Novel pH or Thermosensitive Block Copolymers for Triggered Drug-Delivery Systems

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Over the last decade, polymer micelles and nanoparticles have attracted an increasing interest as efficient drug delivery systems. Polymer micelles from amphiphilic block copolymers are supramolecular core-shell type assemblies of some tens of nanometers in diameter. They are highly stable in aqueous solution because of their low intrinsic critical micelle concentration, which prevents their dissociation upon dilution in the blood stream after intravenous injection. The combination of poly(ethylene oxide) (PEO) with hydrophobic aliphatic polyesters, such as poly(ε-caprolactone) (PCL) or polylactide (PLA), allows to prepare stealthy drug nanocarriers (thanks to PEO), which are biodegradable and biocompatible and capable of encapsulating a hydrophobic drug (due to the aliphatic polyester). In this field, the inclusion of an additional pH-responsive block in the supramolecular assembly is a promising strategy to improve the targeting of tumor tissues by taking advantage of the lower pH at the vicinity of tumor cells. A variety of novel amphiphilic and pH-sensitive copolymers have been synthesized and tested as building blocks for the design of smart nanocarriers able to expose selectively the targeting unit at the vicinity of tumor. Various macromolecular architectures combining PEO, PCL and P2VP have been accordingly synthesized such as linear and star shape di- and triblock copolymers. Their (co)-micellization has been studied in terms of size, particle shape (DLS, TEM) and stealth behavior. Besides, thermo-responsive copolymers combining PEO, polyacrylic acid and poly-N-isopropyl-acrylamide have been synthesized and found efficient in stabilizing stealthy magnetic nanoparticles promising for thermally triggered release of drugs during hyperthermia.