Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
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The *in vivo* antitumor activity of LHRH targeted methotrexate-human serum albumin nanoparticles in 4T1 tumor-bearing Balb/c mice

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Background and Aims: The use of targeted drug delivery systems is a growing trend in cancer treatment to decrease the adverse effect of anti-cancer drugs.
Methods: In this experiment, we sought to conjugate methotrexate-human serum albumin nanoparticles (MTX-HSA NPs) with luteinizing-hormone releasing hormone (LHRH). We carried out the conjugation of LHRH molecules with MTX-HSA NPs via EDC (1-ethyl-3-(diaminopropyl) carbodiimde HCl) cross-linker. The LHRH was intended to target LHRH receptors overexpressed on several types of tumors such as breast cancer. The expression of LHRH receptors on the 4T1 breast cancer cells was confirmed by FITC conjugated LHRH receptor antibody using fluorescence microscopy. Female Balb/c mice bearing 4T1 breast cancer were treated with a single i.v. injection of free MTX, non-targeted MTX-HSA NPs and LHRH targeted MTX-HSA NPs.
Results: The results showed that LHRH targeted MTX-HSA nanoparticles had stronger anti-tumor activity in vivo. By 7 days after treatment, average tumor volume in the LHRH targeted MTX-HSA NPs treated group decreased to 8.67% of the initial tumor volume when the number of attached LHRH molecules on MTX-HSA NPs was the highest, while the average tumor volume in non-targeted MTX-HSA NPs treated mice grew rapidly and reached 250.7% of the initial tumor volume 7 days treatment.
Conclusions: LHRH targeted MTX-HSA NPs could significantly extend the survival time of tumor bearing mice compared with the non-targeted MTX-HSA NPs and free MTX formulations. Mice treated with LHRH targeted MTX-HSA NPs showed slight body weight loss, whereas non-targeted MTX-HSA NPs treatment at the same dose caused a body weight loss of 20–30%.

Keywords: Targeted drug delivery system; LHRH; Methotrexate; Albumin