Hexosomes and Cubosomes from PDMS–PEG block copolymers as Potential Drug Carriers

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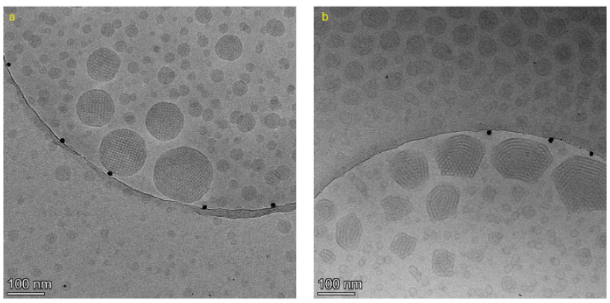
Non-lamellar liquid crystal particles, such as hexosomes and cubosomes, are promising as drug delivery carriers [1]. However, in most cases, they are derived from lipids, which limits the range of characteristic dimensions within particles. Herein, we report for the first time on the preparation of hexosomes and cubosomes from amphiphilic poly(dimethylsiloxane)-poly (ethylene glycol) (PDMS-PEG) block copolymers. PDMS features extremely low glass transition temperatures, i.e, the polymer chains are liquid-like and flexible at molecular lengths much longer than those of hydrocarbon chains in lipids, a condition that is highly favorable for the formation of inverse phases due to the low chain-packing constraints. PDMS-PEG linear block copolymers were synthesized by hydrosilanation from hydride-terminated PDMS (900 g/mol) and allyl methyl ether PEGs (450 and 550 g/mol). ^{1}H NMR and ^{13}C-NMR analyses confirmed the successful conjugation of PDMS and PEG. PDMS$_{900}$-PEG$_{550}$ and PDMS$_{900}$-PEG$_{450}$ show surface activity, reducing the water surface tension to 21 mN/m and 24 mN/m, respectively. Polarized optical microscopy revealed birefringence upon hydration of PDMS$_{900}$-PEG$_{550}$, indicating the formation of anisotropic liquid-crystals. Small-angle X-ray scattering (SAXS) analysis and phase behavior studies confirmed the formation of an inverse hexagonal (H_2) phase for hydrated PDMS$_{900}$–PEG$_{550}$, with characteristic SAXS peak ratios of 1 : √3: √4, and an inverse micellar cubic (I_2) phase with an Fd3m space group for hydrated PDMS$_{900}$–PEG$_{450}$, as evidenced by 14 diffraction peaks observed using synchrotron SAXS. These results suggest that inverse liquid crystal structure and morphology can be tuned by changing PEG chain length. Quantitative structural analysis allowed to determine the radius of the micellar cores and the interfacial area per molecule in the H_2 and I_2 phases [2]. Hexosome and cubosome dispersions in PBS can be prepared from the H_2 and I_2 phases, respectively, via the emulsification-evaporation method, using poly(oxyethylene) stearyl ether (Brij S-100) as a stabilizer, as confirmed by synchrotron SAXS and Cryo-TEM experiments. The colloidal stability of hexosome and cubosome dispersions was monitored using Turbiscan™. Colloidally stable formulations have hydrodynamic sizes of 153.2 ± 4.4 nm (PDI of 0.15 ± 0.05) for PDMS$_{900}$–PEG$_{550}$ hexosomes and 139.4 ± 3.1 nm (PDI of 0.19 ± 0.1) for PDMS$_{900}$-PEG$_{450}$ cubosomes. Additionally, these formulations were studied for the encapsulation and release of ibuprofen as model drug by using High-Performance Liquid Chromatography (HPLC). Cytotoxicity and cell internalization were further evaluated in vitro to assess biocompatibility.

Keywords:
Lyotropic liquid crystals, amphiphilic block copolymers, self-assembly, hexosomes, cubosomes, colloidal stability, drug delivery.



Representative Cryo-TEM images of a) PDMS900-PEG450 cubosomes and b) PDMS900–PEG550 hexosomes.

References:

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