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Core Cross-Linked Nanoparticles from Self-assembling PolyFMA-Based Micelles. Encapsulation of Lipophilic Molecules

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Abstract

The present work describes the preparation of stable organic nanoparticles with potential use as "smart" drug delivery systems capable of encapsulating lipophilic molecules to exert their therapeutic action under the appropriate stimulus. A well-defined self-assembly hydrophilichydrophobic di-block copolymer has been synthesized via atom transfer radical polymerization (ATRP). The hydrophilic block is based on a random copolymer with DMA and HEMA units, while the hydrophobic component is a linear random copolymer of DEA and FMA. Stabilization of the nanoparticles by means of core cross-linking is addressed by Diels-Alder reactions between the furan rings of the hydrophobic blocks and the synthesized bisdienophiles; the influence of both the cross-linking agent and the degree of cross-linking in the process is discussed. The incorporation of a therapeutic agent (pilocarpine) and a lipophilic fluorescent molecule (pyrene) is evaluated. When pyrene was immersed into the micelles, there was a significant boost of the fluorescence emission (from 10- to 40-fold), due to the hydrophobic environment of the inner part of the nanoparticles. Pilocarpine is also able to be encapsulated by the prepared systems. Drug release is triggered by a reduction in the pH of the media and is strongly dependent on the degree of cross-linking achieved.

Keywords: stimulus-response nanoparticles, core cross-linking, drug loading, Diels-Alder reaction, pilocarpine

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