International Journal of Pharmaceutics 379 (2009) 174–180

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Pharmaceutical nanotechnology

Nanoparticles engineered from lecithin-in-water emulsions as a potential delivery system for docetaxel

Nijaporn Yanasarn, Brian R. Sloat, Zhengrong Cui*

Department of Pharmaceutical Sciences, College of Pharmacy, Oregon State University, Corvallis, OR 97331, United States

ARTICLE INFO

Article history:
Received 19 February 2009
Received in revised form 27 May 2009
Accepted 3 June 2009
Available online 11 June 2009

Keywords:
Nanoparticles
Emulsions
Cell uptake
Cytotoxicity
Biocompatibility

ABSTRACT

Docetaxel is a potent anticancer drug. However, there continues to be a need for alternative docetaxel delivery systems to improve its efficacy. We reported the engineering of a novel spherical nanoparticle formulation (~270 nm) from lecithin-in-water emulsions. Docetaxel can be incorporated into the nanoparticles, and the resultant docetaxel-nanoparticles were stable when stored as an aqueous suspension. The release of the docetaxel from the nanoparticles was likely caused by a combination of diffusion and Case II transport. The docetaxel-in-nanoparticles were more effective in killing tumor cells in culture than free docetaxel. Moreover, the docetaxel-nanoparticles did not cause any significant red blood cell lysis or platelet aggregation *in vitro*, nor did they induce detectable acute liver damage when injected intravenously into mice. Finally, compared to free docetaxel, the intravenously injected docetaxel-nanoparticles increased the accumulation of the docetaxel in a model tumor in mice by 4.5-fold. These lecithin-based nanoparticles have the potential to be a novel biocompatible and efficacious delivery system for docetaxel.

1. Introduction

Recently, nanoparticles have gained much attention as a delivery system for anticancer drugs, primarily due to their unique properties that can potentially improve the efficacy of these drugs (Allen and Cullis, 2004). For example, nanoparticles may be used to enhance the solubility of poorly water soluble anticancer drugs and to modify their pharmacokinetics (Gabizon et al., 2003). Nanoparticles may also be engineered to reduce the uptake of the drugs by the reticuloendothelial system and/or to target the drugs to specific tumor cells (Allen, 2002; Emerich and Thanos, 2006). Additionally, there were data showing that nano-sized drug carriers can overcome the multi-drug resistance in many cancer cells (Jabr-Milane et al., 2008).

Docetaxel is a semi-synthetic anticancer agent in the taxane class. It is potent against many solid tumors such as breast cancer, non-small cell lung cancer, ovarian cancer, and prostate cancer (Clarke and Rivory, 1999). In spite of its high efficiency, side effects limit the clinical use of the docetaxel. The current formulation of docetaxel contains Tween 80 and ethanol (50:50, v/v) as the solvent, and adverse reactions due to either the drug itself or the solvent system have been reported in patients (e.g., hypersensitivity, fluid retention) (ten Tije et al., 2003). Therefore, many alternative docetaxel formulations such as liposomes (Immordino et al., 2003), polymeric nanoparticles (Hwang et al., 2008), micelles (Liu et al., 2008), and solid lipid nanoparticles (Xu et al., 2009) have been investigated.

Previously, our laboratory reported the preparation of a nanoparticle formulation from lecithin-in-water emulsions (Cui et al., 2006). Lecithins are components of cell membranes and are regularly consumed as part of a normal diet (Jimenez et al., 1990; Wade and Weller, 1994). They are used extensively in pharmaceutical applications as emulsifying, dispersing, and stabilizing agents and are included in intramuscular and intravenous injectables and other parenteral nutrition formulations (Lixin et al., 2006; Williams et al., 1984). In the present study, we investigated the feasibility of using the nanoparticles as a carrier for docetaxel. Our data showed that the docetaxel can be incorporated in the nanoparticles, and the docetaxel in the nanoparticles was more effective in killing tumors cells in culture than free docetaxel. Our data also showed that the docetaxel-loaded nanoparticles were biocompatible and tended to increase the accumulation of the docetaxel in tumors pre-established in mice.

2. Materials and methods

2.1. Materials

Docetaxel was purchased from LC Laboratories (Woburn, MA). Lecithin (soy, refined) was from MP Biomedicals, LLC (Santa

* Corresponding author. Tel.: +1 541 737 3255; fax: +1 541 737 3999.
E-mail address: Zhengrong.cui@oregonstate.edu (Z. Cui).

0378-5173/$ – see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.ijpharm.2009.06.004