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Synthesis and Characterization of pH-Responsive Nanocarriers Based on POEOMA-b-PDPA Block Copolymers for RNA Delivery

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Abstract : Drug delivery systems are designed to allow adequate protection and controlled delivery of drugs to specific locations. These systems aim to reduce side effects and control the biodistribution profile of drugs, thus improving therapeutic efficacy. This study involved the synthesis of polymeric nanoparticles, based on amphiphilic diblock copolymers, comprising a biocompatible, poly (oligo (ethylene oxide) methyl ether methacrylate (POEOMA) as hydrophilic segment and a pH-sensitive block, the poly (2-diisopropylamino)ethyl methacrylate) (PDPA). The objective of this work was the development of polymeric pH-responsive nanoparticles to encapsulate and carry small RNAs as a model to further develop non-coding RNAs delivery systems with therapeutic value. The responsiveness of PDPA to pH allows the electrostatic interaction of these copolymers with nucleic acids at acidic pH, as a result of the protonation of the tertiary amine groups of this polymer at pH values below its pKa (around 6.2). Initially, the molecular weight parameters and chemical structure of the block copolymers were determined by size exclusion chromatography (SEC) and nuclear magnetic resonance (1H-NMR) spectroscopy, respectively. Then, the complexation with small RNAs was verified, generating polyplexes with sizes ranging from 300 to 600 nm and with encapsulation efficiencies around 80%, depending on the molecular weight of the polymers, their composition, and concentration used. The effect of pH on the morphology of nanoparticles was evaluated by scanning electron microscopy (SEM) being verified that at higher pH values, particles tend to lose their spherical shape. Since this work aims to develop systems for the delivery of non-coding RNAs, studies on RNA protection (contact with RNase, FBS, and Trypsin) and cell viability were also carried out. It was found that they induce some protection against constituents of the cellular environment and have no cellular toxicity. In summary, this research work contributes to the development of pH-sensitive polymers, capable of protecting and encapsulating RNA, in a relatively simple and efficient manner, to further be applied on drug delivery to specific sites where pH may have a critical role, as it can occur in several cancer environments.

Keywords : drug delivery systems, pH-responsive polymers, POEOMA-b-PDPA, small RNAs
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