Amphiphilic Diblock Copolymer based on PPDO and PEG: Synthesis, Characterization, and Micellization

Remant Bahadur K.C.[a], Shanta Raj Bhattarai[a], Santosh Aryal[a], D.R. Lee[b], Hak Yong. Kim[*].
[a] Department of Bionanosystem engineering, Chonbuk National University, Chonju 561-756, Republic of Korea.
[b] Department of Textile Engineering, Chonbuk National University, Chonju 561-756, Republic of Korea.

Introduction: Significant efforts have been paid to the formulation of therapeutic agents in biocompatible nano-composites such as nano-particles, nano-capsules, and micelles conjugate systems etc [1]. These nanocomposites offer a potentially suitable means to deliver small molecular weight hydrophobic drugs as well as macromolecules such as proteins, peptides, and genes by either localized or targeted delivery to the interested site. Amphiphilic biodegradable block copolymers with suitable hydrophilic segment that ensures the enough circulation time of vehicle in blood stream and possesses effective targeting efficiency in the form of corona are commonly used for this purpose [2]. Core of micelles serve as a reservoir to the incorporated hydrophobic drugs, mechanically it protects the encapsulated drug from the enzymatic degradation. Encapsulated drug releases in a control way during hydrolytic degradation of polymer. In the current research an amphiphilic diblock copolymers based on poly (1,4-dioxan-2-one) (PPDO) and methoxy poly (ethylene glycol) (PEG) were synthesized and employed for the formulation of a reproducible polymeric nanoparticles. Here, PEG has been selected as hydrophilic segment, due to its well know out-standing physicochemical properties [3] and PPDO as hydrophobic segment, due to its reputed biodegradable, biocompatible and mechanical properties [4]. Insertion of PPDO in the amphiphilic copolymer can improve its flexibility and hydrophobicity, which is the important step to elaborate the application of biopolymers in biological system

Methods: Poly p-dioxanone-*b*- poly (ethylene glycol) (PPDO-*b*-PEG) was synthesized by the ring opening melt polymerized of p-dioxanone initiated by the hydroxyl end group of methoxy poly (ethylene glycol) (PEG) in the presence of stannous 2-ethylhexonoate (Sn (Oct) $_2$) as catalyst. Well-characterized polymer was employed for the preparation of miceller nanoparticles by co-solvent evaporation technique [5].

Results/Discussion: Encapsulation of drug into the miceller system is not only to protect from enzymatic degradation but also to achieve a control release to the desire site of action. Fast release potentially causes precipitation of drug in the vascular system where as the slow release allows for accumulation of polymeric micelles at target sites. Polymerization and diblock molecular composition was studied by different physiochemical methods (^{1}H-NMR, FT-IR) and thermo gravimetric analysis (TGA). Molecular weight of narrow distribution with polydispersity below 2 was inferred from gel permeation chromatography (GPC). Self-assembly of polymer into a miceller nanoparticles was studied by the comparative spectroscopic study (^{1}H-NMR) of polymer in non-selective (A) and selective (B) solvent. It shows the geometric variation of polymer in nonselective and selective solvent.

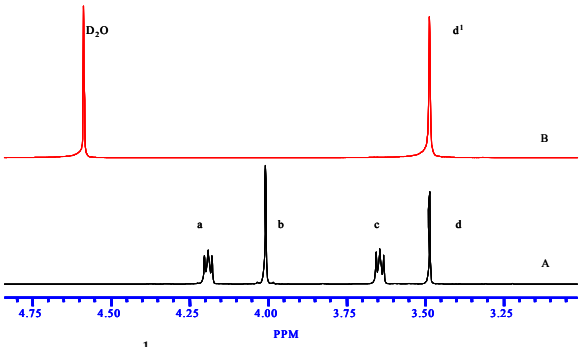

Figure 1. ^{1}H-NMR spectrum of PPDO-b-PEG (R_1) in (A) $CDCl_3$ and (B) D_2O

Spherical particles of average size 35 nm with smooth texture were observed in Atomic force microscope [AFM]. Size and size distribution studied by dynamic light scattering [DLS] show the particles of average size 100 nm with a uni-modal distribution.

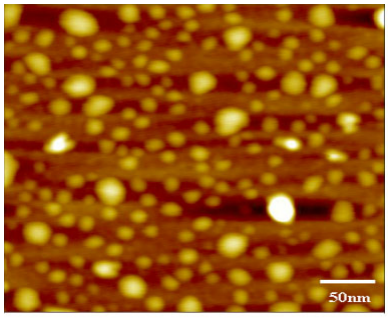

Figure 2. Atomic microscopy of PPDO-b-PEG (R1)

Conclusions: Amphiphilic block copolymers based on p-dioxanone and PEG synthesized by the conventional method were well characterized by different spectroscopic and chromatographic techniques. The well-characterized polymer was successfully self-assembled into a miceller system in the aqueous medium as employed by co-solvent evaporation method. Monodisperse and spherical shape were the characteristic feature of the polymeric nanoparticles.

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