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Dendron-based micelles: A potential nanocarrier platform

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Abstract

Dendron-based amphiphilic copolymers possess unique features such as well-defined structure, self-assembling capability, multivalency, and precise controllability over functionalities and hydrophilicity. To assess their potential as a nanocarrier, we have synthesized novel PEGylated dendron copolymers (PDC) with controlled hydrophilic-lipophilic ratios (HLs) ranging from 52:48 to 91:9. A hydroxyl-terminated generation 3 polyester dendron bearing a focal acetylene moiety was conjugated with poly(ε-caprolactone) (PCL) by 'click' chemistry followed by PEGylation of the dendron surface with multiple methoxy poly(ethylene glycol) (mPEG) moieties. We then systematically compared their self-assembly properties with those of linear-block copolymer (LBC) counterparts. The critical micelle concentrations (CMCs) of PDCs were measured as low as 1.17×10^{-8} M, which was up to 2 orders of magnitude lower than those of the LBCs, demonstrating superior thermodynamic stability of the PDC micelles. TEM images revealed that the PDCs formed spherical micelles (20-30 nm in diameter) with narrow size distributions, which was further supported by dynamic light scattering measurements. To understand the differences in self-assembly between PDCs and LBCs at the molecular level, we also utilized atomistic molecular dynamics (MD) simulations. Individual PDC copolymers were observed to adopt a stable conical shape in water, which is ideal for precise packing into spherical structures. Interestingly, the core was more completely covered by PEG in PDC micelles, which may result in longer circulation half-lives and enhanced accumulation at the therapeutic target site. The low CMCs, controlled micelle morphologies and release properties, and high PEG surface coverage all indicate the promising potential of the PDCs as a nanocarrier platform.

Biography

Seungpyo Hong received his PhD degree from the University of Michigan in 2006 and completed his postdoctoral training at MIT in 2008. He is currently Assistant Professor in the Department of Biopharmaceutical Sciences, College of Pharmacy at the University of Illinois at Chicago. He has published more than 40 papers in reputed journals and served as a reviewer for a number of funding agencies and professional journals. His research achievements have been recognized by the related communities, resulting in him receiving awards including 2012 AAPS New Investgator Award in Pharmaceutics and Pharmaceutical Technologies, Hans Vahlteich Award, and Charles Overberger Award.