Thermo-sensitive nanoparticles from poly(L-lactic acid)/poly(ethylene glycol) alternating mutiblock copolymer for potential anticancer drug carrier

Kun Na[1] Dong Won Kim[2] and You Han Bae[3]

[1]Division of Biotechnology, The Catholic University of Korea, Korea.
[2]Department of Clinical Pathology, Gwangyang Health Collage
[3]Department of Pharmaceutics and Pharmaceutical Chemistry,
University of Utah, USA.

Abstract

In order to produce biodegradable thermo-sensitive nanoparticles, alternating multi-block copolymers (MBC) weresynthesized by coupling dicarboxylated poly(ethylene glycol) (PEG MW 2000) with poly(L-lactic acid) (PLLA)/PEG/PLLA triblock copolymers. Three different multiblock copolymers were synthesized by varying PLLA molecular weight (800 (MBC1), 1600 (MBC2), and 2800 (MBC3)). The MBC formed self-assembled nanoparticleswith a unimodal size distribution during a dialysis process. The nanoparticles had a spherical shape with a size range of 90-330 nm and critical aggregation concentrations in a range of 5.6-12.6 g/mL, depending on PLLA length in MBC. The thermo-sensitivity of MBC nanoparticles was monitored by the changes inparticle size and interior structure as a function of temperature. The particle size slightly decreased on increasing temperature from 37 to 42oC. The interior structure of the nanoparticles responded to temperature by altering microviscosity. The microviscosity, measured by the anisotropy (r value) of a fluorescence probe, of MBC1 nanoparticles significantly changed with increasing temperature (r= 0.187 at 25℃ and 0.216 at 42℃), while MBCs 2 and 3 showed negligible changes in the microviscosity. This indicates that the

temperature-dependent interior structure of the nanoparticles relied on the portion of PLLA in MBC. The thermo-sensitivity affected to the drug release behavior and cell cytotoxicity. At 42℃, doxorubicin (DOX) loaded MBC1 nanoparticles showed enhanced cytotoxicity against Lewis Lung Carcinoma (LLC)cells by facilitated DOX release.

Keywords : Biodegradable polymer, alternating multi-block copolymers, PEG, PLLA, thermo-sensitivity, enhanced drug release, cytotoxicity