European Polymer Journal 45 (2009) 2060–2067

Contents lists available at ScienceDirect

European Polymer Journal

journal homepage: www.elsevier.com/locate/europolj

Thermo- and pH-sensitive comb-type grafted poly(*N*,*N*-diethylacrylamide-co-acrylic acid) hydrogels with rapid response behaviors

Hongliang Liu, Mingzhu Liu *, Liwei Ma, Jun Chen

Department of Chemistry and State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Tianshui Road No. 222, Lanzhou 730000, PR China

ARTICLE INFO

Article history:
Received 23 November 2008
Received in revised form 20 March 2009
Accepted 25 March 2009
Available online 5 April 2009

Keywords:
Hydrogel
Graft
Poly(*N*,*N*-diethylacrylamide-co-acrylic acid)
Rapid response

ABSTRACT

Poly(*N*,*N*-diethylacrylamide) with a terminal hydroxyl end group (PDEA-OH) was synthesized by radical telomerization of *N*,*N*-diethylacrylamide (DEA) monomer using 2-hydroxyethanethiol as a chain transfer agent. Macromonomer of thermo-sensitive PDEA was synthesized by condensation reaction of PDEA-OH with acryloyl chloride. The macromonomer was characterized by FTIR and ^{1}H NMR, and the molecular weight was determined by GPC. Thermo- and pH-sensitive comb-type grafted poly(*N*,*N*-diethylacrylamide-co-acrylic acid) (PDEA-co-AA) hydrogels (GHs) were successfully prepared by grafting PDEA chains with freely mobile ends onto the backbone of a cross-linked (PDEA-co-AA) network. The results showed that the deswelling behavior of the hydrogels was dependent on the test temperature. At 45 °C (beneath the VPTT of the hydrogels), both the normal-type hydrogels (NHs) and comb-type grafted P(DEA-co-AA) hydrogels had lower deswelling rates. While at 60 °C (far beyond the VPTT of the hydrogels), the deswelling rates of the GHs were faster than that of the NHs. Furthermore, pulsatile stimuli-responsive studies indicated that the GHs had excellent thermo-reversibility and were superior to the NHs in the magnitude of their swelling ratios to temperature changes. However, the reversibility to pH changes was poor for both the NHs and the GHs.

1. Introduction

Many polymeric intelligent stimuli-sensitive hydrogels undergo abrupt changes in response to environment stimuli: such as temperature [1–5], pH [6,7], electric field [8] and ionic strength [9,10]. These gels, especially responding to both temperature and pH, are expected for use in various devices, including drug delivery systems [11,12], separations [13] and immobilizations of enzymes [14].

For thermo-sensitive hydrogels, the polymers of several *N*-substituted poly(acrylamides) exhibit thermo-response behavior, such as poly(*N*-isopropylacrylamide), poly(*N*,*N*-diethylacrylamide), poly(*N*-cyclopropylacrylamide) and poly(*N*-ethylacrylamide). Polymers of this type undergo a thermally induced and reversible phase transition. The temperature at which this occurs is commonly referred to as the lower critical solution temperature (LCST). Below the LCST, polymer chains are well soluble in aqueous media and the hydrogel is in a swollen, hydrated and hydrophilic state; above the LCST, on the other hand, the polymer chains of gel network collapse and aggregate abruptly, and the volume of gel dramatically shrinks at the same time [15,16].

In case of pH-sensitive hydrogels, either acid (–COOH) or basic (–NH_2) pendent groups are contained in the network. One of the frequently studied pH-sensitive polymers is poly(acrylic acid) (PAA), which extends and shrinks at pH values above and below the pK_a of PAA (about 4.75), respectively.

For several potential hydrogel applications, a fast response is needed. One of the most useful methods to enhance the response rate is to produce comb-type grafted hydrogels by tailoring the gel architecture at the molecular level [17,18]. Recently, Zhang and co-workers [19] prepared a dual temperature and pH-sensitive poly(*N*-isopropylacrylamide-co-AA) (P(NIPA-co-AA)) hydrogel with

---

* Corresponding author. Tel.: +86 931 8912387; fax: +86 931 8912582.
E-mail address: mzliu@lzu.edu.cn (M. Liu).

0014-3057/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.eurpolymj.2009.03.019

comb-type grafted chains by copolymerization of PNIPA macromonomers with NIPA monomers and AA monomers. They investigated the different deswelling behavior between the normal-type and comb-type grafted hydrogels, as well as the effects of simultaneous changes of both temperature and pH value on the prepared dual thermo- and pH-sensitive hydrogels.

In contrast to previous studies, we selected poly(*N*,*N*-diethylacrylamide) (PDEA) [20] which has a LCST of 33 °C [21] in aqueous media as the thermo-sensitive component. Compared with *N*-isopropylacrylamide (NIPA), *N*,*N*-diethylacrylamide (DEA) lacks amide hydrogen, and it can only form a single intermolecular hydrogen bond as proton acceptor with water, but cannot form an intramolecular hydrogen bond as proton donor. This structure difference makes the volume transition of PNIPA gels abruptly, while that of PDEA gels continuously [22]. This different swelling behavior of PDEA can be expected to be more suitable to application in the life sciences [23]. In the work reported in this paper, we synthesized thermo- and pH-sensitive comb-type grafted poly(*N*,*N*-diethylacrylamide-co-acrylic acid) (PDEA-co-AA) hydrogels, and the swelling behavior of the hydrogels to temperature and pH was investigated. It is expected that these thermo- and pH-sensitive comb-type grafted P(DEA-co-AA) hydrogels have an excellent foreground in biomedical fields for stimuli-responsive drug delivery systems.

2. Experimental

2.1. Materials

Acrylic acid (AA) (A.P. grade) (Chemical Co. Tianjin, China) was distilled under reduced pressure prior to use. *N*,*N*-diethylacrylamide (DEA) was synthesized according to literature [24]. *N*,*N*′-Azobisisobutyronitrile (AIBN) (C.P. grade) (Shanghai Fourth Reagents Plant, Shanghai, China) was recrystallized from methanol. 2-Mercaptoethanol (ME) (Shanghai Fourth Reagents Plant, Shanghai, China), Ammonium persulfate (APS) (Tianjin Chemical Company, Tianjin, China) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamide (TEMED) (Chemical Co. Shanghai, China) were A.P. grade and used as received. *N*,*N*′-methylenebisacrylamide (NNMBA) (C.P. grade) (Medicine Co. Shanghai, China) was recrystallized from ethanol. The other reagents were A.P. grade and were used without further purification. Water for all reactions, solution preparation, and polymer purification was double distilled.

2.2. Polymer synthesis

The PDEA macromonomer was prepared as follows: First, the PDEA polymer with a terminal hydroxyl end group (PDEA-OH) was synthesized by radical telomerization of the DEA monomer using ME as a chain transfer agent. DEA (6.35 g, 50 mmol), ME (0.078 g, 1 mmol), and AIBN (0.082 g, 0.5 mmol) were dissolved in tetrahydrofuran (THF) (20 mL) in a three-necked flask. Polymerization was carried out at 70 °C for 15 h under nitrogen atmosphere. After concentrating the reactant by THF evaporation, the reactant was poured into petroleum ether to precipitate PDEA-OH. PDEA-OH was collected by filtration and was purified by repeated precipitation in petroleum ether from acetone. Polymer was isolated by freeze-drying from aqueous solution. For the second step of preparation of PDEA macromonomer, PDEA-OH was dissolved in acryloyl chloride (large excess), and the reaction was stirred at 40 °C for 2 h under nitrogen atmosphere. The purification process for the macromonomer followed the same process for PDEA-OH.

2.3. Characterization of the polymers

Fourier transform infrared (FTIR) spectroscopy was carried out with Nicolet Nexus 670 FTIR Spectrometer. The sample was prepared with the KBr pellet technique. ^{1}H NMR spectra were recorded on a Bruker-300 spectroscopy using $CDCl_3$ as the solvent and tetramethylsiliane (TMS) as the internal reference. The molecular weight of semi-telechelic PDEA-OH was determined by gel permeation chromatography (GPC, Water 515 pump with Waters 2410 refractive-index detector) using THF as the mobile phase and polystyrene as the standard.

2.4. Synthesis of P(DEA-co-AA) hydrogels

To synthesize the comb-type grafted P(DEA-co-AA) hydrogels, the DEA and AA monomers, PDEA macromonomer, cross-linker NNMBA, and initiator APS were dissolved in 3 mL of distilled water in a glass vial, and dry nitrogen gas was bubbled into the solution for 10 min to remove the dissolved oxygen. The polymerization was carried out at 20 °C for 24 h by injecting 20 μL TEMED (accelerator). After the reaction, the produced gel was cut into discs (13 mm in diameter and 3 mm in thickness), and gel discs were immersed in distilled water for 5 d at room temperature with water being changed twice every day to remove unreacted materials and allow the hydrogels to equilibrium. As a control, the normal-type P(DEA-co-AA) hydrogels were prepared and purified by the same method as described above without adding PDEA macromonomer. The feed compositions of the monomers and other reactants are listed in Table 1. The comb-type grafted P(DEA-co-AA) hydrogels and normal-type P(DEA-co-AA) hydrogels were denoted as GHs and NHs, respectively.

2.5. Preparation of buffer solutions with different pH

Hydrochloric acid/potassium hydrogen phthalate, sodium hydroxide/potassium hydrogen phthalate and sodium hydroxide/sodium dihydrogen phosphate were used to prepare buffer solutions with different pH ranges from 2 to 4, 4 to 6 and 6 to 8, respectively. Hydrochloric acid/potassium chloride and ammonium chloride/ammonium hydroxide were used to prepare solutions of pH 1.5 and 9.3, respectively. On the basis of the Donnan theory on the polymer swelling, one can expect that the swelling is dependent on salt concentration. In order to eliminate the influence of salt concentration, sodium chloride was used to adjust ionic strength to 0.1 mol L^{-1}. The pH of all solutions was determined by pHS-3B model pH meter.