indeed explains the very common problems of low PTX loading contents and burst release. In the case of PCL–PEG/SN38, the two boundaries can be tuned by mixing organic solvents to get two curves closer and even intersected, at which the micellization and drug precipitation occurred simultaneously, leading to efficient drug encapsulation. In addition, the micellization boundaries of other amphiphilic copolymers were investigated [1]. This work may provide guidance for loading hydrophobic drugs into micelles with suppressed burst release.

Keywords: amphiphilic block copolymers, hydrophobic drugs, co-precipitation, drug loading efficiency

Reference

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PEG-polypeptide conjugated with LHRH as an efficient vehicle for targeted delivery of doxorubicin to breast cancer

Shixian Lv[a,b], Zhaohui Tang[a], Mingqiang Li[a,b], Wantong Song[a], Xuesi Chen[a,*]
[a]*Key Laboratory of Polymer Ecomaterials, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, China*
[b]*University of Chinese Academy of Sciences, Beijing 100039, China*
*Corresponding author.
E-mail addresses: lvshixian@ciac.ac.cn (S. Lv), xschen@ciac.ac.cn (X. Chen).

Nano-scaled drug delivery systems have been attracting great attention in cancer therapy due to their great advantages over conventional chemotherapeutic agents [1]. Among these nanomedicines, tumor-targeted nanoparticles modified with active targeting ligands show better antitumor effect compared to the non-targeted nanoparticles owing to their increased tumor accumulation. Because of the overexpression of the luteinizing hormone-releasing hormone (LHRH) receptors in a lot of tumors, the LHRH peptide has been used as an ideal targeting ligand for constructing nanoparticles for targeted drug delivery. To develop a simple LHRH targeted drug delivery system, an amphiphilic methoxy poly(ethylene glycol)-*b*-poly(l-glutamic acid)-*b*-poly(l-phenylalanine) (mPEG-*b*-P(Glu)-*b*-P(Phe)) tri-block copolymer was synthesized and utilized (Fig. 1). PEG provided prolonged blood circulation, middle PLG domain was designed for doxorubicin (DOX) loading through electrostatic interactions and LHRH modification through EDC/NHS method, and P(Phe) could facilitate the self-assembly and enhance the stability of the nanoparticles through hydrophobic/aromatic interactions. ^{1}H NMR analysis showed that the LHRH moieties conjugated to each mPEG-*b*-P(Glu)-*b*-P(Phe) copolymer chain were approximately 1.2. DOX was successfully loaded into the targeted nanoparticles by simple mixing of free DOX and the copolymers in the aqueous solution with a DOX loading content of 9.94%. *In vitro* MTT assays showed that the DOX-loaded targeted nanoparticles (DOX–TNPs) exhibited higher cell proliferation inhibition in MCF-7 human breast cancer cells compared to the DOX-loaded non-targeted nanoparticles (DOX–NPs) and free DOX. The IC_{50} value of DOX–TNPs in MCF-7 cells following 24 h incubation was 1.8 or 2.2-fold less than that incubated with DOX–NPs or free DOX, respectively. The *in vivo* studies on MCF-7 tumor bearing nude mice demonstrated that the tumor volume of DOX–TNPs treated group was 2.7 and 1.9 fold smaller than that treated with free DOX and DOX–NPs at the same dose, respectively. While, body weight loss of DOX–TNPs treated group was lower than these control groups, which might be attributed to their enhanced drug accumulation by active targeted delivery. With convenient fabrication and versatile functions, this delivery system is promising for targeted cancer therapy in the future.

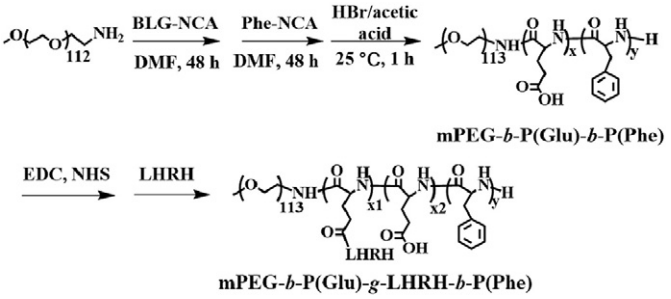

Fig. 1. Synthesis pathway for mPEG-*b*-P(Glu)-*b*-P(Phe) and LHRH modified mPEG-*b*-P(Glu)-*g*-LHRH-*b*-P(Phe) copolymers.

Keywords: polypeptide, LHRH, drug delivery, chemotherapy, doxorubicin

Reference

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pH and reduction-sensitive disulfide cross-linked polyurethane micelles for bio-triggered anti-tumor drug delivery

Shuangjiang Yu, Chaoliang He*, Qiang Lv, Hui Zheng, Zhaohui Tang, Huayu Tian, Xuesi Chen
Key Laboratory of Polymer Ecomaterials, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, China
*Corresponding author.
E-mail addresses: yushuangjiang@ciac.ac.cn (S. Yu), clhe@ciac.ac.cn (C. He).

Polymeric micelle-based nano-carriers have exhibited a great potential in cancer therapy. Nevertheless, how to enhance the micellar stability and reduce the burst release is a key issue for improving the drug delivery efficiency *in vivo*. In order to enhance the stability of micellar nano-vehicles, various strategies by reversibly cross-linking the core or shell of the micelles with stimuli-cleavable linkages have been developed [1,2]. In our previous work, a disulfide cross-linked polyurethane micelle was developed. The doxorubicin (DOX)-loaded disulfide cross-linked micelles exhibited reduced cytotoxicity *in vitro* but displayed enhanced tumor suppression efficacy *in vivo*, likely due to the increased tumor accumulation of the drug-loaded cross-linked micelles [3].

Herein, a pH and reduction dual responsive cross-linked polyurethane micelle (PRS-CLPUM) was fabricated for multiple stimuli-responsive drug delivery. The micelles were composed of PEG chains as a hydrophilic shell, and piperidine and intermolecular disulfide linkages in the polyurethane blocks were responsible for the pH- and reduction-sensitivity (Fig. 1). With DOX as a model drug, the drug-loaded PRS-CLPUMs exhibited superior stability under extracellular conditions, whereas DOX release was triggered in response to acidic conditions or an intracellular reduction agent *in vitro*. Confocal laser scanning microscopy and flow cytometric analysis indicated that the intracellular drug release of the DOX-loaded PRS-CLPUMs was