Dendritic architecture enhances the structural stability of self-assembled dendron micelles in the presence of serum proteins

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Dendrimers and linear-block copolymer (LBC)-based micelles are two types of nanocarriers that have been largely studied. The multivalent interactions enabled by the hyperbranched dendrimers and the modularity, along with high drug loading capability, of the LBC-based micelles are key features of each platform. Our group previously developed PEGylated dendron-based copolymers (PDC), which incorporated these key characteristics into a single system. The PDCs self-assemble into dendron micelles (DMs) with high thermodynamic stability as measured by low critical micelle concentrations (in an order of 10^{-9} M), demonstrating their potential as efficient nanocarriers. In addition, because the dendritic PEG chains can form a dense inert layer on the surface of DMs, this hybrid design is expected to minimize non-specific interactions between the nanocarriers and biological components. These non-specific interactions are known to negatively affect the ability of nanocarriers to deliver their cargos. For instance, non-specific micelle-serum protein interactions can cause micelle disintegrations and subsequently a premature release of loaded drugs. In this study, we hypothesized that DMs are more stable than LBC-based micelles (LMs) in the presence of serum proteins because their dense PEG outer layers can lower micelle-serum protein interactions. To test our hypothesis, we compared the integrities of DMs and LMs in the presence of serum proteins using a FRET method. Our results showed that DMs have superior stability over their LM counterparts. The half-life of DMs was approximately 2 times longer than that of the LMs in a 50% fetal bovine serum solution. These results indicate that the dendritic PEG outer layers reduce the binding and/or penetration of serum proteins into the micelles. While additional studies are required to fully understand the effect of the dendritic PEG layers on micelle-serum protein interactions and corresponding biological consequences, our results support that DMs have great potential as a novel drug delivery platform.