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Poly(hydroxyethyl acrylate-co-coumaryl acrylate) as a photo-responsive amphiphile

Ju Hyup Lee, Jin-Chul Kim *

College of Biomedical Science and Institute of Bioscience and Biotechnology, Kangwon National University, 192-1, Hyoja 2 dong, Chuncheon, Kangwon-do 200-701, Republic of Korea

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ABSTRACT

Poly(hydroxyethyl acrylate-co-coumaryl acrylate)s P(HEA-CA)s were prepared as a photo-responsive amphiphile by a free radical polymerization. Their CA residues were readily dimerized under UV light irradiation (365 nm, 400 W). Their interfacial activity increased in proportional to the CA content. P(HEA-CA)s were self-assembled into microspheres in aqueous phase due to their amphiphilicity which were confirmed by TEM. And the mean diameter was higher with higher CA content. In addition, P(HEA-CA)s could emulsify mineral oil in distilled water. The emulsions prepared with higher CA content were more stable in terms of the droplet size change. They could be destabilized by UV light irradiation.

1. Introduction

Several kinds of photo-responsive drug carriers, namely liposome [1], cubosome [2], microgel [3] and emulsion [4], were developed by taking advantage of coumarin and its derivative. Coumarins can be photo-dimerized because a cyclobutane bridge is formed between two molecules under the irradiation of a UV light. At the same time, the de-dimerization can take place under a UV irradiation because the cyclobutane bridge is photo-cleavable [5]. Photo-responsive liposomes were prepared by incorporating coumarin derivatives into the liposomal membrane [6] or by modifying the surface with coumarin-containing polymers [7]. The photo-dimerization and de-dimerization were claimed to fluctuate the liposomal membrane and cause a release from the liposome. Photo-responsive cubic phases were prepared by including coumarins in the water channel of cubic phase [8]. The diffusivity of a solute through the water channel will decrease upon the photo-dimerization because the dimer can block the water channel more effectively than the monomer. So the release from the cubic phase will be suppressed by a UV light irradiation. On the other hand, a photo-responsive microgel were prepared by taking advantage of hydrophobic interaction between polymeric β-cyclodextrin and Tween 20-coumarin conjugate [9]. The hydrocarbon chain of the conjugate was supposed to be included in the cavity of β-cyclodextrin, and the coumarin residues were to interact one another. So Tween 20-coumarin conjugate would act as a cross-linker for polymeric β-cyclodextrin. Another photo-responsive microgel was prepared by taking advantage of an electrostatic interaction between poly(ethyleneimine) and carboxymethoxycoumarin, and of a hydrophobic interaction among the coumarin residues [10].

In this study, poly(hydroxyethyl acrylate-co-coumaryl acrylate)s P(HEA-CA)s were prepared as a photo-responsive amphiphile. Due to the coumarin residue, the copolymer will be photo–reactive and the photo-reactivity was observed by determining the dimerization degree under the UV irradiation. Since P(HEA-CA)s has both a hydrophilic segment (hydroxyethyl acrylate segment) and a hydrophobic comonomer (coumaryl acrylate), the copolymers will be amphiphilic and the amphiphilicity was investigated by measuring the air/water interfacial tensions of the copolymers solutions. The amphiphilic property of P(HEA-CA)s was appreciated by observing their self-assembling property in an aqueous phase and their emulsifying ability. The photo-reactive property of the copolymer was appreciated by observing the effect of the UV irradiation on the size change of the oil drop of emulsion which was prepared using a P(HEA-CA) as an emulsifier.

2. Experiment

2.1. Materials

Acryloyl chloride was purchased from TCI (Tokyo, Japan). Hydroxyethyl acrylate (HEA), 7-hydroxy coumarin and dimethylformamide (DMF) were purchased from a Sigma Chemical Co. St. Louis, MO, USA). a-a′-Azobis(isobutyronitrile) (AIBN) was provided

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* Corresponding author. Tel.: +82 33 250 6561; fax: +82 33 253 6560.
E-mail address: jinkim@kangwon.ac.kr (J.-C. Kim).

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by Junsei Chemical Co. (Japan). Water was doubly distilled in a Milli-Q water purification system (Millipore Corp, MA, USA) until the resistivity was 18 MΩ/cm. All other reagents were in analytical grade.

2.2. Preparations of coumaryl acrylate

Coumaryl acrylate was prepared by a method described elsewhere [11]. 2 g of NaOH was put to 275 ml of absolute alcohol in a 500 ml-round bottom flask, and then 8.1 g of 7-hydroxy coumarin was put to the alcohol. The mixture was heated to 60 °C and it was stirred using a magnetic bar for 30 min at the same temperature. The mixture was cooled down to a room temperature and further cooled to 0 °C–5 °C by keeping in a freezer. Acryloyl chloride (4.47 ml) was dropped to the cold mixture over 60 min and the reaction was performed by gently stirring the mixture for 90 min using a magnetic bar at the same temperature. The product (acrylic coumarin) was precipitated out by pouring the reaction mixture into 400 ml of cold water (4 °C), and the precipitate was separated by filtrating through Buchner funnel (Dong IL, South Korea). The filtrate was washed with cold water (4 °C) and dried in an oven. For further purification, the filtrate was re-crystallized in methanol.

2.3. Preparation of P(HEA-CA)s

P(HEA-CA)s were prepared by a free radical reaction. HEA (3 g) and various amounts of CA (0 g–0.17353 g) were dissolved in 26 mL of DMF contained in a 250 ml 3-neck round bottom flask so that the molar ratio of HEA/CA was 97/3, 99/1, 99.5/0.5, and 100/0. AIBN (0.0436 g), an initiator, was put in the solution and the reaction mixture was degassed by purging with nitrogen gas stream for 30 min. The reaction was performed for 12 h around 75 °C with the solvent being refluxed. The reaction mixture was cooled to a room temperature, and the product was precipitated out by pouring it in 200 ml of diethylether. And the precipitate was separated by filtering through a filter paper (Whatman No. 2). For the purification, the precipitate was dissolved in DMF and it was re-precipitated in the non-solvent. After filtration, the filtrate was dried in an oven. The copolymer prepared using the reaction mixture where the molar ratio of HEA/CA was 100/0, 99.5/0.5, 99/1, and 97/3 will be termed as P(HEA-CA) (100/0), P(HEA-CA) (99.5/0.5), P(HEA-CA) (99/1), and P(HEA-CA) (97/3), respectively.

2.4. ^{1}H NMR spectroscopy

^{1}H NMR spectra of P(HEA-CA)s were obtained on a Bruker DPX 400 MHz spectrometer (Karlsruhe, Germany, in the Central Laboratory Center of Kangwon National University). P(HEA-CA)s were dissolved in DMSO-d6.

2.5. Dimerization of CA residue of poly(HEA-CA)s

Aqueous solution (2%, w/v) of P(HEA-CA)s were prepared by dissolving the copolymer in distilled water. A UV light (365 nm, 400 W) was irradiated to the copolymer solutions for 10 min. The dimerization degree was determined by a following equation [12].

$$\text{Dimerization}(\%) = \left(1 - \frac{A_t}{A_o}\right) \times 100$$

where, A_o is the absorbance of P(HEA-CA)s solution at 320 nm before being exposed to UV irradiation, and A_t is the absorbance after being exposed to a UV irradiation.

2.6. Measurement of air/water interfacial tensions

Aqueous solutions (0.1%, w/v) of P(HEA-CA)s were prepared by dissolving the copolymers in distilled water. The copolymer solutions of which concentration ranges from 0.0005% to 0.1% were prepared by diluting the mother solution two times subsequently with distilled water. The air/water interfacial tensions of the copolymer solutions were determined on a surface tension meter (SEO, DST 60, South Korea).

2.7. Preparation and characterization of P(HEA-CA)s assemblies

P(HEA-CA)s were dissolved in distilled water so that the concentration of each solution was 10% (w/v). The shape of the assemblies was investigated on a TEM (LEO-912AB OMEGA, LEO, Germany at Korean Basic Science Institution located in Chuncheon, Korea) after they were stained with phosphotungstic acid solution (2% in distilled water) [13,14]. On the other hand, in order to investigate the effect of a UV irradiation on the size of P(HEA-CA)s assemblies, a UV light (365 nm, 400 W) was irradiated to the copolymer solutions for 30 min. And then, the mean diameters of P(HEA-CA)s assemblies contained in UV-treated solutions and in UV-untreated solutions were determined on a light scattering machine (Plus 90, Brookhaven Instrument, USA).

2.8. Preparation of O/W emulsions using P(HEA-CA)s as an emulsifier

Aqueous phases were prepared by dissolving P(HEA-CA)s (0.08 g) in 4 ml of distilled water contained in a 10 ml vial. P(HEA-CA)s were contained in the aqueous phase as an emulsifier. Mineral oil (1 ml) was put in the aqueous phase, and the two phase mixture was emulsified by homogenizing on a vortexing mixer (Scientific Industries, Inc. G-560) for 1 min and then in a bath-type sonicator (Sonic and materials, Gex-750) for 2 min [15,16]. Emulsions prepared using P(HEA-CA) (100/0), P(HEA-CA) (99.5/0.5), P(HEA-CA) (99/1), and P(HEA-CA) (97/3) as an emulsifier will be abbreviated as emulsion (100/0), emulsion (99.5/0.5), emulsion (99/1), and emulsion (97/3), respectively.

2.9. Stability of oil droplet size of emulsion

The stability of oil droplet size of emulsion was observed by a method described elsewhere [17]. Emulsions contained in glass vials were stored at a room temperature under dark condition for 72 h. The images of the emulsions were obtained on a photomicroscope (Olympus, CX31, Japan) at a given time, and the mean diameters of the oil droplets were determined on an image analyzer (Media Cybernetics, Image-Pro Plus version 5.1). In order to investigate the effect of UV irradiation on the stability of oil droplet size, emulsions were subjected to the UV irradiation (365 nm, 400 W) for 10 min. And then the photos of the UV-irradiated emulsions were obtained on a photomicroscope at a given time for 40 min, and the mean diameters of the oil droplets were determined on the image analyzer.

3. Results and discussion

3.1. ^{1}H NMR spectroscopy of P(HEA-CA)s

Fig. 1 shows the ^{1}H NMR spectrum of P(HEA-CA) (97/3). The peak at 4.75 ppm is the signal of the hydroxyl group of HEA, the peak at 3.55 ppm is the signal of the ethyl group of HEA, the peaks in the range of 6.5–7 ppm are the signal of the coumaryl proton. The area of the hydroxyl group signal of HEA was 59.75, and that of the coumaryl proton signal was 1. Accordingly, the molar ratio of HEA/CA of P(HEA-CA) (97/3) was calculated to be 98.3:1.7. In the