Polymeric nanoparticles and their biomedical applications are rapidly heading to the forefront of drug delivery and diagnostic. Herein, it is reported the self-assembly of PEO outer-shell block copolymer micelles resistant to non-specific protein adsorption and possessing a pH-responsive PDPA inner core able to carry poorly water-soluble bioactive drugs.

Monodisperse block copolymer micelles were produced from PEO\(_{113}\)-b-PG\(_{2MA}\)\(_{30}\)-b-PDPA\(_{50}\) in phosphate buffer saline (PBS) solution. The micellar size (\(R_H = 21\) nm) and micellar molecular weight (\(M_w (\text{micelles}) > 10^6\) kDa) were found to be in the range to avoid renal clearance and still below the cut-off size of the leaky pathological vasculature (\(D_H < 200\) nm) making them candidates for the use in cancer therapy based on the EPR effect [1]. These micelles were placed in contact with in 10% \(v/v\) human plasma dissolved in PBS. The dynamic light scattering experiments revealed that the micellar aggregates are especially stable for up to 24 h in such a condition.

The anticancer drug paclitaxel could be loaded at ~ 7% \(w_{\text{drug}}/w_{\text{polymer}}\) into the PDPA core via physical entrapment without destabilization of the micellar system. The encapsulation efficiency was ~ 70% and the drug release profiles at pH 7.4 and 5.0 are shown in Figure 1.

Figure 1. Drug release profiles from PTX-loaded PEO\(_{113}\)-b-PG\(_{2MA}\)\(_{30}\)-b-PDPA\(_{50}\) micelles at pH 5.0 (○) and 7.4 (□) (left); molecular structure of the block copolymer sample and pH-behavior of the self-assembly block copolymer micelles (right).

The paclitaxel complete release from the micelles takes about 120 h at pH 7.4 whilst only 18 h are required to achieve the same at pH 5.0. These results suggest that at pH < \(pK_{a(PDPA)}\) (\(pK_{a(PDPA)} = 6.8\)) the block copolymer micelles are physically destabilized (pH-induced dissociation) thus accelerating the release of the anticancer drug selectively at tumor sites since the extracellular pH in most tumours is lower (pH 5.7-7.2) than in normal tissues [2].


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