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Microparticles produced by the hydrogel template method for sustained drug delivery

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ABSTRACT

Polymeric microparticles have been used widely for sustained drug delivery. Current methods of microparticle production can be improved by making homogeneous particles in size and shape, increasing the drug loading, and controlling the initial burst release. In the current study, the hydrogel template method was used to produce homogeneous poly(lactide-co-glycolide) (PLGA) microparticles and to examine formulation and process-related parameters. Poly(vinyl alcohol) (PVA) was used to make hydrogel templates. The parameters examined include PVA molecular weight, type of PLGA (as characterized by lactide content, inherent viscosity), polymer concentration, drug concentration and composition of solvent system. Three model compounds studied were risperidone, methylprednisolone acetate and paclitaxel. The ability of the hydrogel template method to produce microparticles with good conformity to template was dependent on molecular weight of PVA and viscosity of the PLGA solution. Drug loading and encapsulation efficiency were found to be influenced by PLGA lactide content, polymer concentration and composition of the solvent system. The drug loading and encapsulation efficiency were 28.7% and 82% for risperidone, 31.5% and 90% for methylprednisolone acetate, and 32.2% and 92% for paclitaxel, respectively. For all three drugs, release was sustained for weeks, and the *in vitro* release profile of risperidone was comparable to that of microparticles prepared using the conventional emulsion method. The hydrogel template method provides a new approach of manipulating microparticles.

1. Introduction

Polymeric microparticle drug delivery systems have been widely explored for controlled delivery of active pharmaceutical ingredients. Microparticles provide several advantages as drug delivery vehicles, such as protection of encapsulated drug from unfavorable environmental conditions and ability to control drug release profile for a specified period of time (Tran et al., 2011a). In particular, the potential to control drug release profile over an extended period of time is one of the most desirable attributes (Wei et al., 2012). Suitable drug candidates that may benefit greatly from such controlled drug delivery systems based on polymeric microparticles include those that have a broad therapeutic window, require a low daily dose and are used for the long-term treatment of disease.

Poly(lactide-co-glycolide) (PLGA) is probably the most extensively used polymer in microparticle drug delivery systems (Tran et al., 2011a). This copolymer of lactide and glycolide degrade by simple hydrolysis when exposed to an aqueous environment such as inside the human body. PLGA has been used in a host of drug products approved by Food and Drug Administration (FDA), such as Zoladex Depot® (goserelin), Lurpon Depot® (leuprolide), Sandostatin LAR® Depot (octreotide acetate), Nutropin Depot® (somatotropin), Trelstar® (triptorelin), Somatulin® Depot (lanreotide), Risperidal® Consta® (risperidone), Vivitrol® (naltrxone) and Bydureon® (exenatide). PLGAs are available at various molecular weights (or intrinsic viscosities) and lactide/glycolide ratios with either ester end-caps or free carboxylic acid end-caps. The properties of PLGA have been shown to influence important microparticle characteristics, such as the amount of drug loading, loading efficiency and drug release both *in vitro* and *in vivo* (Yeo and Park, 2004; Su et al., 2011; Amann et al., 2010). Previous studies have demonstrated that the rate of hydrolysis, and therefore, drug release is heavily dependent on the PLGA molecular weight and monomer composition. Consequently, it is possible to design PLGA-based microparticle drug delivery systems with tailored polymer degradation characteristics and release patterns by varying the PLGA composition.

In addition to polymer composition and properties, there are other formulation- and process-related parameters that may affect microparticle performance. Formulation-related factors include

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