

“One-Pot” Synthesis of Biocompatible Shell Cross-Linked Micelles via ATRP in 2-Propanol/Water

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We report the one-pot synthesis of shell cross-linked (SCL) micelles based on a novel ABC triblock copolymer using Atom Transfer Radical Polymerisation (ATRP) in a 9:1 2-propanol/water mixture at 40°C. The triblock copolymer was prepared using a poly(ethylene oxide) macro-initiator (PEO), which was used to polymerize first 2-(dimethylamino)ethyl methacrylate (DMA), followed by a biocompatible 2-(methacryloyloxy)ethyl phosphorylcholine (MPC) monomer. The resulting PEO₁₁₃-PDMA₃₀-PMPC₅₀ underwent spontaneous self-assembly to form PMPC-core micelles *in situ* due to the well known co-nonsolvency behaviour of PMPC chains in alcohol/water mixtures. In the same reaction solution, cross-linking of the PDMA chains in the inner shells was conducted using 1,2-bis(2-iodoethoxy)ethane for five days at 20°C, followed by purification using silica chromatography. The resulting SCL micelles were then dialyzed against water. This solvent switch causes SCL micelle swelling due to solvation of the PMPC chains, which no longer reside within the micelle cores but instead join the hydrophilic PEO chains in the micelle coronas. The final SCL micelle diameter depended on the target degree of cross-linking (20-100 %) and the PMPC block length, as judged by dynamic light scattering and atomic force microscopy (AFM). AFM imaging of the SCL micelles prepared at a target degree of cross-linking of 30 % provided evidence for their ‘nanocage’ structure when absorbed onto mica from water.