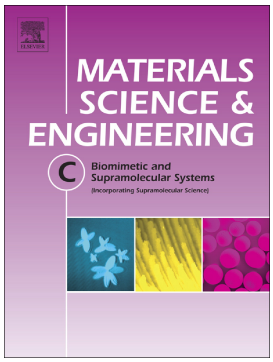

Y-shaped copolymers of poly(ethylene glycol)-poly(ϵ-caprolactone) with ketal bond as the branchpoint for drug delivery

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Y-shaped Copolymers of Poly(ethylene glycol)-Poly(ε-caprolactone) with Ketal Bond as the Branchpoint for drug delivery

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Abstract

In this study, a Y-shaped amphiphilic block copolymer consisting of hydrophilic poly(ethylene glycol) (mPEG) and two poly(ε-caprolactone) (PCL) as the hydrophobic arms with a ketal linker was synthesized (mPEG-Ketal-$(PCL)_2$). The structure of the copolymer with different compositions was characterized by ^1H NMR, gel permeation chromatography (GPC) and differential scanning calorimetry (DSC). The amphiphilic property endows the copolymer with the ability to be self-assembled into micelles for encapsulating anticancer drug doxorubicin (DOX), and the effect of copolymer with different PCL length on drug loading properties were tested. The morphology, size, pH responsiveness, drug release profile and *in vitro* anticancer activity of the DOX loaded micelles were also studied. *In vitro* drug release studies showed that over 50% of the DOX was released at pH5.0 in 24 h because of hydrolysis of ketal linker in the copolymers. The confocal laser microscopy and flow cytometry experiments showed that the DOX-loaded micelles could be effectively internalized by Hela cells, the ketal bond in the backbone was broken in acid endo/lysosomal compartments and triggered the fast release of DOX. The *in vitro* antitumor efficacy of the DOX loaded mPEG-Ketal-$(PCL)_2$ micelles was better than that of non-pH sensitive ones. *In vivo* studies showed that the mPEG-Ketal-$(PCL)_2$ micelles enhanced the DOX blood circulation time and had good tumor-targeting efficiency.

Key words: pH-sensitive; Y-shaped copolymer; Polymeric micelles; Drug delivery

1. Introduction

Polymeric micelles, self-assembled from amphiphilic block copolymers, have received significant attention as anticancer drug carriers [1-8]. Taking advantage of the high permeability and retention effect (EPR) of tumor tissue, the passive targeting drug delivery would be achieved, which enhanced drug accumulation in tumor and increased therapeutic efficiencies. To date, most widely studied amphiphilic polymers for drug delivery including diblock copolymers and triblock linear copolymers [9]. Compared with linear copolymers, nonlinear

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