Physicochemical Characteristics of Hydrotropic Polymer Micelles Bearing Superparamagnetic Iron oxide and Paclitaxel

Hong Yeol Yoon[1], Ki Young Choi[1,2], Gurusamy Saravanakumar[1], Ah Young Kim[1,2], Kwangmeyung Kim[2], Jae Hyung Park[1,3], Ick Chan Kwon[2], Kinam Park[4]

[1]Departments of Advanced Polymer and Nanopharmaceutical Sciences, Kyung Hee University, Gyeonggi-do 446-701, Korea

[2]Biomedical Research Center, Korea Institute of Science and Technology, Seoul 136-791. Korea

[3]BioImaging Research Center, Gwangju Institute of Science and Technology, Gwangju 500-712, Korea

[4]Departments of Pharmaceutics and Biomedical Engineering, Purdue University, IN 47907, USA

Introduction

Over the past several years, multifunctional nanoparticles that can deliver imaging agents or therapeutic drugs have been developed because of their potential for various biomedical applications [1]. Such nano-sized particular systems have been successfully used for diagnosis, imaging, and treatment of cancer since they can be passively accumulated at the tumor site via EPR (enhanced permeability and retention) effect [2]. Self-assembled polymeric micelles from amphiphilic block copolymers can enclose poorly water-soluble drugs and diagnostic agents in their hydrophobic inner core and can deliver them to the tumor site. In recent years, novel hydrotropic polymer micelles of poly(ethylene glycol)-block-poly(2-(4-(vinyl benzyl oxy)-*N,N*-diethyl nicotinamide)) (PEG-b-P(VBODENA) have been developed as a drug delivery carrier for paclitaxel (PTX), and they showed an excellent loading capacity of PTX, compared to other polymeric micelles [3]. In this study, we aimed to evaluate the potential of hydrotropic micelles as the carrier for both of PTX and magnetic nanoparticles.

Methods

Ferric chloride hexahydrates ($FeCl_3 \cdot 6H_2O$), 1-octadecene, and oleic acid were purchased from Aldrich (St. Louis, MO, USA). PTX was obtained from Samyang Genex (Daejeon, Korea). Poly(ethylene glycol)-block-poly(2-(4-vinyl benzyloxy)-N,N'-diethylnicotinamide)) (PEG-b-P(VBODENA)) was synthesized as reported previously [4]. Oleic acid-coated superparamagnetic iron oxide nanoparticles (MNP) were synthesized by thermal decomposition method [5]. MNP and PTX-loaded hydrotropic micelles were prepared using the dialysis method. The loading amount of PTX was determined by using a HPLC (Agilent Technologies, USA), in which the mobile phase consisted of acetonitrile:water (45:55, v/v). The loading amount of MNP was analyzed by the Inductively Coupled Plasma Spectrometer (ICP, Leeman Lab, USA). Particle size and stability of the micelles were measured using the fiber-optics particle analyzer (FPAR-1000, Otsuka electronics, Japan). Micelles morphology was obtained using the Field Emission Transmission Electron Microscopy (FE-TEM, JEM-2100F, JEOL, Japan). MNP5-PTX (2.6mg/kg Fe) was dispersed in PBS (pH 7.4), and 200μl of the solution was intravenously injected through the tail of athymic nude mice bearing SCC-7 tumors at limb. *In-vivo* T_2-weighted images were obtained using the 1.5Tesla whole body clinical MR scanner (GE Medical System) under the following conditions: TR = 3500ms, TE = 56.9ms, field of view (FOV) = 6 x 6 cm^2, and section thickness = 0.8mm.

Results

The MNP and PTX were readily encapsulated into the hydrotropic micelles using the dialysis method. Figure 1 shows the TEM images for micelles bearing MNP and PTX. The result indicated that the particles size decreased as the loading contents of PTX increased. MNPs were evenly dispersed at the inside of nanoparticles. From *in vitro* release test of PTX, it was found that PTX could release from nanoparticles in a sustained manner. The magnetic property of MNP was significantly enhanced after being encapsulated into the micelles. When the nanoparticles were intravenously injected into the tumor-bearing mice, they were selectively accumulated at the tumor, which was demonstrated from the MR imaging of the mice.

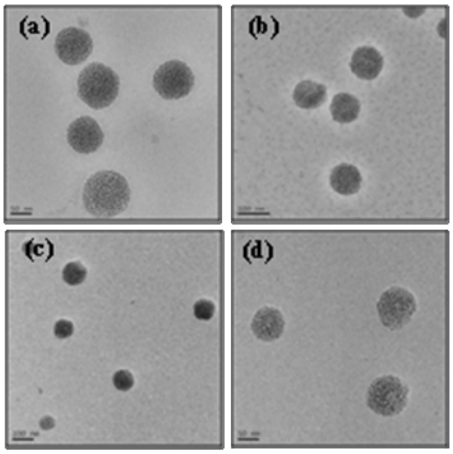

Figure 1. FE-TEM images of (a) MNP5, (b) MNP5-PTX10, (c) MNP5-PTX20, (d) MNP5-PTX30.

Conclusions

PTX and MNP were successfully encapsulated into the hydrotropic micelles. The resulting nanoparticles might have a potential as the carrier of PTX and magnetic nanoparticles for cancer therapy as well as imaging.

References:

1. Nasongkla N et al., Nano Lett, 2006:**6**: 2427-2430.
2. Talelli M et al., Langmuir, 2009:**25**:2060-2067.
3. Huh KM et al., J Control Release, 2005:**101**:59-68.
4. Lee SC et al., Biomacromolecules, 2007:**8**: 202-208.
5. Park J et al., Nat Mater, 2004:**3**:891-895.