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Short communication

Methacrylic acid-triggered phase transition behavior of thermosensitive hydroxypropylcellulose[☆]

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ABSTRACT

Methacrylic acid (MAA)-triggered phase transition of thermosensitive hydroxypropyl cellulose (HPC) was studied. The phase transition temperature of 0.1 wt.% HPC aqueous solutions was dramatically reduced from 41 °C to 8 °C as the MAA concentration increased from 0 wt.% to 4 wt.%. The sharp decrease of HPC phase transition temperature triggered by MAA may be attributed to strong hydrogen bonding between MAA and HPC. It may be proposed that the hydrogen bonding of MAA with HPC restricts the interaction of water with HPC and so reduces the solubility of HPC in water and improves the hydrophobic association of HPC. Furthermore, MAA attaching on HPC polymer chains was polymerized to form surfactant-free PMAA nanogels around ambient temperature when HPC collapsed forming PMAA nanogels. Effect of MAA concentration and polymerization temperature on the size and size distribution of PMAA nanogels was investigated.

1. Introduction

The temperature phase transitions of thermosensitive polymers, hydrogels, and micro/nano-gels have been intensively studied due to their significant importance in fundamental research and practical applications (Hu, Tong, & Lyon, 2010; Scherzinger, Lindner, Keerl, & Richtering, 2010). In particular, intelligent polymer systems with temperature dependent phase transitions can be engineered to find applications in drug delivery, tissue engineering, biosensors, protein and DNA separation, and cell-releasing materials (Buchholz et al., 2001; Cohen Stuart et al., 2010; Oh et al., 2004). For instance, thermogelling polymer system has been developed for tissue engineering applications (Kretlow, Klouda, & Mikos, 2007). Such body temperature-induced hydrogels avoid the toxicity issue of chemically crosslinked hydrogels and open an avenue to minimally invasive surgery through the injection of thin polymer solutions at room temperature. Thermosensitive nanogels self-assemble into colloidal crystal materials that promise to be designed for biosensor application (Holtz & Asher, 1997). Hydrophilic–hydrophobic switch of thermo-sensitive polymers has been developed for smart polymer surface culturing cell sheet at 37 °C above the phase transition temperature 32 °C of poly(N-isopropylacrylamide) (PNIPA). As PNIPA polymer becomes hydrophilic at room temperature, the cell sheet can automatically detach from the PNIPA surface without chelating agents or enzymes that may damage cell. Another important application of thermo-responsive polymer systems includes DNA and protein separation (Root, Hammock, & Barron, 2008).

In recent years, researchers have extensively investigated the phase transition behavior of thermosensitive, natural polymers such as hydroxypropylcellulose (HPC), hydroxypropylmethyl cellulose (HPMC), and methylcellulose (MC) (Lu, Hu, & Gao, 2000). One important finding is that the phase transition behavior can be manipulated through interpolymer hydrogen bonding between the thermo-sensitive polymer and poly(acrylic acid). Lu, Hu, and Schwartz (2002) discovered that the phase transition temperature of 1 wt.% hydroxypropylcellulose (HPC) aqueous solution dramatically shifted from 41 °C to 16 °C under the interaction of 1 wt.% poly(acrylic acid) at pH = 3.2. Due to interpolymer hydrogen bonding, PAA screens the hydrogen bonding interaction of HPC with water and thus leads to the strong hydrophobic interaction of HPC macromolecules at a low temperature. Furthermore, the phase transition temperature of HPC/PAA aqueous solution can be tailored by varying the solution pH, HPC molecular weight, and PAA molecular weight and concentration. The PAA-induced phase transition behavior of HPC could be applied to the tuning viscosity and solubility of HPC in pharmaceutical, food, and personal care products. Meanwhile, Lu et al. (2002) for the first time synthesized surfactant-free PAA nanogels using HPC template directly in the HPC aqueous solution around room temperature, while a

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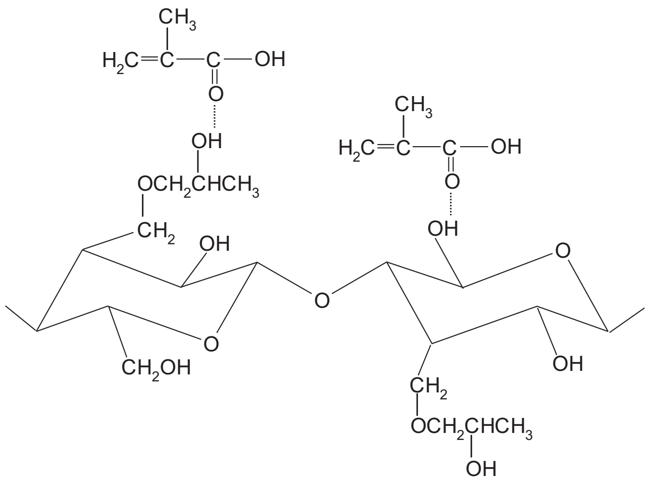

Fig. 1. Schematic hydrogen bonding between hydroxypropylcellulose (HPC) and methacrylic acid (MAA).

conventional method is inverse emulsion polymerization for the synthesis of PAA nanogels (Kriwet, Walter, & Kissel, 1998). An innovative polymerization of PAA nanogels provides a process for making "green" PAA nanogel without surfactants and organic solvents (Liao, Shao, Wang, Qiu, & Lu, 2012).

Herein, we report methacrylic acid (MAA)-triggered temperature phase transition of hydroxypropylcellulose (HPC) linear polymer. MAA dissolves in the HPC aqueous solution and induces the phase transition at a temperature lower than the phase transition temperature of the HPC aqueous solution without the weak acid. Such phase transition phenomena may be explained through the hydrogen bonding interaction of HPC with the weak acid MAA as schematically shown in Fig. 1. MAA can attach to the surface of HPC polymer chains through such hydrogen bonding. As the monomer MAA polymerizes to form PMAA polymer chains around the HPC macromolecule, PMAA could form much stronger hydrogen bonding with HPC which induces the phase transition of HPC around room temperature. HPC polymer chains collapse to form nano-scale particles and then PMAA attaching onto the HPC "template" forming nanogels. In this novel synthesis method, HPC acts as a template for making surfactant-free PMAA nanogels. Understanding of the weak acid-induced phase transition of thermosensitive polymer is of significant importance in the aqueous synthesis of PMAA nanogels and other interpenetrating (IPN) smart nanogels with PMAA networks.

2. Materials and methods

2.1. Materials

Hydroxypropylcellulose ($M_w = 1 \times 10^5$, degree of substitution (DS) = 3.0), methacrylic acid (MAA), methylenebisacrylamide (BIS), ammonium persulfate (APS), N, N, N′, N′-tetraethylmethyldiamine (TEMED) were purchased from Aldrich and were used as received.

2.2. UV–vis spectrophotometer

UV–vis spectrophotometer characterization of phase transition of HPC aqueous solution 0.1 wt.% HPC aqueous solutions having different concentrations of MAA were measured at 0.2 °C/min by means of Lambda 35 UV–vis spectroscopy (Perkin Elmer, USA), respectively.

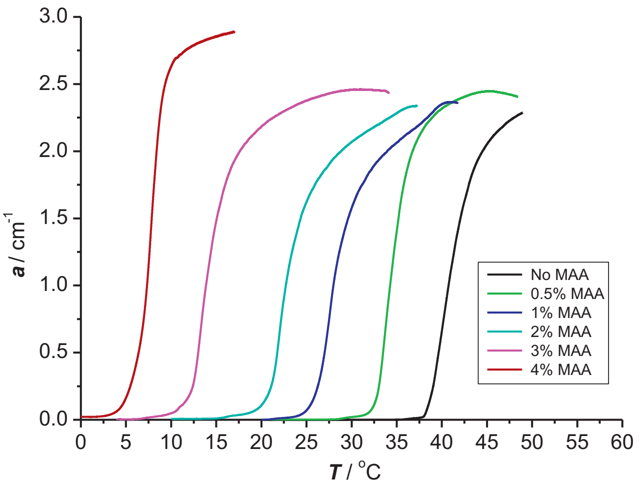

Fig. 2. Effect of MAA concentration on the phase transition of HPC.

2.3. Preparation of PMAA nanogels at different polymerization temperatures

20 g of 1.0 wt.% HPC, 0.40 g MAA, and 0.10 g BIS dissolved in 74.3 g DI water under stirring for 30 min. After the HPC/MAA solution was purged with N_2 for 40 min at 18 °C, 5 g water solution containing 0.10 g APS was added. 0.10 g TEMED was added in the solution to initiate polymerization. The reaction proceeded 1 h at 18 °C and PMAA nanogels formed. The same formulation and procedure were applied to the preparation of PMAA nanogels at different polymerization temperatures of 22 °C, 6 °C, and 30 °C.

2.4. Preparation of PMAA nanogels at different MAA concentrations

20 g of 1.0 wt.% HPC, 0.30 g MAA, and 0.10 g BIS dissolved in 74.4 g DI water under stirring for 30 min. The HPC/MAA solution was purged with N_2 for 40 min. After stabilizing for 20 min at 24 °C, 5 g water solution containing 0.10 g APS was added in the solution. And 0.10 g TEMED was added in the solution to initiate polymerization. The reaction proceeded for 1 h at 24 °C and a PMAA nanogel formed. The same formulation and procedure were applied to the preparation of PMAA nanogels at different MAA concentrations of 0.6 wt.%, 0.8 wt.%, and 1.0 wt.%.

2.5. Characterization of size and size distribution of PMAA nanogels with dynamic light scattering (DLS)

The size and size distribution of PAA nanogel dispersion were measured by dynamic light scattering with a BI-9000 AT digital time correlator (BI-200SM, Brookhaven Co., Ltd.) under pH = 6.3 and 25 °C at a scattering angle of 90°. Light source is a He–Ne laser with 35 mW and 633 nm.

3. Results and discussion

3.1. Methacrylic acid (MAA)-triggered phase transition behavior of thermosensitive hydroxypropylcellulose (HPC)

The effect of methacrylic acid (MAA) concentration on the phase transition of 0.1 wt.% hydroxypropylcellulose (HPC, degree of substitution 3.0, $M_w = 10^5$) is shown in Fig. 2. The phase transition temperature of 0.1 wt.% HPC aqueous solution was reduced from 41 °C, without MAA, to 8 °C, with 4 wt.% MAA. The decreasing phase transition temperature with increasing MAA concentration

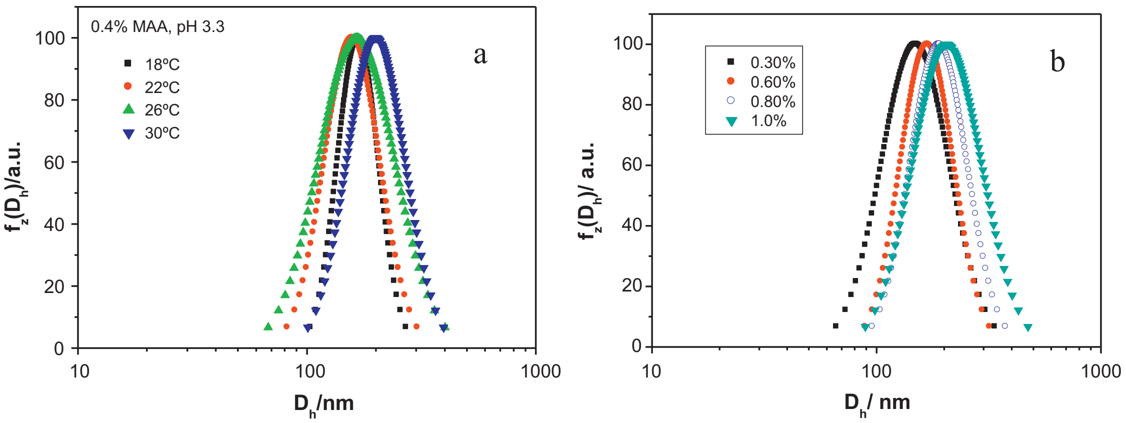

Fig. 3. (a) Size and size distribution of PMAA nanogels prepared in four different polymerization temperatures of 18 °C, 22 °C, 26 °C, and 30 °C and (b) size and size distribution of PMAA nanogels prepared in four different MAA concentrations of 0.3 wt.%, 0.6 wt.%, 0.8 wt.%, and 1.0 wt.%.

is attributed to the formation of hydrogen bonding between the hydroxyl (—OH) group of HPC polymer and MAA carboxyl group (—COOH). Such hydrogen bonding screens the access of water to the HPC polymer chains and reduces the solubility of the HPC in water, thus resulting in the increase of the hydrophobic association of the HPC interpolymers. At a lower MAA concentration of 0.5 wt.%, the HPC phase transition temperature is 34 °C. With increasing MAA concentration from 1.0 wt.% to 4.0 wt.%, the phase transition temperature of HPC/MAA aqueous solution was dramatically reduced from 28 °C to 8 °C. As compared with 1% MAA, 1% acrylic acid (AA) induced the phase transition of HPC at 37 °C, 9 °C higher than the phase transition temperature of HPC with 1% MAA (Liao, Shao, Wang, Qiu, & Lu, 2012). 2% MAA induced the phase transition of HPC at 22 °C, while 2% AA induced phase transition temperature of HPC was 32 °C. The sharp decrease of the phase transition temperature is attributed to a much stronger hydrophobic association of inter-HPC polymers induced by an increasing concentration of MAA.

3.2. *Effect of polymerization temperature on the synthesis of PMAA nanogels*

Due to the hydrogen bonding between HPC and MAA, MAA can attach on to the HPC polymer chains. Therefore, we successfully synthesized PMAA nanogels with very narrow size distribution. Firstly, we studied the effect of polymerization temperature on size and size distribution of the resulting PMAA nanogels, as shown in Fig. 3a. The syntheses of surfactant-free PMAA nanogels were carried out at 0.2 wt.% HPC, 0.1 wt.% of initiator APS and catalyst TEMED, and 0.1 wt.% crosslinker BIS at polymerization temperatures of 18 °C, 22 °C, 26 °C, and 30 °C, respectively. Before reaction, the pre-reaction solutions at four different temperatures are clear. After initiation, monomer MAA absorbed on the HPC polymer chains polymerized immediately to form poly(methacrylic acid) (PMAA) polymer chains. Because of the hydrogen bonding of PMAA to HPC, HPC chains underwent phase transition and dehydrated to form a shrunken structure at 18 °C, much lower than 41 °C. Therefore, the PMAA chains around HPC also dehydrated to form PMAA nanogels in the presence of crosslinker BIS. The formulation of PMAA nanogels was indicated by a light blue of the solution at a low pH (<3.5). However, we found that as MAA was polymerized at pH > 6.0, the solution was still transparent. This means that no PMAA nanogels formed as MAA ($pK_a = 5.2$) was neutralized, where no hydrogen bonding exists between HPC and PMAA due to the ionization of MAA and PMAA.

The resulting PMAA nanogels were measured by DLS measurement at 25 °C. The size and size distribution of surfactant-free PMAA nanogels are shown in Fig. 3a. The results showed that an increasing polymerization temperature from 18 °C to 26 °C did not affect the average size of about 160 nm of PMAA nanogels, which had a narrow size distribution polydispersity index (PDI) of about 0.1. As the polymerization temperature further increased up to 30 °C, the average size D_h of PMAA nanogels became bigger, 200 nm, while the size distribution still kept narrow.

Table 1
Effect of MAA concentration on size and size distribution of PMAA nanogels.

MAA content (wt.%)	Average diameter (nm)	PDI
0.30	149.8	0.119
0.60	168.9	0.078
0.80	190.3	0.090
1.0	205.6	0.137

3.3. *Effect of monomer MAA concentration on the size and size distribution of PMAA nanogels*

Effect of MAA concentration on the size and size distribution of the resulting PMAA nanogels was shown in Fig. 3b. The results show that an increasing MAA concentration led to the bigger average size of the resulting PMAA nanogels. In polymerization system with the same HPC concentration of 0.2 wt.%, a higher monomer MAA concentration resulted in a faster growth of PMAA nanogels, thus forming a larger size of the resulting PMAA nanogels. Interestingly, the size distributions of the PMAA nanogels prepared at four different MAA concentrations were narrow, about 10% relative polydispersity index (PDI) (Table 1). Our green route to the synthesis of surfactant-free PMAA nanogels will have significant impact on the real applications of PMAA nanogels in the field of nanomedicine (Wu et al., 2010).

4. Conclusion

In conclusion, our results show that monomers MAA can trigger the phase transitions of thermosensitive hydroxypropyl cellulose (HPC) aqueous solution at lower temperatures. The phase transition temperature decreased with increasing the concentration of the weak acid MAA due to the strong hydrogen bonding between HPC and MAA and the hydrophobic association. As MAA attaching on the HPC polymer chains polymerized and formed PMAA that induced stronger hydrogen bonding with HPC, PMAA nanogels formed with the collapse of HPC directly in aqueous media. Therefore, we developed a green route to the synthesis of surfactant-free PMAA nanogels using HPC as a template. The resulting PMAA nanogels demonstrated very narrow size dispersity. Such green PMAA nanogels promise to be developed for use in controlled drug delivery, bioadhesive, and other novel nanobiomaterials.

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