were measured using HPLC. The loading efficiency of 17-AAG-loaded nanofibers was slightly above 50% which resulted from loss of 17-AAG and polymers during electrospinning. The controlled release of 17AAG from nanofibers lasted for more than 1 month. Cumulative amounts of released 17AAG after 1 month were nearly 40% in a single nozzle electrospun PLGA nanofiber (Fig. 1).

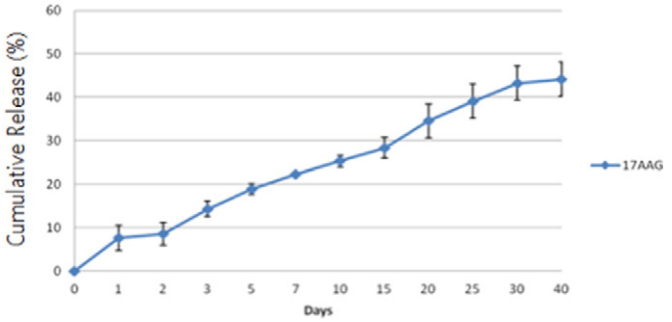

Fig. 1. *In vitro* release profiles of 17-AAG from PLGA nanofibers.

Keywords: PCL/PLGA nanofibers, 17-AAG, electrospinning, single nozzle, dual nozzle

References

[1] E.D. Boland, G.E. Wnek, D.G. Simpson, K.J. Pawlowski, G.L. Bowlin, Tailoring tissue engineering scaffolds using electrostatic processing techniques: a study of poly(glycolic acid) electrospinning, J. Macromol. Sci. Pure 38 (2001) 1231–1243.
[2] X. Huang, C.S. Brazel, On the importance and mechanisms of burst release in matrix-controlled drug delivery systems, J. Control. Release 73 (2001) 121–136.

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Enhanced solubility, stability, and antitumor activity of the VESylated gemcitabine prodrug by co-assembly with TPGS

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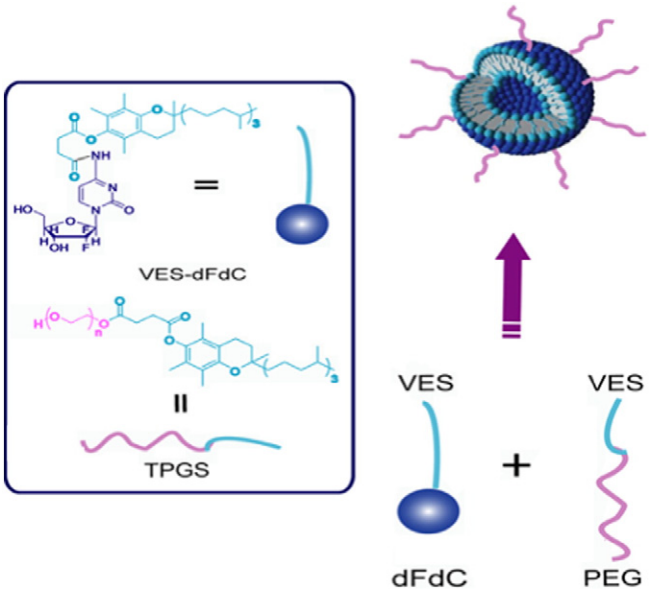
A VESylated gemcitabine (VES-dFdC) prodrug, which can be self-assembled into nanoparticles in water, is described. VES-dFdC was designed to improve the efficacy of gemcitabine and to overcome its limitations such as short half-life, systemic toxicity, and drug resistance [1]. However, VES-dFdC based nanoparticles were not sufficiently stable, and prone to precipitate in PBS or serum. Moreover, it is challenging to make a concentrated suspension of VES-dFdC nanoparticles in water, which renders it not suitable for i.v. injection. Here, TPGS, which has the same VES moiety as the VES-dFdC prodrug, was selected to co-assembly with VES-dFdC prodrug to improve the stability and concentration of the nanoparticles in PBS or serum (Scheme 1). Stable colloidal suspensions were obtained without aggregation in PBS at VES-dFdC/TPGS molar ratios from 1/0.5 to 1/1.5. The concentration of VES-dFdC prodrug increased to 18 mg/mL with the VES-dFdC/TPGS ratio at 1/1.5. All the nanoparticles showed neutral surface charges from −0.156 to +0.388 mV. With increasing amount of TPGS, the sizes of co-assemblies increased initially and then decreased, as determined by the dynamic light scattering (DLS). Interestingly, TEM revealed that, with increasing amount of TPGS, the morphology of nanoparticles changed from nano-sized capsule to micelle. The anticancer efficacy of these stable colloidal suspensions at a VES-dFdC/TPGS molar ratio of 1/1 was evaluated in nude mice with pre-established BxPC-3 tumors. The results showed that compared with native gemcitabine, VES-dFdC/TPGS nanoparticles resulted in enhanced antitumor activity.



Scheme 1. Illustration of co-assemblies of VES-dFdC prodrug and TPGS.

Keywords: Co-assembly, TPGS, VES-dFdC, nanocapsules, micelle

Acknowledgments

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Reference

[1] J. Zhang, L. Miao, S. Guo, Y. Zhang, L. Zhang, S. Andrew, Y. William, L. Huang, Synergistic anti-tumor effects of combined gemcitabine and cisplatin nanoparticles in a stroma-rich bladder carcinoma model, J. Control. Release 182 (2014) 90–96.

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Cisplatin complexes stabilized poly(glutamic acid) for controlled delivery of doxorubicin

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Doxorubicin hydrochloride (DOX · HCl), an anthracycline antibiotic, is used in the first line treatment for a wide range of cancers. In order to reduce the side effects of free DOX · HCl, many nanocarriers have been developed. We have already developed a green and

convenient method for the encapsulation of DOX · HCl through the electrostatic interaction with methoxy poly(ethylene glycol)-*block*-poly(l-glutamic acid) (mPEG-*b*-PLG) in aqueous solution [1]. However, the DOX · HCl-loaded mPEG-*b*-PLG micelles [DOX(L)] are unstable in blood circulation, which results in a fast release of free DOX · HCl after administration. Therefore the blood circulation time of the DOX(L) is comparable to that of free DOX · HCl.

Cisplatin (CDDP) is another commonly used anticancer agent for a variety of cancers. CDDP can be conjugated with carbonyl groups of poly(l-glutamic acid) chains through coordination bond that is much more stable than electrostatic interaction. In addition, considering that the combination of CDDP and DOX · HCl has enhanced therapeutic efficacy as compared with CDDP or DOX · HCl alone. Here CDDP was used to stabilize DOX · HCl-loaded mPEG-*b*-PLG micelles.

First, mPEG-*b*-PLG and DOX · HCl were self-assembled into spherical DOX · HCl-loaded mPEG-*b*-PLG micelles in aqueous solution. Then, CDDP was added in to stablize the micelles and form CDDP-complexed and DOX · HCl-loaded mPEG-*b*-PLG nanoparticles (CDDP-DOX · HCl-NPs) (Fig. 1). The loading efficiency of both two drugs was almost 100%, and the drug loading content (DLC) of DOX was 11.8%, the DLC of CDDP was 15.8%. *In vitro* experiment showed that the release rate of DOX · HCl and CDDP from the CDDP-DOX · HCl-NPs was increased with the decrease of environmental pH. Pharmacokinetics study in rats showed that CDDP complexation could significantly prolong the blood circulation time of DOX · HCl-loaded mPEG-*b*-PLG micelles. The CDDP-DOX · HCl-NPs exhibited superior antitumor activity and reduced systemic toxicity as compared to free drugs in *in vivo* experiments on Balb/C nude mice bearing MCF-7 tumor with the tumor suppression rate of 87%, indicating that the CDDP-complexed-DOX · HCl-loaded mPEG-*b*-PLG nanoparticles have great potential for cancer chemotherapy.

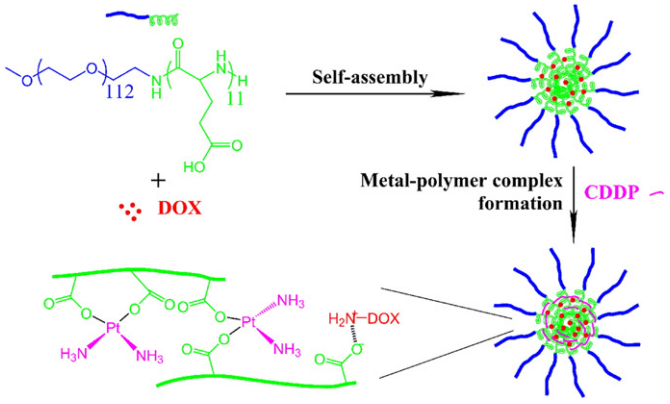

Fig. 1. Schematic illustration of CDDP-complexed-DOX · HCl-loaded mPEG-*b*-PLG nanoparticles.

Keywords: poly(l-glutamic acid), doxorubicin, cisplatin, drug delivery, nanoparticles

Reference

[1] M.Q. Li, W.T. Song, Z.H. Tang, S.X. Lv, L. Lin, H. Sun, Q.S. Li, Y. Yang, H. Hong, X.S. Chen, Nanoscaled poly(l-glutamic acid)/doxorubicin-amphiphile complex as pH-responsive drug delivery system for effective treatment of non small cell lung cancer, ACS Appl. Mater. Interfaces 5 (2013) 1781–1792.

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A dual-targeting strategy to enhance photodynamic efficacy using a pH-responsive polymeric micelles

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A dual-targeting (cellular and subcellular targeting) strategy was designed to enhance the efficacy of a porphyrin-based photodynamic therapy (PDT) system by using a folic acid (FA) modified and pH-responsive polymeric micelle (Fig. 1a). For this system, a cationic porphyrin was used as a mitochondria-specific photosensitizer, and a crosslinked tri-block copolymer micelle as the carrier [1,2]. The copolymer carrier exhibits multiple purposes: (1) modified by polyethylene glycol (PEG) chains, the micelle displays enhanced water dispersibility and biocompatibility; (2) with a targeting ligand (FA) on its surface, the system can specifically target the folate receptor (FR)-positive cells, and cause much higher cytotoxicity towards these cells; (3) with a unique pH-sensitive structure, the carrier can dissociate under lysosomal pH as a result of protonation of tertiary amines and disruption of the crosslinking bonds, leading to the release of the mitochondria-targeted photosensitizer (Fig. 1b). Our results showed that the singlet oxygen treatment led to the loss of mitochondrial membrane potential and the subsequent mitochondria damage and cell apoptosis; and the micelle system with FA on its surface can damage the mitochondrial and kill the cell more efficiently. This dual-targeting and pH-responsive drug release strategy may provide a more efficient PDT action for future anticancer applications.

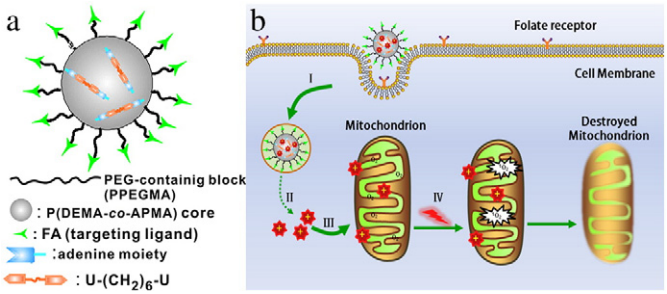

Fig. 1. (a) Structures of the polymeric micelle. (b) Schematic illustration of the effect of the dual-targeting nanosystem.

Keywords: dual-targeting, pH-responsive, photodynamic therapy, mitochondrial apoptosis

References

[1] S. Fulda, L. Galluzzi, G. Kroemer, Targeting mitochondria for cancer therapy, Nat. Rev. Drug Discov. 9 (2010) 447–464.
[2] J. Fan, F. Zeng, S. Wu, X. Wang, Polymer micelle with pH-triggered hydrophobic-hydrophilic transition and de-cross-linking process in the core and its application for targeted anticancer drug delivery, Biomacromolecules 13 (2012) 4126–4137.

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