**A novel micellar-like polymeric nanoparticle for paclitaxel delivery: *in vitro* and *in vivo* evaluation**

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**Introduction:** Paclitaxel (PTX) is one of the most effective chemotherapeutic drugs for the treatment of a variety of cancers. However, it is associated with serious side effects caused by PTX itself and the Cremophor EL emulsifier. Micellar-like polymeric nanoparticles (NPs) have been promising carriers for drugs with poor water solubility because their core-shell structure can readily incorporate lipophilic drugs into their lyophobic polymeric cores, while the hydrophilic shell can provide stabilization for the NPs without the need for additional stabilizer and prolong the circulation of the NPs in blood. The aim of this study was to develop micellar-like polymeric NPs for PTX from PCL-PEG-PCL (PCEC) triblock copolymer, intended to be intravenously administered, able to improve the therapeutic index of the drug and devoid of the adverse effects of Cremophor® EL.

**Methods:** PTX-loaded micellar-like polymeric NPs were prepared by thin film method [1].

**Results:** The prepared PTX-loaded polymeric NPs (with drug loading content of 28.98%) exhibited homogeneous spherical shapes with an average diameter of around 100 nm (Fig. 1A and B). It is clearly seen from the TEM image that the NPs possessed a core-shell morphology which is characterized by a hydrophobic core surrounded by a hydrophilic PEG corona. The *in vitro* release showed a biphasic pattern: a fast release rate in the first 6 days followed by a slow uniform release afterwards for about 20 days in 10 mM PBS containing 1M sodium salicylate (Fig. 1C). DSC thermograms indicated that PTX formulated in the NPs existed as an amorphous state or a solid solution in the polymeric matrix (Fig.1D). Figure 2 indicated that drug-free NPs did not exhibit detectable cytotoxicity to the HepG2 cells during test period. The cytotoxicities of PTX and PTX-loaded polymeric NPs exhibited both time and concentration dependent. When the PTX concentration was higher than 2.5μg·mL$^{-1}$, cytotoxicities of PTX-loaded polymeric NPs were significantly lower than that free PTX formulation. This result indicated that NPs formulation greatly reduced the cytotoxicity of the Cremophor EL/ethanol mixture in the free PTX formulation in the cell culture system. Figure 3 showed the in vivo anti-tumor efficacy of PTX-loaded polymeric NPs and Taxol® in EMT6 breast tumor-bearing mice. Taxol® and PTX-loaded polymeric NPs with drug loading content of 28 wt. % were given by intravenous injection each second day (five times) at a dose of 20 mg/kg/day for 10 days. Compared with saline control group, the group treated with PTX-loaded NPs inhibited tumor growth significantly (Fig.3A). At the end of the experiment, the group treated with PTX-loaded NPs showed better antitumor activity than the group treated with Taxol®, with tumor inhibition rates of 85.79% and 63.37%, respectively. To mice treated with Taxol®, a large decrease in body weight was observed. While to the mice treated with PTX-loaded NPs, the decrease in body weight was limited to 5% of the initial weight (Fig.3B).

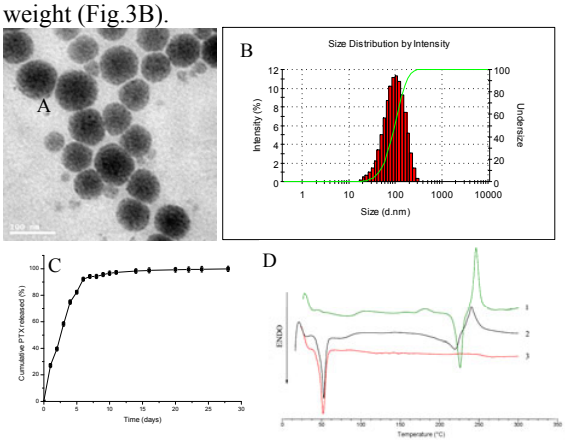


Fig. 1 Characterization of PTX-loaded micellar-like polymeric NPs: (A) TEM image. (B) Size and size distribution. (C) *In vitro* release profiles (n=3). (D) DSC thermograms of (1) pure PTX; (2) physical mixture of PTX and blank NPs; (3) PTX-loaded NPs.

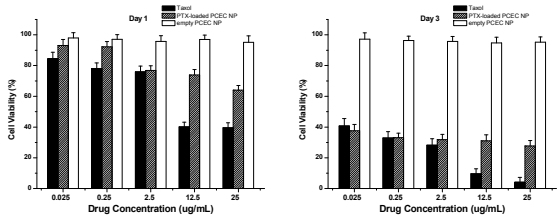


Fig. 2 Viability of HepG2 liver cancer cells cultured with PTX-loaded polymeric NPs and Taxol® at the same PTX dose and empty NPs with the same amount of NPs (n=6).

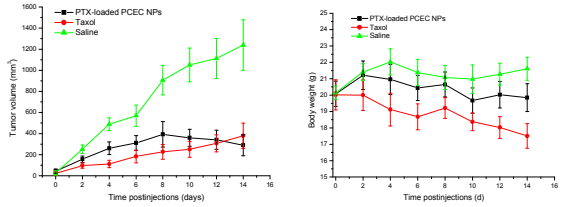


Fig. 3 *In vivo* anti-tumor efficacy (A) and body weight changes (B) after intravenous treatment of PTX-loaded polymeric NPs and Taxol® on EMT6 breast tumor bearing BALB/c mice. (n=10).

**Conclusions:** We have successfully developed micellar-like polymeric NPs loaded with PTX based on PCL-PEG-PCL copolymers using thin film method. *In vitro* and *in vivo* studies indicated that the PTX-loaded polymeric NPs may be considered as an effective anticancer drug delivery system for cancer chemotherapy.

**References:**

[1] Wang Y.Int J Pharm. 2007; 337:63-73