exist in equilibrium with aqueous solution and retain an internal bicontinuous structure unchanged. In contrary to liposomes or micelles cubosome is more resistant to mechanical or osmotic rupture. The cubic phase nanoparticle delivery system can be used to improve the oral bioavailability of poorly water-soluble drugs. The structure and dynamics of lipidic mesophases, and their interactions with guest molecules can be tailored by applying additives, thereby achieving novel materials with improved functions for drug delivery. [1, 2]

Here we present lipid-liquid crystalline nanoparticles as effective and safe anticancer drug delivery system. Doxorubicin, a model drug that contains an amine group and a hydrophobic part, was loaded into the cubic phase and cubosomes. As the pH sensitive release is crucial for a delivery system to release drugs at the target tumor cells, the release behavior of DOX was evaluated by using electrochemistry and UV-vis spectroscopy in two buffered solutions at pH 5.5 and 7.4. The release behavior in vitro indicated that the DOX was removed from nanoparticles faster at pH 5.5 than at pH 7.4.The size and morphology of the prepared nanoparticles were characterized using dynamic light scattering and cryo-transmission electron microscopy. The inner cubic structure of the prepared materials was confirmed by SAXS. SAXS and DLS results demonstrate that the introduction of DOX does not significantly modify the inner structure of the cubosome, as well as their size and charge. A bicontinuous cubic phase of cubic Im3m was obtained with the particle size of each cubosome formulation of about 170 nm. The cytotoxicities of cubosomes and cubosomes containing DOX were evaluated using *in vitro* cytotoxicity assay on the glioma cells.

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[1] E. Nazaruk, M. Szlęzak, E. Górecka, R. Bilewicz, Y. M. Osornio, P. Uebelhart, E. M. Landau, *Langmuir*, 2014, ***30***, 1383.

[2] E. Nazaruk, E. Górecka, R. Bilewicz**,** *J. Colloid and Interface Sci.,* 2012, **385**, 130.