PDA Journal
of Pharmaceutical Science and Technology

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PDA J Pharm Sci and Tech **2013**, *67* 135-145
Access the most recent version at doi:10.5731/pdajpst.2013.00908

Sustained Delivery of Amphotericin B and Vancomycin Hydrochloride by an Injectable Thermogelling Tri-Block Copolymer

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ABSTRACT: Because traditional drug delivery poses many disadvantages such as poor compliance of patients and a drug plasma level variation, novel drug delivery systems containing controlled release drug vehicles become attractive. In this study, a kind of tri-block copolymer consisting of polycaprolactone (PCL) and poly(ethylene glycol) (PEG), PCL-PEG-PCL, were synthesized by a rapid microwave-assisted and a conventional synthesis method to form an in situ gelling system that provides a controlled release of drugs over a long period of time. Copolymer characterization was performed using a gel permeation chromatography, the ^{1}H-NMR, and a phase transition behavior evaluation. Vancomycin hydrochloride and amphotericin B were used as drug models here. This study confirmed that the synthesis of the copolymer using microwave irradiation was the most effective method to prepare this smart copolymer. Results also demonstrated the better performance of the microwave-synthesized copolymer regarding its phase behavior. It was shown that gelatin temperatures were also affected by the hydrophilicity of the drug model, the copolymer concentration, and the media. It was indicated that the hydrogels could sustain the delivery of model drugs for about 17 to 20 days. As the drugs used in this study were both large molecules and the main release mechanism was copolymer bulk erosion rather than simple diffusion, the effect of drug and copolymer concentration on the drug release profile was not so significant.

KEYWORDS: Tri-block copolymer, PCL-PEG-PCL, Vancomycin, Amphotericin B, In situ forming gel, Drug release, Microwave

LAY ABSTRACT: Different studies have been carried out to improve drug delivery systems. Smart drug vehicles such as thermoresponsive and in situ forming hydrogels made of tri-block copolymers are promising systems in this field. Thermoresponsive hydrogels can release loaded molecules in response to the changing temperature. In situ forming hydrogels are the kind of thermoresponsive materials that are injectable fluid (sol) at room temperature and gel at body temperature. Pharmaceuticals release gradually from the gel over long periods of time. Here we investigated the in situ forming hydrogel based on poly(caprolactone)–poly(ethylene glycol)–poly(caprolactone) as a drug delivery system. Vancomycin hydrochloride and amphotericin B were used in this study as a model. The results indicated that this system can control release pattern of drug perfectly for approximately 20 days.

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