Synopsis of Original Research Paper

Design of Polymeric Micelles for Novel Carriers in Drug Delivery Systems

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Supramolecular structures, such as lipoproteins and viruses, occur *in vivo* as natural carner systems. In mimicking such vehicles, we have been studying micelle-forming polymeric drugs as a novel type of drug carrier. Polymeric micelles based on AB block copolymers of polyethylene oxide (PEO) and poly-β-benzyl-L-aspartate (PBLA) were prepared. Such polymeric micelles are expected to physically incorporate drugs. AB block copolymers were synthesized using amino-terminated PEO to initiate the polymerization of β-benzyl-L-aspartate-N-carboxyanhydride (BLANCA). The composition and molecular weights of the block copolymers were established by ^{1}H-NMR. Micellar solutions of PEO-PBLA block copolymer were characterized by dynamic light scattering. Fluorescence probe techniques were used to study the polymeric micelles. From changes in the fluorescent intensity and shifts in the excitation spectrum of pyrene upon micellization, critical micelle concentrations (CMC) of PEO-PBLA block copolymers were obtained. The vibrational structure of monomer pyrene fluorescence was altered in PEO-PBLA micellar solutions consistent with low polarity within the PBLA core. In PEO-PBLA micellar solutions, 1,3- (1,1'dipyrenyl)-propane intramolecular eximer emission, relative to monomer emission was very small ; this indicated very low mobility of PBLA segments within the micellar core. Further evidence for the limited motion of PBLA segments in the micellar core was obtained by ^{1}H NMR. This limited motion of the PBLA segments in the micellar core is in contrast to low molecular weight surfactants which commonly show a higher degree of motion within their cores. The ability of PEO-PBLA micelles to solubilize hydrophobic molecules was studies by UV and fluorescence spectroscopy using pyrene. Enhanced solubility of pyrene was determined with increasing concentrations of PEO-PBLA. Then, potential of entrapping Adriamycin (ADR) within micelles based on PEO-PBLA block copolymers was investigated. The loading process involved bringing ADR and PEO-PBLA into an aqueous milieu from N,N-dimethylformamide (DMF) through a simple dialysis procedure. Evidence for the physical entrapment of ADR within the micelles was derived from fluorescence spectroscopy, where considerable quenching of fluorescence was observed for ADR associated with the micelles. In addition, quenching experiments, using a water-soluble quencher (iodide (I^-)), showed that the fluorescence of ADR, present in micellar solutions, was largely uneffected by I^-, whereas the fluorescence of free ADR was readily quenched. As a result of the entrapment of ADR within the polymeric micelles, the drug slightly binds serum albumin as evidenced by gel permeation chromatography (GPC). In contrast, free ADR readily binds serum albumin in aqueous solutions. The finding suggests that ADR is stably entrapped within PEO-PBLA micelles. The ADR imbued within the micelles is expected to display markedly dissimilar pharmacokinetics relative to free ADR.