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## ACCEPTED MANUSCRIPT

Reverse micelles prepared from amphiphilic polylactide-*b*-poly(ethylene glycol) block copolymers for controlled release of hydrophilic drugs

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## **Graphical abstract**

PLA-b-PEG block copolymers were dissolved in a toluene-ethanol mixture, followed by addition of distilled water or heparin solution to yield blank (A) or heparin-loaded reverse micelles (B).

#### **Abstract**

This work aims to evaluate the potential of reverse micelles prepared from amphiphilic polylactide-b-poly(ethylene glycol) (PLA-b-PEG) block copolymers for controlled release of hydrophilic drugs. Different PLA-b-PEG diblock and triblock copolymers were synthesized by ring-opening polymerization of D- or L-lactide in the presence of a PEG macroinitiator. Reverse micelles were prepared by self-assembly of copolymers in a solvent/co-solvent/water system. Toluene was used as solvent, and ethanol as cosolvent to solubilize appropriate amount of water. The resulting nano-sized reverse micelles were able to encapsulate heparin in the hydrophilic core. Dynamic light scattering (DLS) and transmission electron microscopy (TEM) were used to determine the size and morphology of reverse micelles. The results show that reverse micelles are spherical in shape with sizes below 100 nm. Drug loaded reverse micelles were embedded in biocompatible membranes by mixing with 10% PLA solution in toluene with 1:3 volume ratio. In vitro release studies were realized in phosphate buffer saline (PBS) at 37°C. Heparin was almost totally released within 24h. Triblock copolymer reverse micelles exhibited faster drug release than diblock ones probably due to the more compact micelle structure of the latter. Therefore, PLA-b-PEG reverse micelles could be promising for applications as carrier of hydrophilic drugs when embedded in biocompatible membranes.

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