

Examination of Thermo- and pH-Responsiveness of Ion Group Functionalized MPEG-b-PCL Diblock Copolymers

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Abstract. Here, we examined the thermo- and pH-responsiveness of the MPEG-b-PCL diblock copolymer (MC) with carboxyl (MC-COOH) and amine (MC-NH₂) groups at the chain ends of the PCL segment.

Keywords: phase transition, pH, sol-to-gel, ion, hydrophobicity.

1. Introduction

Recently, considerable effort has been devoted to developing thermo- and pH-responsive block copolymers that undergo a phase transition as the function of temperature [1]. In the development of thermo- and pH-responsive block copolymers, much work has been done to incorporating biodegradable segments into the poly(ethylene oxide) (PEO) block with the purpose of creating biodegradable block copolymers. Previously we have reported methoxy poly(ethylene glycol) (MPEG)-poly(ϵ -caprolactone) (PCL) diblock copolymers that undergo gel-to-sol phase transition at body temperature [2]. The MPEG-PCL (MC) copolymer series with hydrophilic and hydrophobic block as amphiphilic segments can form an ordered crystalline structure in aqueous solutions. The formation and destruction of an ordered crystalline structure depended on the MPEG and PCL blocks [3].

Thus, we hypothesized that introducing anionic (carboxyl) and cationic (amine) groups at the chain ends of the PCL segment could alter the ordered crystalline structure of the MC copolymer. The ordered crystalline structure in the MC with carboxyl anionic groups (MC-COOH) and amine cationic groups (MC-NH₂) could closely pack or aggregate to induce an aggregated gel through intra- and inter-molecular interactions as the temperature is varied above room temperature.

In the present work, we describe the preparation of MC-COOH with carboxyl anionic groups and MC-NH₂ with amine cationic groups and then examined the sol-to-gel phase transitions as a function of temperature and pH. We additionally studied the critical micelle concentration (CMC) of the MC-COOH and MC-NH₂ in an aqueous medium of different pH.

2. Experimental Section

2.1. Synthesis of MPEG-PCL diblock copolymers

MC diblock copolymer (750-2500) was prepared using a block copolymerization method reported previously [2].

2.2. Synthesis of MC-COOH and MC-NH₂

MC (2 g, 0.62 mmol) and toluene (75 mL) were introduced into a flask. The MC solution was distilled by azeotropic distillation to remove water. Toluene was then distilled off to give 15 mL in final volume. For

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MC-COOH, glutaric anhydride (0.14 g, 1.23 mmol) and acetic acid (0.9 mL) was added to MC solution at room temperature under nitrogen. For MC-NH₂, firstly, 4-Nitrophenyl chloroformate (0.25 g, 1.23 mmol) and triethylamine (0.12 mL) was added to MC solution and stirred for 24 h at room temperature under nitrogen to give a MC polymer with oxy-nitrophenoxy end group. Then, Diamino butane (1.03 g, 11.7 mmol) and THF (10 mL) was added to MC polymer with oxy-nitrophenoxy end group in THF (15 mL) solution. A reaction mixture was poured into a mixture of n-hexane and ethyl ether (v/v=4/1) to precipitate a polymer, which was separated from the supernatant by decantation to give each block copolymer.

2.3. Viscosity Measurements

Each block copolymer (0.5 g, 0.15 mmol) was individually dissolved in 4-mL vials with DW or different pH to make 20 wt% concentrations and was stored at 4 °C. After 24 h, the viscosity of the copolymer solutions were measured by using a Brookfield Viscometer DV-III ultra with programmable Rheometer and circulating baths with programmable controller TC-502P. The viscosity of polymer solutions was investigated by using T-F spindle at 0.1 rpm from 10 to 60 °C in increments of 2 °C.

2.4. Determination of CMC

The CMC was determined using pyrene as a fluorescence probe. 1 mL of pyrene solution in THF (1.2 mM) was added to 1000 mL of DW. THF was removed by a rotary evaporator at 30 °C for 2 h to give pyrene solution in water (1.2×10^{-6} M). Stock solutions of each copolymer were prepared by dissolving MC, MC-COOH, and MC-NH₂ samples in distilled water or different pH under stirring. From the stock solution a series of concentration was prepared by dilution. The pyrene solution was added by the copolymer solution. The solutions after filtration using 0.45 μm membrane filter were allowed to stand overnight at room temperature to equilibrate. The sizes of the resultant micelles were measured by electrophoretic light scattering (FPAR-1000, Otsuka, Japan). The micelle concentration in these experiments varied from 0.5×10^{-7} to 1.0 mg/mL. The pyrene concentration in copolymer solution was 6×10^{-7} M. For the measurements of pyrene excitation spectra scan speed was set at 240 nm/min and, emission and excitation slit widths were set at 2.5 nm. For the excitation spectra, the emission wavelength was 373 nm. Fluorescence intensities of the pyrene entrapped in the micelle core were determined by an F-4500 fluorescence spectrophotometer (Iex 338 nm, Hitachi Co. LTD, Japan) at room temperature.

3. Results

The MPEG-PCL diblock copolymer (MC) was synthesized via the ring-opening polymerization of the monomer CL using the terminal alcohol of MPEG (M_n , 750 g/mol). Then MC-COOH with carboxyl anionic groups and MC-NH₂ with amine cationic groups were prepared in good yield by using of MC. The MC-COOH and MC-NH₂ diblock copolymer solutions were prepared by dissolution at different pH in 20 wt% concentrations. The solutions exhibited opaque emulsion sol form at room temperature. The viscosities of the MC-COOH and MC-NH₂ solution were equal to 1 cP at low temperatures. At intermediate temperatures, the viscosities of the MC-COOH and MC-NH₂ solution increased to a sharp maximum then dropped rapidly, indicating the formation and disruption of the opaque gel state. The different behaviour of sol-to-gel phase transition exhibited at MC-COOH and MC-NH₂ diblock copolymers. The micelle formation characteristics of the MC-COOH and MC-NH₂ diblock copolymers prepared in different pH were examined. The resulting micelle depended on the characteristics of the anionic and cationic end groups of the MC-COOH and MC-NH₂ diblock copolymers.



Fig. 1: Sol-to-gel phase transition of the MC-COOH diblock copolymers.

4. References

- [1] M. S. Kim, J. H. Kim, B. H. Min, H. J. Chun, D. K. Han, H. B. Lee, Polymeric Scaffolds for Regenerative Medicine, *Polymer Reviews*, 2011, 51, 1-30.
- [2] M. S. Kim, H. Hyun, K. S. Seo, Y. H. Cho, G. Khang, H. B. Lee, Preparation and characterization of MPEG-PCL diblock copolymers with thermo-responsive sol-gel-sol behavior, *Journal of Polymer Science Part A: Polymer Chemistry*, 2006, 44, 5413-5423.
- [3] J. I. Kim, S. H. Lee, H. J. Kang, D. Y. Kwon, D. Y. Kim, W. S. Kang, J. H. Kim, M. S. Kim, Examination of phase transition behavior of ion group functionalized MPEG-b-PCL diblock copolymers, *Soft Matter*, 2011, 7, 8650-8656.