Synthesis and Characterization of Thermosensitive and Supramolecular Structured Hydrogels

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ABSTRACT: New kinds of thermosensitive and supramolecular structured hydrogels were synthesized via copolymerization of *N*-isopropylacrylamide (NIPA) with photocurable and biodegradable polypseudorotaxanes as cross-linkers under UV irradiation. The polypseudorotaxanes were prepared by supramolecular self-assemblies of α-cyclodextrins threaded onto amphiphilic LA−PEG−LA copolymers end-capped with methacryloyl groups. The structure of the hydrogels was characterized in detail with FTIR, ^{1}H NMR, XRD, DSC, and TGA techniques. The analytical results have demonstrated that the channel-type crystalline structure of inclusion complexes (ICs) remains in as-obtained hydrogels. Their swelling behavior was measured gravimetrically in the temperature range from 22 to 67 °C. It was observed that the cross-linked hydrogel made of only the macromer guest shows also thermosensitive. However, this stimuli-responsive property disappears when α-CDs are threaded onto the polymeric backbone and reappears when PNIPA blocks are introduced. The theromsensitivity of these hydrogels could be modulated by changing the PNIPA content as well as the α-CD to macromer ratio.

Introduction

Recent advances in supramolecular chemistry are primarily associated with achievements in the study on self-assembly processes according to the guest−host type. Macrocyclic compounds are most often used as host molecules, among which cyclodextrins (CDs) have enjoyed the widest application.[1] CDs are a series of cyclic oligosaccharides consisting of six to eight glucose units, named α-, *β*-, and *γ*-CD, respectively, which possess internal hydrophobic cavities capable of accommodating various organic and polymeric compounds. Since the first report released in 1990 by Harada and colleagues that α-CD can form inclusion complexes (ICs) with poly(ethylene glycol) (PEG),[2] a wide variety of polymeric inclusion complexes based on CDs have been prepared and characterized.[3−8] Among the ICs ever reported, stimuli-responsive polyrotaxanes are of special interest. Many research groups have studied rotaxane-derived molecular shuttle in response to external stimuli, e.g., light, pH, and polarity of the environment.[9−14]

Meanwhile, hydrogels resulted from self-assemblies of CDs have drawn increasing attention, for both their intrinsic scientific value and their potential applications in various fields. These hydrogels can be divided into two categories according to their formation principle: physically and chemically cross-linked supramolecular structured hydrogels. A great deal of work has been conducted in this field by Yui,[15] Ritter,[16] Li,[17] and Tonelli[18] et al. Stimuli-responsive supramolecular structured hydrogels have been particularly interesting. Choi and co-workers have described the control of rapid phase transition induced by supramolecular complexation of *β*-cyclodextrin-conjugated poly(*ϵ*-lysine) with a specific guest, 3-trimethylsilylpropionic acid (TPA).[19] Huh and colleagues prepared a kind of hydrogel by means of inclusion complexation between PEG-grafted dextrans and α-cyclodextrins in aqueous media.[20] The formation of a rapidly induced thermoreversible hydrogel system based on inclusion complexation between PPG-grafted dextran and *β*-CD was also reported.[21] However, dextran as a polymeric backbone in those systems could not be degraded in human body. Therefore, hyaluronic acid (HA) was preferred over dextrin while preparing supramolecular structured hydrogels, which presented temperature- and pH-controlled hydrogelation.[22]

More recently, we have reported a novel gelation process, in which a physical hydrogel was first prepared by inclusion complexation of linear or star-shaped macromers of CL-PEG-CL and LA-PEG-LA having methacryloyl terminals with α-CDs, and subsequently a chemical cross-linked one was formed in situ under UV irradiation in the presence of a photoinitiator, leading to great improvement in hydrogel strength.[23−26] These cross-linked hydrogel polymers are expected to possess different physical and mechanical properties compared with classical polymers because of their topological architectures.[27] To develop a novel kind of stimuli-responsive hydrogels, we intended to incorporate poly(*N*-isopropylacrylamide) (PNIPA) into the hydrogels to make them thermosensitive. As well-known, PNIPA is a representative of stimuli-sensitive polymers exhibiting a lower critical solution temperature (LCST) around 32 °C in distilled water.[28,29] This kind of stimuli-sensitive supramolecular structured hydrogels has the potential to be used as tissue engineered scaffolds, biosensors in human body, and carriers of drug controlled delivery as well as in size-selective separation processes involving materials that can be denatured at high temperatures.[30]

Experimental Section

1.1. Materials. *N*-Isopropylacrylamide (NIPA) (Acros, Belgium), α-CD and stannous 2-ethylhexanoate (Sigma), and 2,2-dimethoxy-2-phenyl acetophenone (DMPA) (Fluka, Switzerland), methacrylic anhydride (Aldrich, USA), and 1-vinyl-2-pyrrolidone (Merck Schuchardt, Germany) were used as

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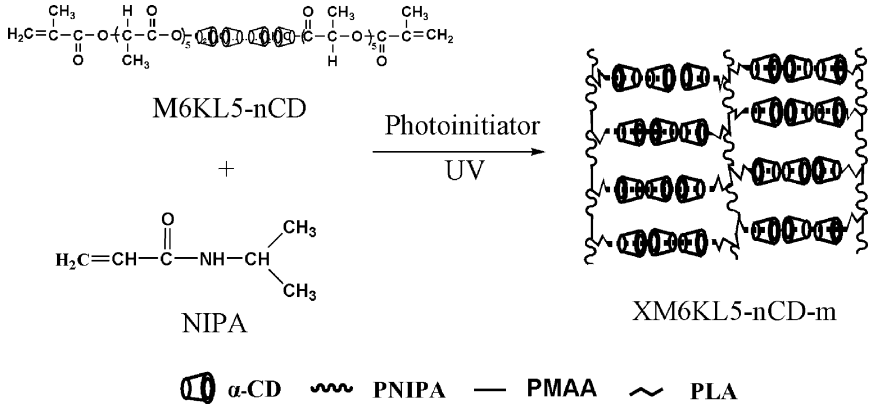
Scheme 1. Preparation Route for Thermosensitive and Supramolecular Structured Hydrogel



received. PEG-1000 (PEG 1K) and -6000 (PEG 6K) were imported from Japan and distributed domestically. L-Lactide (LA) was supplied by Fushun Tianyuan Biomaterials Co. Ltd., China. All other reagents used were of analytical grade.

1.2. Preparation of Photocurable Macromers. Hydroxyl-terminated copolymers of LA-*b*-PEG-*b*-LA were synthesized in toluene by the ring-opening polymerization of LA with PEG 6K as an initiator and $Sn(Oct)_2$ as a catalyst. Afterward, soluble macromers bearing methacryloyl terminals were prepared from the reaction of the copolymers with methacrylic anhydride in the same solvent added. The symbol H6KL*b* denotes the hydroxyl-terminated LA−PEG−LA copolymer, M6KL*b* the methacryloyl end-capped macromer, and XM6KL*b* the dried hydrogel after photocuring, where b stands for the degree of polymerization (DP) of l-lactide oligomer in the macromers. To ensure the solubility of the macromers in water, the value of *b* is controlled to equal 5 in this study.

As a typical example, the synthesis of the macromer M6KL5 was conducted as follows. To remove traces of water, 20 g of PEG 6K and 2.40 g of LA were dissolved in 150 mL of toluene in a round-bottomed flask with a magnetic stirrer. About 50 mL of toluene was distilled off using a water separator. A precisely weighed amount of 67 mg of stannous 2-ethylhexanoate was added, and the resultant mixture was refluxed at 120 °C for 10 h under a nitrogen atmosphere. The reaction was stopped by addition of a fixed quantity of water. Subsequently, 3.08 g of methacrylic anhydride was added. The mixture was again refluxed at 120 °C for 8 h under a nitrogen atmosphere. Then it was cooled to room temperature, and the product was precipitated in a 2:1 (v/v) mixture of diethyl ether with *n*-hexane, filtered, and dried in vacuo at 40 °C to constant weight to give M6KL5; yield 95%. FTIR/cm^{-1}: 2889 (CH_2, CH_3), 1759 (C=O), 1109 (C−O), 1643 (C=C). ^{1}H NMR/ppm (DMSO-d_6): δ 6.10 (s, 2 H, *H*-C=C), 5.77 (s, 2 H, *H*-C=C), 5.12−5.20 (m, 10H, *H*-C(CH_3)C=O), 4.18−4.22 (m, 6H, $-OCH_2CH_2OCO-$, $H_2C=CH(CH_3)COOCH(CH_3)CO$), 3.44−3.56 (m, 540 H, $-OCH_2CH_2O-$), 1.89 (s, 6 H, C=C−CH_3), 1.43−1.49 (m, 30 H, C (CH_3) C=O).

1.3. Preparation of Polypseudorotaxanes. A saturated aqueous solution containing a stoichiometric amount of α-CDs was added to a certain volume of 20% (w/w) macromer solution in water at room temperature. The resultant mixture was sonicated for 10 min and then stood for gelation. A gelation occurred to yield a physical gel network because of the supramolecular self-assemblies between α-CDs and the macromers. The gel formed was directly freeze-dried to give rise to polypseudorotaxanes.

1.4. Formation of Thermosensitive and Supramolecular Structured Hydrogels. When a gelation occurred to yield a physical gel, a certain amount of NIPA and a photoinitiator solution of DMPA in *N*-vinylpyrrolidone (10 mg/mL) were added, respectively. The resultant mixture was stirred and then sonicated for 10 min to ensure NIPA dissolving. Afterward, it was exposed to 365 nm LWUV lamp of 20 W (Institute of Electric-Light Resources, Beijing) for a fixed time span. The supramolecular self-assembly and photocuring processes are illustrated in Scheme 1.

Table 1. Elemental Analytical Result of the Dried Hydrogel Samples

	calculated			found		
composition	N	C	H	N	C	H
XM6KL5-30CD-50	1.68	48.67	7.07	2.41	49.60	7.41
XM6KL5-30CD-100	2.96	50.47	7.38	3.66	51.21	7.82
XM6KL5-30CD-150	3.96	51.88	7.64	4.46	52.55	8.02

To leach out unthreaded α-CDs as well as ICs presumably entrapped in the network, the photocured hydrogel was completely immersed in both DMSO and water for every 3 days at room temperature. The solvent was refreshed daily. Finally, the hydrogel was dried at 70 °C in vacuo to constant weight.

For the sake of expression, the inclusion complex synthesized is designated as M6KL5-*n*CD, the photocured hydrogel made of it as XM6KL5-*n*CD, and in turn the photopolymerized thermosensitive and supramolecular structured hydrogel as XM6KL5-*n*CD-*m*, where *n* stands for a feeding molar ratio of α-CDs to macromer and *m* for that of NIPA to M6KL5. To afford a direct comparison, the corresponding hydrogel sample without α-CDs, denoted as XM6KL5-*m*, was also prepared. The homopolymer of PNIPA was synthesized via photopolymerization in water. In addition, a saturated polypseudorotaxane, named as 1K-10CD, was prepared from the self-assemblies of PEG-1000 with α-CD according to the reference.[2] The elemental analytical results of thermosensitive and supramolecular structured hydrogels are listed in Table 1.

1.5. Characterization. FTIR spectra were measured using Shimadzu IR Prestige-21 FTIR spectrometer at room temperature in the range from 4000 to 500 cm^{-1}, with a resolution of 2 cm^{-1} and 20 scans. Samples were prepared by well dispersing the complexes in KBr and compressing the mixtures to form disks. The ^{1}H NMR spectra were recorded at room temperature on a Bruker ARX 400 NMR instrument with DMSO-d_6 as solvent and tetramethylsilane (TMS) as internal standard.

Gel permeation chromatography (GPC) analysis was carried out with a chromatographic system equipped with a Waters 1515 isocratic HPLC pump and a Waters 2414 refractive index detector. Three columns were in series (Waters styragel HT3, HT4, and HT5, 7.8 × 300 mm). THF was used as eluent at a flow rate of 1.0 mL/min. Monodispersed polystyrene standards were used to obtain a calibration curve. Wide-angle X-ray diffraction (WAXRD) measurements were performed on powder and film samples using Panaltic X'pert PRO X-ray diffractometer. The radiation source used was Ni-filtered, Cu Kα radiation with a wavelength of 0.154 nm. The voltage was set to be 40 kV and the current 40 mA. Samples were placed on a sample holder and scanned from 4.5° to 50° in 2θ at a speed of 0.0017°/s.

Thermogravimetric analysis (TGA) of samples was made using a TA Instrument 2000 thermogravimetric analyzer at a heating rate of 20 °C/min with nitrogen used as purge gas. Differential scanning calorimetry (DSC) measurements were carried out using a DSC-200 PC (Netzsch, Germany) differential scanning calorimeter. The DSC thermograms covered

the temperature range of −60 to 150 °C at a scanning rate of 10 °C/min. Elemental analysis was carried out on an Elementar Vario EL elemental analyzer (Germany).

The swelling behavior of dried hydrogel was studied by a general gravimetric method. Dry films (a diameter of 10 mm and a thickness of 2 mm) were incubated in distilled water at 22 °C, and the swollen weight for each sample was recorded at regular time intervals after excess surface water was blotted carefully with moistened filter paper. The procedure was repeated until there was no further weight increase. While the temperature increased gradually the swollen hydrogel began to shrink. The temperature was maintained constant for 3 h after increasing by every 5 °C, and then the weight of shrunk hydrogel was measured. The swelling ratio (SR) was calculated by the following equation:

$$\mathrm{SR} = (m_1 - m_0) \times 100\%/m_0$$

where m_0 stands for the initial weight of dried gel and m_1 the weight of the swelling gel at a particular temperature and a prescribed time interval.

Results and Discussion

Preparation. In general, the terminal hydroxyl groups of PEGs can initiate the ring-opening polymerization of lactones and lactides in the presence of Sn(Oct)$_2$ to give hydrolytically labile polymeric or oligomeric extensions at each end of the central water-soluble domain. The resultant copolymers further react with (meth)acrylic anhydride or (meth)acryloyl chloride to yield photocurable macromers. A method for preparing photocurable and biodegradable macromers was developed by Hubbell,[31] but it seems to suffer from sustaining vacuum during the ring-opening polymerization and incomplete remove of the resultant triethylamine hydrochloride after end-capping the copolymers with acryloyl chloride. We found that these limits can be easily ruled out by means of one-pot synthesis at reflux temperature of toluene under a nitrogen atmosphere when methacrylic anhydride, rather than acryloyl chloride, was used. With acryloyl chloride as a terminal reagent, it is considered the resulting acrylate more susceptible to oxygen inhibition than methacrylate in the following photopolymerization.[32] Additionally, the GPC data showed the macromers obtained in this study have a unimodal peak with a polydispersity index below 1.08, indicating that they possess the target molecular weight and molecular structure.

α-CDs appeared to act as a powerful gelator, and a rapid physical gelation occurred at room temperature upon a photocurable macromer solution mixing with a saturated aqueous solution of α-CDs. The physical gels formed are thixotropic and reversible, and the sol−gel transition process can be readily controlled by adjusting the α-CD concentration and the composition of the photocurable macromers.[25,26] These gels were freeze-dried to give ICs or polypseudorotaxanes.

The preparation route of thermosensitive and supramolecular hydrogels is described in Scheme 1. In fact, the copolymerization took place in the heterogeneous phase, in which the intermediate ICs served as cross-linkers. Whether the monomer NIPA was dispersed well in the aforementioned physical gels was a key to ensure it incorporating into the matrix chains. Therefore, sound stirring, sonication, and standing operations were prerequisites before photopolymerizing the mixture. A perfect suspension was formed after these physical gels mixing with the monomer NIPA. When the resulting suspension was directly exposed to UV irradiation of $\lambda = 365$ nm at room temperature for a certain time in the presence of a photoinitiator, a rapid photopolymerization was in situ occurred in which the methacryloyl end groups and NIPA were initiated and cross-linked to yield the dimensionally stable hydrogel. As shown in Table 1, the content of nitrogen of all the hydrogel samples increases with the feeding molar ratio of NIPA to M6KL5, indicating the copolymerization proceeded between the ICs or polypseudorotaxanes and NIPA. However, the calculated values are always smaller than what was experimentally measured, which possibly resulted from some CDs leached out in the process of extracting the samples in DMSO and water. Taken together the following structural characterization and the swelling examination, it is proper to prepare the thermosensitive and supramolecular structured hydrogels via this technique.

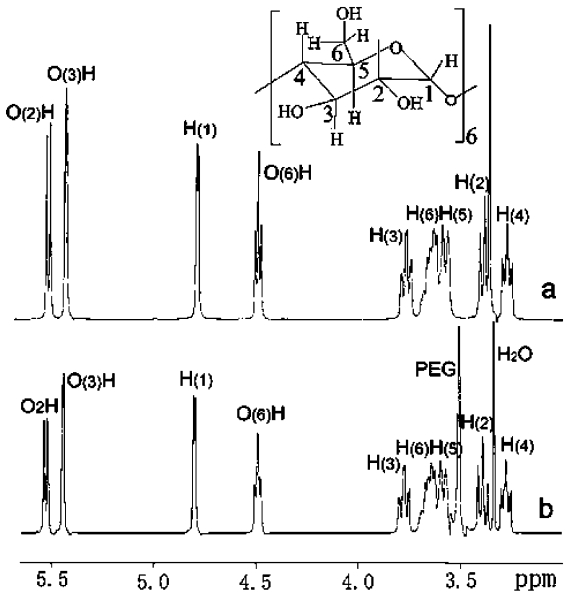


Figure 1. ^{1}H NMR spectrum of the inclusion complex M6KL5-30CD in DMSO-d_6.

Characterization. Upon formation of ICs, chemical shifts of protons in both host and guest molecules vary because their chemical environments change as a consequence of supramolecular interaction. In particular, the internal H(3) and H(5) protons in CDs are sensitive to the complexation effect than H(1), H(2), and H(4) protons located on the outside of the host cavity; therefore, the signals of protons H(3) and H(5) are shifted upfield.[6] Figure 1 shows the ^{1}H NMR spectra of free α-CD (a) and its inclusion complex M6KL5-30CD (b). As can be seen, there exist α-CD and PEG components in the inclusion complex. The peaks are assigned as O(2)H at δ 5.521−5.538, O(3)H at 5.441−5.447, H(1) at 4.791−4.799, and O(6)H at 4.797−4.805 ppm, respectively. Multiple resonances at δ 3.574−3.804 ppm are the chemical shifts of H(3), H(6), and H(5) protons and at 3.254−3.414 ppm those of H_2O, H(2), and H(4) protons. Compared with chemical shift of free α-CD, the largest peak shift of H(5) proton was observed in ICs. The peak shifts of H(3) and H(5) protons were also larger than H(1), H(2), H(4), O(2)H, O(3), and O(6) protons. In addition, the chemical shift of the methylene protons of PEG block in M6KL5 also changes upfield in ICs. This result suggests there is supramolecular interaction between the photocurable macromer and α-CDs.

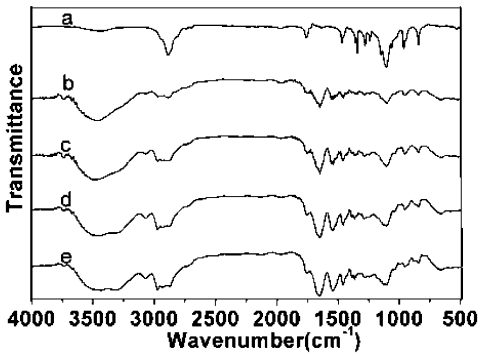


Figure 2. FTIR spectra of M6KL5 (a), XM6KL5-25 (b), XM6KL5-50 (c), XM6KL5-100 (d), and M6KL5-150 (e).

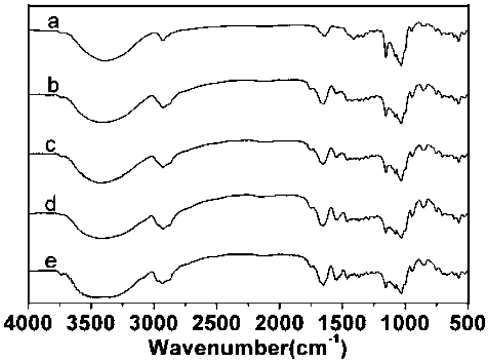


Figure 3. FTIR spectra of α-CD (a), XM6KL5-30CD-25 (b), XM6KL5-30CD-50(c), XM6KL5-30CD-100 (d), and XM6KL5-30CD-150 (e).

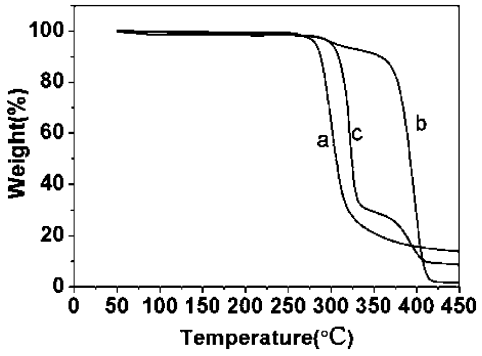


Figure 4. TGA curves of α-CD (a), M6KL5 (b), and M6KL5-30CD (c).

FTIR spectra of M6KL5 (a), XM6KL5-25 (b), XM6KL5-50 (c), XM6KL5-100 (d), and XM6KL5-150 (e) are presented in Figure 2. M6KL5 spectrum exhibits bands at 1103 and 1755 cm^{-1}, which are attributed to the C−O−C stretching mode and the characteristic stretching vibration of carbonyl, respectively. Upon introducing PNIPA segment, the observed is the characteristic absorbance band of PNIPA in the spectra. The amide I band (C═O stretch) emerges at 1651 cm^{-1}, the amide II band (N−H vibration) at 1547 cm^{-1}, and the methyl groups (in isopropyl group) at 1362−1386 cm^{-1}. Moreover, the intensity of the amide I band increases as the NIPA to M6KL5 molar ratio augments.

Furthermore, Figure 3 depicts the FTIR spectra of free α-CD (a), M6KL5-30CD-25 (b), M6KL5-30CD-50 (c), M6KL5-30CD-100 (d), and M6KL5-30CD-150 (e). The pure α-CD spectrum displays extremely strong band around 3380 cm^{-1}, assigned to the symmetric and asymmetric O−H stretching mode. The broad hydroxyl band is shifted to higher frequency at 3415 cm^{-1} owing

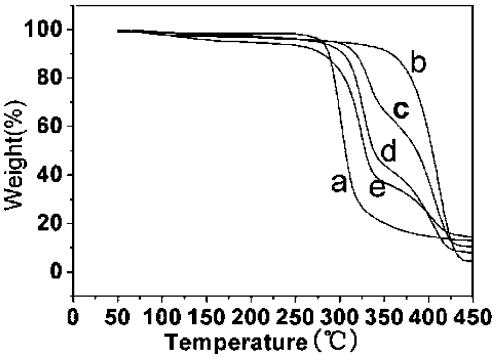


Figure 5. TGA curves of α-CD (a), XM6KL5-100 (b), XM6KL5-10CD-100 (c), XM6KL5-30CD-100 (d), and XM6KL5-60CD-100 (e).

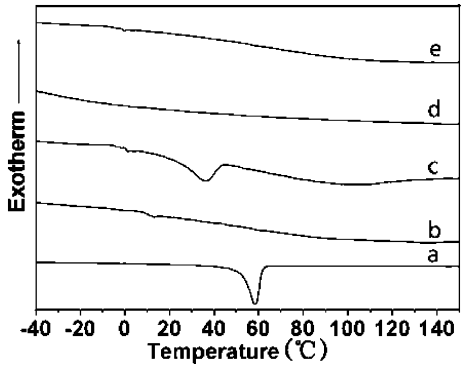


Figure 6. DSC curves of XM6KL5 (a), PNIPA (b), XM6KL5-100 (c), pure α-CD (d), and XM6KL5-30CD-100 (e).

to formation of ICs, which is most likely a result of the noncovalent interaction between O−H of α-CD and the macromer backbone. Not only the characteristic bands of PNIPA but also that of α-CD appear in the spectra of the dried supramolecular structured hydrogel samples. Moreover, there are evident differences in the positions and intensities of the spectra between free α-CD and free M6KL5-m (c) in Figure 2, suggesting a supramolecular interaction indeed existed rather than a simple physical mixture of them.

TGA thermal analysis is a powerful technique from which the supramolecular interaction between host and guest molecules in ICs can be determined, and the host−guest ratio can also be evaluated. The supramolecular structured gel undergoes a two-step thermal degradation process. The first step is mainly attributed to the decomposition of α-CDs, while the second mainly to that of the guest copolymer. Here, the temperature is set at which 10% of mass loss has occurred as the decomposition temperature (T_d) to assess the thermal stability of the supramolecular structured hydrogels obtained from the physical and chemical cross-linking gelation.[33] As shown in Figure 4, the T_d values for free α-CDs (a) and M6KL5 (b) are 290 and 358 °C, respectively. Upon forming ICs (c), this value for α-CDs increases by 19 °C, and that for M6KL5 by 23 °C, as compared with their free counterparts. TGA thermograms of dried gel XM6KL5-100 (b), XM6KL5-10CD-100 (c), XM6KL5-30CD-100 (d), and XM6KL5-60CD-100 (e) are shown in Figure 5. The T_d data for the component α-CDs and XM6KL5-100 are 318 and 365 °C in the supramolecular structured hydrogel XM6KL5-10CD-100 (c), 305 and 370 °C in XM6KL5-30CD-100 (d), and 293 and 384 °C in XM6KL5-60CD-100 (e), all higher than those for pure α-CDs and XM6KL5-100 (362 °C). This fact clearly

Table 2. Feed Composition of Different Dried Hydrogel Samples

code	composition	host/ mmol	guest/mmol	NIPA/ mmol	H_2O/g	concn NIPA/ mg/g	dose of initiator/μL	irradiation time/min
A_0	XM6KL5	0	0.17	0	4.54	0	50	10
A′	XM6KL5-30CD	0.6	0.02	0	4.54	0	50	10
A_3	XM6KL5-10CD-100	0.6	0.06	6	5.64	90	46	10
A_3'	XM6KL5-100	0	0.06	6	5.64	90	46	10
B_1	XM6KL5-30CD-25	0.6	0.02	0.5	4.54	12	50	10
B_2	XM6KL5-30CD-50	0.6	0.02	1	4.54	25	50	10
B_3	XM6KL5-30CD-100	0.6	0.02	2	4.54	50	50	10
B_4	XM6KL5-30CD-150	0.6	0.02	3	4.54	75	50	10
B_3'	XM6KL5-100	0	0.02	2	4.54	50	50	10
C_3	XM6KL5-60CD-100	0.6	0.01	1	4.27	26	47	10
C_3'	XM6KL5-100	0	0.01	1	4.27	26	47	10

implies that the thermal stability of individual component is substantially improved as long as an inclusion complex is formed between them. In addition, this two-step weight loss behavior can be used to estimate the ratio of still threaded α-CDs to the copolymer in the supramolecular structured hydrogels. The molar ratios of the threaded α-CDs to XM6KL5-100 in the samples of XM6KL5-10CD-100, XM6KL5-30CD-100, and XM6KL5-60CD-100 are 10, 27, and 43, respectively. Although there is a partial overlap of two weight-loss steps, this method is appropriate to evaluate the amount of α-CDs threaded onto the hydrogel network chains.

Figure 6 shows the DSC curves of XM6KL5 (a), PNIPA (b), XM6KL5-100 (c), α-CD (d), and XM6KL5-30CD-100 (e). There is a distinct endothermic peak at 59 °C in the sample XM6KL5, corresponding to the melting point of PEO block crystalline. For PNIPA, a fluctuation is observed at 12 °C, probably resulted from the glass transition temperature. Regarding XM6KL5-100, the melting point of PEO block crystalline shifts to a lower temperature, which is absent upon forming ICs as depicted in curve (e). This clearly indicates the PEO blocks have been included in the channel of the host α-CD lattice so as to impede the crystalline phase formation.

The XRD patterns of pure α-CD (a), M6KL5 (b), XM6KL5-100 (c), M6KL5-30CD (d), PEG1K-10CD (e), and XM6KL5-30CD-100 (f) are given in Figure 7. The diffraction peaks of pure α-CD appear at 12.31°, 13.92°, and 22.02°, respectively. Meanwhile, the macromer M6KL5 presents two strong peaks at 19.31° and 23.49°. Since a diffraction pattern of a physical mixture is simply the superposition of each crystalline component,[34] the diffractogram of the physical gel M6KL5-30CD makes the diffraction pattern rather different from that of either M6KL5 or α-CD. This is a significant evidence for a different type of the crystalline structure formed in the inclusion complex of M6KL5 with α-CD. Meanwhile, the pattern of M6KL5-30CD is quite similar to that of PEG1K-10CD, which had been proved to possess a tubular or channel-type crystalline structure.[2] Therefore, M6KL5-*n*CD also assumes this crystalline structure as such. The main sharp reflection peak at $2\theta = 19.98°$ ($d = 4.45$ Å) represents the characteristic peak of the formed channel-type crystalline structure of necklace-like ICs. Besides, the diffractogram of XM6KL5-30CD-100 shows a pattern quite different from those of the host α-CDs and the guest XM6KL5-100 (c). Thus, it can be deduced that there still exists the channel-type crystalline structure in the thermosensitive and supramolecular structured hydrogels. After forming these thermosensitive hydrogels, however, the main characteristic peak shifts slightly to around $2\theta = 19.72°$ ($d = 4.60$ Å).

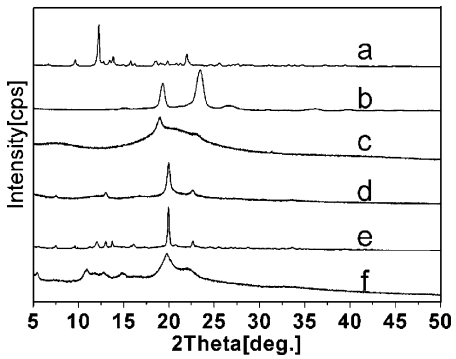


Figure 7. XRD patterns of pure α-CD (a), M6KL5 (b), XM6KL5-100 (c), M6KL5-30CD (d), PEG1K-10CD (e), and XM6KL5-30CD-100 (e).

Swelling Behavior of the Hydrogels. According to feed compositions shown in Table 2, a series of hydrogels were prepared and their swelling ratios were measured in distilled water at 22 °C. After reaching the swelling equilibrium, these hydrogels were left at 27, 32, 37, 42, 47, 52, 57, 62, and 67 °C in turn in the thermostatic water bath for 3 h before measuring the swelling ratio changes.

As depicted in Figure 8, the hydrogel made of pure macromer M6KL5 has the higher SR than the corresponding supramolecular structured hydrogels. Interestingly, the SR of these supramolecular structured hydrogels is found to increase with the increasing content of NIPA. Figure 9 shows that the SR is also directly correlated with the concentration of solutions used to prepare hydrogels. When the NIPA to M6KL5 molar ratio keeps constant, the SR of the hydrogel increases with the decreasing concentration of solution. On the other hand, the equilibrium water uptakes

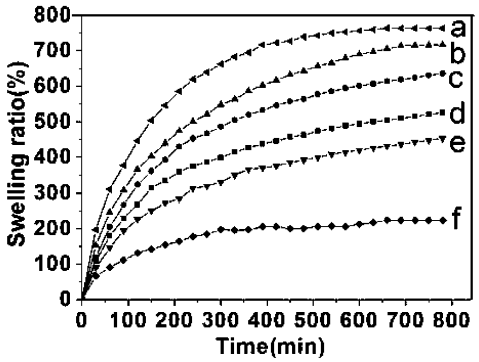


Figure 8. Swelling kinetics of different hydrogels measured gravimetrically in distilled water at 22 °C: (a) XM6KL5, (b) XM6KL5-30CD-150, (c) XM6KL5-30CD-100, (d) XM6KL5-30CD-50, (e) XM6KL5-30CD-25, and (f) XM6KL5-30CD.

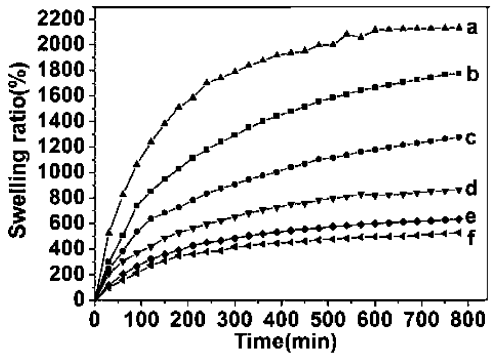


Figure 9. Swelling curves of different hydrogels at 22 °C (code given in Table 2): (a) C_3', (b) B_3', (c) A_3', (d) XM6KL5-10CD-100, (e) XM6KL5-30CD-100, and (f) XM6KL5-60CD-100.

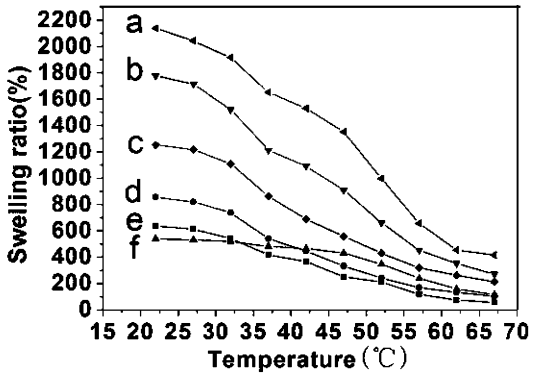


Figure 10. Swelling curves of hydrogels at different temperatures (code given in Table 2): (a) C_3', (b) B_3', (c) A_3', (d) XM6KL5-10CD-100, (e) XM6KL5-30CD-100, and (f) XM6KL5-60CD-100.

decrease with the increasing amount of α-CDs threaded onto the network chains. It is most likely due to the fact that the channel-type crystalline structure formed by the self-assemblies of α-CDs impairs water to enter the hydrogel matrix.[24]

The temperature dependence of the swelling ratios of the hydrogels from 22 to 67 °C with a same amount of NIPA added is shown in Figure 10. It presents two different stimuli-responsive trends related to the composition with and without α-CDs. For the sample coded as A_3', B_3', and C_3' as listed in Table 2, the lower the whole concentration of solution involved, the more significant changes the SR would have with the temperature. Additionally, the temperature sensitivity is highly correlated with the amount of α-CDs threaded on the hydrogel network chains. The more the amount of α-CDs incorporated, the less markedly varies the SR with the temperature.

To detect the thermosensitivity of hydrogels at varying temperatures, the swelling behavior of the samples containing the same amount of α-CDs is profiled in Figure 11. Surprisingly, the first observation was that the hydrogel resulted from only the macromer guest, i.e., XM6KL5, also showed thermosensitive. This stimuli-responsive property disappeared when α-CDs were threaded onto the polymeric backbone, as seen in the sample XM6KL5-30CD. It reappeared when PNIPA blocks were introduced. Moreover, the longer the PNIPA block, the more thermosensitive is the hydrogel. For the sample XM6KL5-30CD-150 and XM6KL5-30CD-100, their SR curves cross that of XM6KL5-30CD in the vicinity of 50 °C and continue to go down with rising temperature. Meanwhile, the SR of the sample XM6KL5-30CD-50 goes below the curve of XM6KL5-30CD at about 62.5 °C. Such fact implies that α-CDs threaded onto the hydrogel network chains could be subjected to a strong pressing action caused by the collapse of PNIPA blocks. Consequently, the PNIPA blocks are expected to work as the driving force to cause the α-CDs to move along the polymer chains following the temperature up or down. Furthermore, a great number of hydroxyl groups exist in each α-CD threaded onto the polymer backbones, which can be used as active positions for cell recognition and further chemical modifications. Hence, these hydrogels can be regarded as promising smart biomaterials used for tissue engineered scaffolds, biosensors in human body, and carriers of drug controlled release.

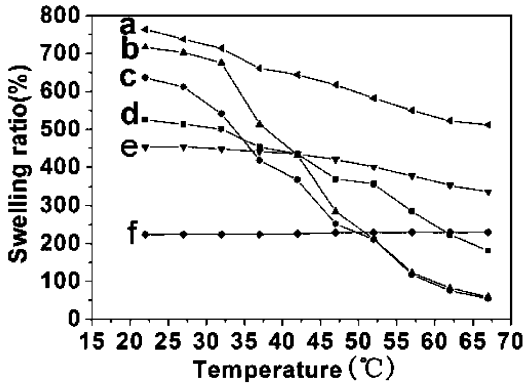


Figure 11. Temperature dependence of equilibrated swelling ratios of hydrogels in the temperature range from 22 to 67 °C: (a) XM6KL5, (b) XM6KL5-30CD-150, (c) XM6KL5-30CD-100, (d) XM6KL5-30CD-50, (e) XM6KL5-30CD-25, and (f) XM6KL5−30CD.

Conclusions

In this study, a novel type of hydrogel with both supramolecular structure and thermosensitive nature was synthesized via copolymerization of NIPA with photocurable and biodegradable polypseudorotaxanes as cross-linkers. The channel-type crystalline structure of inclusion complexes comprising α-CDs threaded onto the macromer chains was found to remain in the hydrogels after copolymerization. Their stimuli-responsive property can be tailored by changing the content of PNIPA as well as the ratio of α-CD to macromer. What is more, the PNIPA blocks are expected to work as the driving force to cause the CDs to move along the macromer chains following the temperature up or down. The potential biomedical applications of these thermosensitive and supramolecular structured hydrogels in tissue engineered scaffolds, biosensor in human body, and carriers of drug controlled release are now under investigations.

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