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ORIGINAL RESEARCH

Preparation and swelling behavior of pH/temperature responsive semi-IPN hydrogel based on carboxymethyl xylan and poly(*N*-isopropyl acrylamide)

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Abstract In this study, carboxymethyl xylan was synthesized from wheat straw xylan and then pH/temperature dual-responsive hydrogels based on the carboxymethyl xylan (CMX) and poly(*N*-isopropylacrylamide) (PNIPAm) were firstly synthesized through semi-interpenetrating polymer network synthetic route. The temperature-responsive behavior was investigated by swelling experiment and DSC test, showing that the CMX content played an important role in the phase transition, and the CMX–PNIPAm hydrogel had higher pH sensitivity compared with PNIPAm hydrogel. The CMX content and the interconnected pore structure within the network improved the swelling, and the CMX–PNIPAm hydrogels had a high de-swelling rate. Addition of AAc in the hydrogels can improve pH sensitivity but decrease temperature sensitivity. The excellent swelling reversibility in response to temperature was verified through the oscillatory experiments of swelling and de-swelling. It is expected that the CMX–PNIPAm hydrogels could be used in biomedical fields as an intelligent material, especially for drug delivery.

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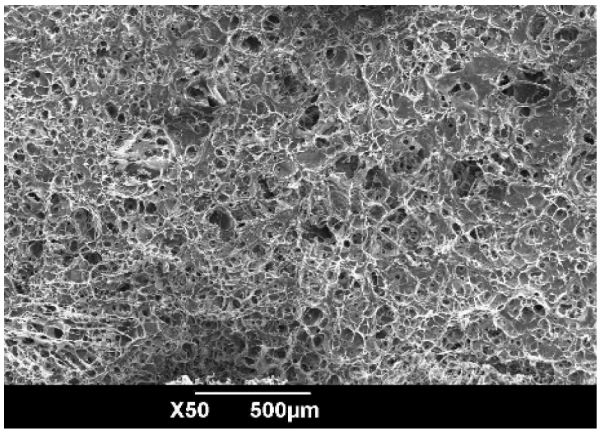
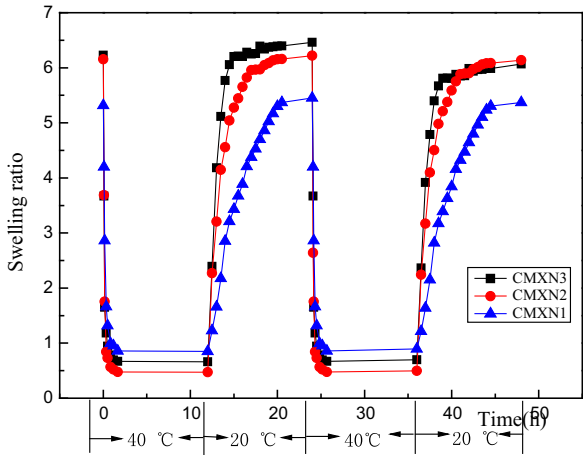
Graphical abstract





Keywords Hydrogel · Carboxymethyl xylan · Semi-interpenetrating · Reversible response

Abbreviations

BIS	*N*-Methylene bisacrylamide
CMX	Carboxymethyl xylan
^{13}C-NMR	C-Nuclear magnetic resonance
DSC	Differential scanning calorimetry
FT-IR	Fourier transform infrared spectroscopy
GC	Gas chromatography
LCST	Lower critical solution temperature
PNIPAm	Poly(*N*-isopropylacrylamide)
SEM	Scanning electron microscopy
semi-IPN	Semi-interpenetrating polymer network

Introduction

Xylan, as the major component of hemicelluloses, is one of the most abundant polysaccharides in plants. It is widely used in many fields, for example, to produce xylitol as a functional food additive (Ebringerova et al. 2005) and the biomedical field for drug delivery (Sun et al. 2013). In addition to the advantages of biodegradability and low-toxicity, many beneficial effects of xylans have been reported, including anti-inflammatory effects, immune function, bone tissue regeneration, and so on (Ebringerová and Heinze 2000; Bush et al. 2016). It is reported that carboxymethylation of polysaccharides is a functional modification to prepare bio-based materials with useful properties, such as films, emulsions, suspensions, and for binding and maintaining water (Heinze 1998). Some polysaccharides have been modified into carboxymethyl polymer for preparing intelligent polymeric hydrogels, such as carboxymethyl chitosan (Guo and Gao 2007; Azarova et al. 2016) and carboxymethyl cellulose (Ma et al. 2007; Dai et al. 2018; Bajpai and Shrivastava 2005). The carboxymethylation of xylan was also investigated because carboxymethyl xylan (CMX) is more hydrophilic than xylan and can decrease the surface tension of water (Petzold et al. 2006a, b). CMX can be used to synthesize pH-sensitive hydrogel because of the presence of carboxyl groups; however, CMX-based hydrogel has not been studied.

Intelligent polymeric hydrogels have become a research interest because of their sensitivity to environmental stimuli. The preparation of smart hydrogel is one of the study focuses, due to its widespread applications in many fields, such as drug delivery system (Huynh et al. 2009), cell encapsulation vehicle (Roy and Gupta 2003), tissue engineering scaffold (Lee and Mooney 2001; Jeong et al. 2002), and wound dressing (Razzak et al. 2001). Temperature sensitive hydrogels, especially PNIPAm gel, have attracted extensive interest, because the lower critical solution temperature (LCST) is close to the human body temperature. Semi-interpenetrating polymer network (semi-IPN) technology is an important method to prepare thermo- and pH-sensitive hydrogels because of its advantages, such as excellent sensitivity to

stimulus (Guo and Gao 2007) and high mechanical strength (Lee and Chen 2001). In recent years, a particular interest in the preparation of the semi-IPN hydrogels is the introduction of natural polysaccharides (Dragan 2014; Sun et al. 2016). The incorporation of natural polysaccharides could adjust the LCST of the hydrogels and improve the biodegradability and biocompatibility of the hydrogels as well as the swelling and de-swelling rate (Zhang et al. 2005a, b). A variety of natural polysaccharides have been used to achieve these excellent performances, such as carboxymethyl chitosan (Guo and Gao 2007), carboxymethyl cellulose (Ma et al. 2007), sodium alginate (Zhang et al. 2005b), dextran (Zhang et al. 2004b), konjac glucomannan (Liu et al. 2010), and kappa-carrageenan (Chen et al. 2009).

Xylan-based hydrogels have attracted more and more attention of researchers in recent years. Bush et al. (2016) have prepared a hemicellulose xylan/chitosan composite hydrogel, and the thermal-responsive and injectable composite hydrogel, which is liquid at room temperature and gels at physiological temperature, was suitable for the use of bone tissue regeneration. Xylan-based temperature/pH sensitive hydrogels were also prepared for controlled drug release (Gao et al. 2016). The semi-IPN hydrogels have been prepared by incorporating phosphorylated poly(vinyl alcohol) (P-PVA) into the hemicelluloses-g-poly(acrylic acid) polymeric network, where the P-PVA was uniformly dispersed and the strong hydrogen bonding interaction was occurred, leading to effective increase of thermal stability and compressive strength (Peng et al. 2014). Xylan/poly(-methacrylic acid) semi-interpenetrating network hydrogel was prepared, and the hydrogel presented porous structure, and the interconnected porous channels increased when the content of xylan was increased in the hydrogels (Sun et al. 2016). We have already gained some achievements in the study of xylan-based hydrogels. A xylan-based pH-sensitive and biodegradable hydrogel was prepared (Sun et al. 2013), and the hydrogel was used as a carrier for oral drugs because of the excellent pH-sensitivity and biodegradability. With acetylsalicylic acid as a model drug, the release dynamics of the drug-loaded hydrogels closed to zero-order drug release kinetics for 6 h. Moreover, the xylan/poly(acrylic acid) magnetic nanocomposite hydrogel (Sun et al. 2015) and a novel hemicellulose-based magnetic hydrogel (Li et al. 2014) were prepared. The prepared hydrogels exhibited porous structure, excellent thermal stability, pH-sensitivity, and good paramagnetic property.

In this paper, xylan was isolated from wheat straw and then modified by the carboxymethylation in ethanol/water medium with sodium monochloroacetate, and the obtained CMX was characterized by FT-IR and ^{13}C NMR spectroscopies. The CMX and poly(*N*-isopropylacrylamide) (PNIPAm) was used to synthesize pH/temperature dual-responsive semi-interpenetrating hydrogel. The pH/temperature responsive behaviors and the reversibility of swelling and de-swelling were investigated.

Experimental section

Materials

Wheat straw was collected from Changan Region in Xi'an city of China and ground to pass a 1 mm size screen. The xylan material was isolated from the wheat straw. *N*-isopropylacrylamide (NIPAm) and *N*,*N*-methylene bisacrylamide (BIS) were obtained from J&K Chemical LTD. Ammonium persulfate (APS), anhydrous sodium sulfite, and sodium monochloroacetate were purchased from Tianjin Fuchen Chemical Reagent Co. (China). Acrylic acid (AAc) was obtained from Shanghai Chemical Reagent Co. (China). All chemicals used were of analytical grade.

Preparation of pure xylan

Wheat straw powder was delignified with sodium chlorite under pH 4.0 (adjusted by acetic acid) at 75 °C for 2 h to obtain holocellulose. Hemicelluloses were isolated from the holocellulose using 10% KOH at 25 °C for 10 h with a solid to liquor ratio of 1:20 (g/mL). The obtained hemicelluloses contained 80.4 wt% xylose and 12.5 wt% arabinose (related to the total sugar content), which was determined by gas chromatography (GC) analysis.

To prepare pure xylan, the obtained hemicellulosic material was further treated with 0.05 M HCl at 50 °C for 4 h with a solid to liquor ratio of 1:20 (g/mL). Gas chromatography analysis showed that the obtained xylan contains 93 wt% xylose and 5 wt% arabinose. The xylose content was close to that material for

preparing carboxymethyl xylan used by Petzold et al. (2006a). The weight-average molecular weight of the xylan is 18,600 g mol^{-1}, which was determined by gel permeation chromatography (GPC) on a PL aquagel-OH 50 column (300 × 7.7 mm, Polymer Laboratories Ltd).

Synthesis of carboxymethyl xylan

The carboxymethylation of xylan was performed according to the conventional method for carboxymethylation of polysaccharides (Heinze and Pfeiffer 1999; Petzold et al. 2006a, b). Xylan sample (2.0 g) and NaOH (1.5 g) were added into a three-necked flask containing 10 mL distilled water for alkalization at 40 °C for 30 min. Next, 90 mL of ethanol/water mixture with a ratio of 9:1 (v/v) was added into the slurry medium. After the addition of sodium monochloroacetate (2.4 g) and sodium hydroxide (0.5 g), the reaction temperature was increased to 70 °C for 2 h. The reaction mixture was neutralized to pH 5.5, and the resulting product was collected by filtration and washed with 75% aqueous ethanol (v/v). The product was dried at 45 °C for 24 h in a vacuum oven.

The prepared CMX was dissolved in distilled water with a solid to liquor ratio of 1:20 (g/mL) at 50 °C for 2 h. The pH of the solution was adjusted accurately to 6.0, and then the CMX solution was poured in 3 volumes of ethanol for solid–liquid separation for 15 min. The supernatant liquid was filtered off, and the solid product was washed with 75% aqueous ethanol (v/v) for at least five times.

Characterization of CMX

FT-IR and ^{13}C NMR spectroscopies were applied to evaluate the chemical structure of carboxymethyl xylan. The dried sample was analyzed by FT-IR spectrophotometer (Nicolet 510) with KBr discs containing 1% finely ground sample. For ^{13}C-NMR spectroscopy, 100 mg of the sample was dissolved in 1 mL D_2O completely, and the solution was transferred into the NMR tube, and the NMR spectrum was recorded on a Bruker AMX 400 spectrometer at room temperature. The ^{13}C NMR spectrum of the CMX was measured by using the pulse program of 'zgig30', and 2000 scans was performed.

Synthesis of hydrogels

The CMX–PNIPAm semi-interpenetrating hydrogels were synthesized in aqueous solution using free radical initiator system, and Scheme 1 displays synthetic scheme of CMX–PNIPAm hydrogel. As listed in Table 1, various ratios of CMX and NIPAm were dissolved in distilled water. As the redox initiation system, 1 wt% APS and 3 wt% anhydrous sodium sulfite were added into the mixed solution with a rapid stirring speed, and then BIS was added slowly as the crosslinker. The prepared hydrogels were collected after the gelation was completed. PNIPAm hydrogel, xylan-PNIPAm, and CMX–PNIPAm/AAc were also prepared as the above described method, and the feed compositions are listed in Table 1. All hydrogels were cut into cubes (5x5x5 mm) and immersed in distilled water for 24 h to remove the residual monomers, and then the hydrogels were pre-frozen at − 20 °C and then freeze-dried at − 50 °C for 48 h.

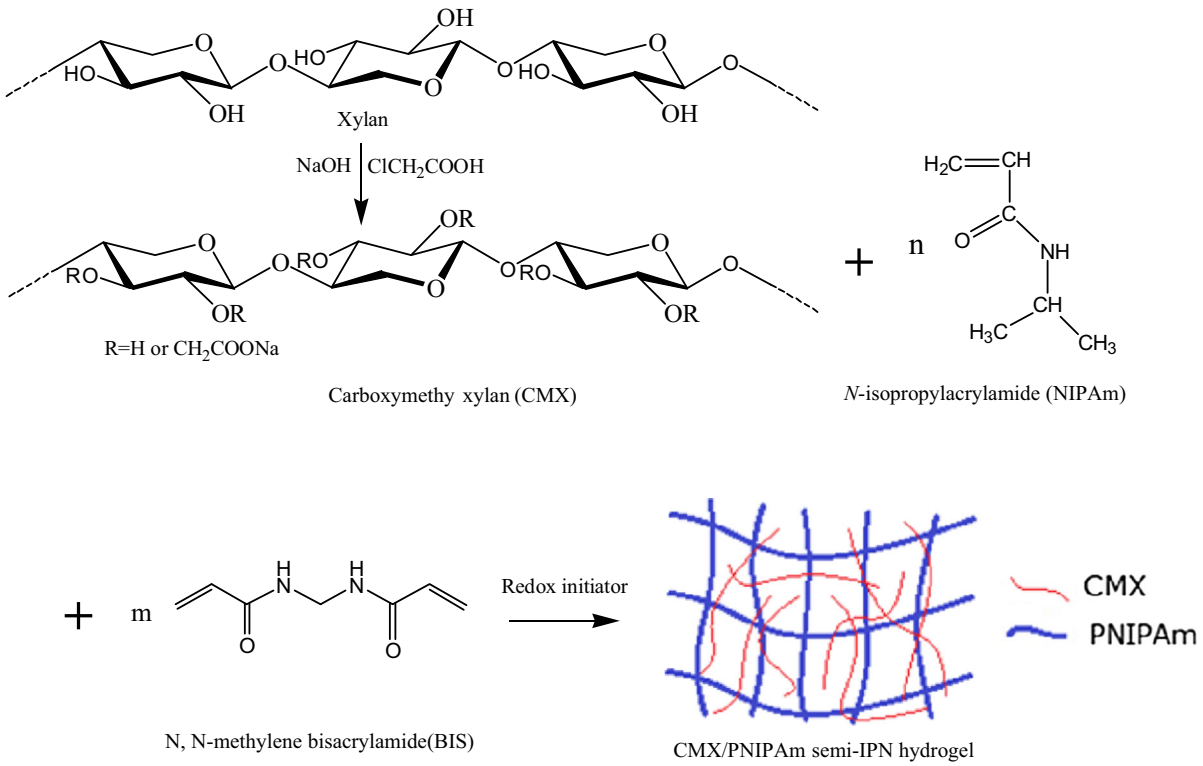
Characterization of the CMX–PNIPAm hydrogels

FT-IR spectra of the prepared hydrogels were recorded on a FT-IR spectrophotometer (Nicolet 510) after dried hydrogel samples were ground and pressed into KBr discs. The morphology of the hydrogels was observed by a scanning electron microscope instrument under different magnifications (SEM, S-2460 N, Hitachi, Tokyo, Japan) after the swollen hydrogels were freeze-dried to maintain the porous structure without any collapse.

Thermo-behavior of the hydrogels

The thermo-behavior of the hydrogels was studied through the determination of the equilibrium swelling ratios of the hydrogels at different temperatures. The swelling experiment was conducted in triplicate by conventional gravimetric method. The hydrogel samples were immersed into distilled water at the temperatures ranging from 20 to 50 °C. The swollen hydrogels were taken out and the surface water was removed using filter paper, and then weighed as soon as possible. The equilibrium swelling ratio (S_{eq}) was calculated as follows:

$$S_{eq} = (W_e - W_d)/W_d \quad (1)$$



Scheme 1 Synthetic scheme of CMX–PNIPAm hydrogel

Table 1 Feed compositions for synthesis of different hydrogels

Samples composition	PNIPAm	Xylan-PNIPAm	CMX–PNIPAm				CMX–PNIPAm/AAc	
	NIP[a]	XN[a]	CMXN1[a]	CMXN2	CMXN3	CMXN4	CMXNA1[a]	CMXNA2
NIPAm	100	83.3	90.9	83.3	76.9	71.4	76.9	71.4
Xylan	0	16.7	0	0	0	0	0	0
CMX	0	0	9.1	16.7	23.1	28.6	15.4	14.3
AAc	0	0	0	0	0	0	7.7	14.3

[a]Abbreviations of the PNIPAm hydrogel (NIP), xylan-PNIPAm hydrogels (XN), CMX–PNIPAm hydrogels (CMXN), and CMX–PNIPAm/AAc hydrogels (CMXNA), respectively

where the terms W_d is the weight of the dry hydrogel; and W_e is the weight of the swollen hydrogel at equilibrium state.

In order to characterize the thermo-behavior of the hydrogels, the DSC test (TA Instruments, USA) was conducted to determine the LCST of the hydrogels. The swollen hydrogel samples were analyzed at the temperatures ranging from 15 to 45° under N_2 atmosphere with a heating rate of 2 K min^{-1}.

pH-Response of the hydrogels

The pH sensitivity of the prepared hydrogels was tested in triplicate by gravimetric method in buffer solutions of desired pH (1.5–11.0) at 20 °C, and ionic strength was adjusted to I = 0.1 M using NaCl. The weight of the swollen hydrogel in different pH buffer solution was measured, and the equilibrium swelling ratio was calculated by the formula (1).

Swelling and de-swelling behaviors of the hydrogels

The swelling and de-swelling behaviors of the prepared hydrogels were also studied in triplicate by gravimetric method as above. All dried hydrogel samples were swelled in distilled water at 20 °C, and taken out at 30 min intervals and weighted after removing the excess surface water with a filter paper. The de-swelling behaviors of the swollen hydrogels was studied at 40 °C. At predetermined time intervals, the shrinking hydrogels were taken out and weighted after blotting the excess water on the surface of hydrogel. Water uptake and water retention at time t were defined as follows:

$$\text{Water uptake}\,\% = (W_t - W_d)/(W_e - W_d) \times 100\% \quad (2)$$

$$\text{Water retention}\,\% = (W_t - W_d)/(W_e - W_d) \times 100\% \quad (3)$$

where W_t is the weight of the hydrogel at swelling time t; and W_d and W_e are defined as above.

The temperature-dependent swelling reversibility of the CMX–PNIPAm hydrogels were determined by alternately immersing in distilled water at 40 °C and 20 °C. The swelling ratios of the hydrogels were measured by gravimetric method. The swelling and de-swelling test were carried out repeatedly with a period of 24 h.

Results and discussion

Characterization of CMX

The FT-IR spectra of xylan and carboxymethyl xylan are shown in Fig. 1. According to the previous studies (Fang et al. 2002; Sun et al. 2005), the absorption bands at 1614, 1464, 1252, 1040, and 892 cm^{-1} were associated with native hemicelluloses in spectrum (a). The prominent band at 1040 cm^{-1} was originated from the C–O–C stretching of pyranoid ring of xylan. The occurrence of small band at 1166 cm^{-1} was due to the presence of arabinose residues. There was a sharp band at 892 cm^{-1}, which arose from the C1 group frequency or ring frequency, and this band is characteristic of β-glucosidic linkages between the sugar

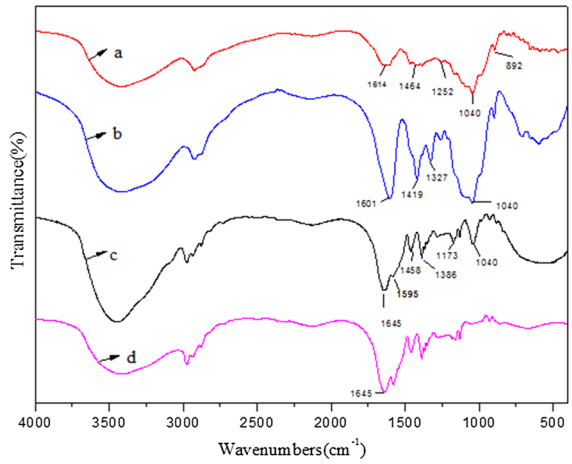


Fig. 1 FT-IR spectra of xylan (spectrum a), carboxymethyl xylan (spectrum b), CMX–PNIPAm hydrogel (spectrum c) and PNIPAm hydrogel (spectrum d)

units. The broad band at 1614 cm^{-1} was probably attributed to adsorbed water (Fang et al. 2002; Sun et al. 2005). IR spectrum (b) of CMX displayed the representative absorption peaks for carboxymethyl groups, and the strong absorption peak at 1601 cm^{-1} was attributed to the presence of COO^- group (Sun et al. 2013), and the $-CH_2$ scissoring and –OH bending vibration resulted in the two absorptions at 1419 and 1327 cm^{-1}, respectively. The characteristic absorptions of carboxymethyl xylan appeared obviously, confirming the successful carboxymethylation of xylan.

Figure 2 shows ^{13}C NMR spectrum of carboxymethyl xylan. The characteristic signals of the main chain of xylan are depicted between 104 and 75 ppm. The substituents on xylan chain resulted in a substantial downfield shift of the nearest carbon atom resonance and moderate upfield shifts of the signals of the neighboring carbon atoms (Tranquilan-Aranilla et al. 2012). The signals at 103.9, 78.6, 75.9, 75.0, and 65.2 ppm were assigned to C-1, C-4, C-3, C-2, and C-5, respectively, of the β-D-xylpyranosyl units of the xylan (Lawther et al. 1995). As shown in Fig. 2, the signal of the carboxylate groups appeared at 180.6 ppm (Petzold et al. 2006a; Lawther et al. 1995), and the observed splitting peak may be attributed to different possible positions of carboxymethyl substituents on the xylan polymer chain (Tranquilan-Aranilla et al. 2012). The signals at 58.7 ppm were assigned to the methylene carbon

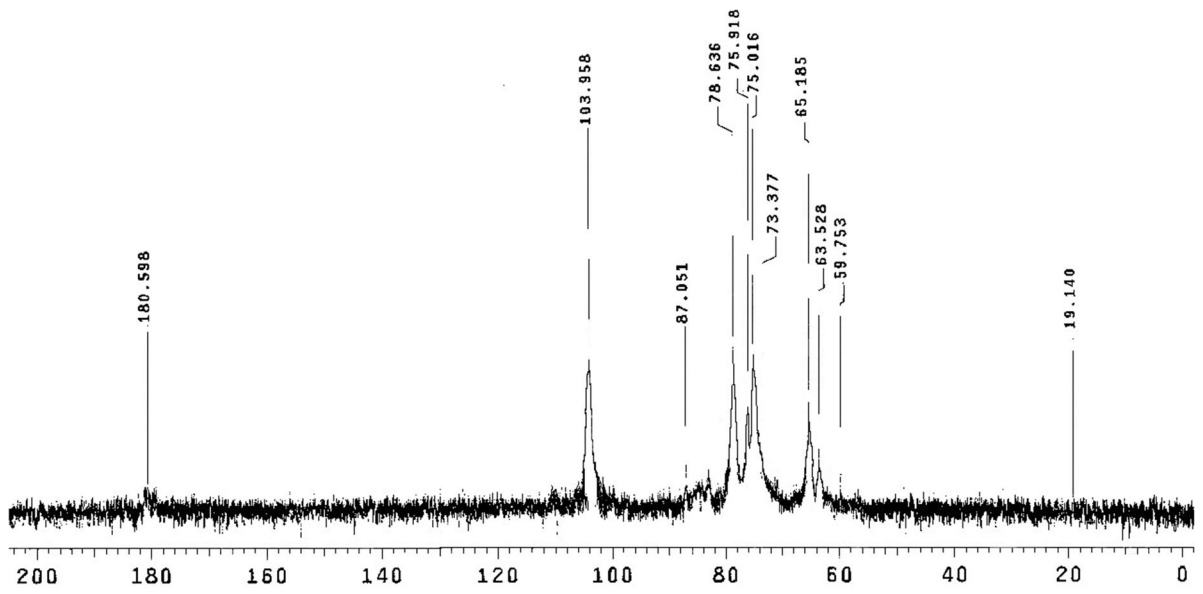


Fig. 2 ^{13}C NMR spectrum of CMX in D_2O

atom of the carboxymethyl groups. These observations confirmed the carboxymethylation of xylan, and the degree of substitution of anhydroxylose by carboxymethyl groups was found to be 0.78, which was determined by ^{1}H-NMR.

Characterization of the CMX–PNIPAm hydrogels

Compared with the IR spectrum of CMX (spectrum b) in Fig. 1, the spectra of CMXN2 hydrogel (spectrum c) and PNIPAm hydrogel (spectrum d) showed a new peak appearing at around 1645 cm^{-1} which was the representative absorption band of the carbonylamide and N–H stretching in PNIPAm. The two absorption bands at around 1458 cm^{-1} and 1368 cm^{-1} were attributed to the asymmetric bending vibration of $–CH_3$ groups and the symmetric vibration coupling of the double $–CH_3$ on the $–CH(CH_3)_2$, respectively. The peak at 1173 cm^{-1} was assigned to the contraction vibration of C–C in the $–CH(CH_3)_2$ groups. Because low amount of CMX was used for the synthesis of the CMX–PNIPAm hydrogels, the representative absorptions of the CMX at around 1600 cm^{-1} and 1040 cm^{-1} correspondingly weakened. Importantly, the characteristic absorptions of PNIPAm and CMX were found in the spectrum, and this suggested the successful synthesis of the CMX–PNIPAm hydrogel (Ma et al. 2007; Lee and Chen 2001).

The SEM photographs of the hydrogel (CMXN2) are showed in Fig. 3, and the surface of the hydrogel displayed a uniform morphology at × 50. From the SEM photographs at × 400, it was observed that different sizes of pores were formed within the hydrogel, and it is obvious from Fig. 3c that these pores were connected with each other, which resulted in the formation of the interconnected pore channels. The pore channels provided the way for the water to diffuse in and out of the hydrogels, resulting in the increases of the swelling and de-swelling rates of the hydrogels, and this also would improve the temperature sensitivity of the hydrogels and make the porous and thermo-sensitive hydrogels have potential applications as biomaterial (Teli et al. 2007), and the porous network could provide enough space and channels for the loading and releasing of drugs (Cheng et al. 2003).

Temperature dependence of the swelling ratio

As shown in Fig. 4, the swelling ratios of the CMX–PNIPAm hydrogels displayed obvious temperature dependence over the temperatures ranging from 20 to 50 °C. It was clear that the equilibrium swelling ratios of all hydrogels decreased with an increase in temperature without any exceptions, and a sharp decrease occurred at the transition temperature, thus the CMX–PNIPAm hydrogel demonstrated

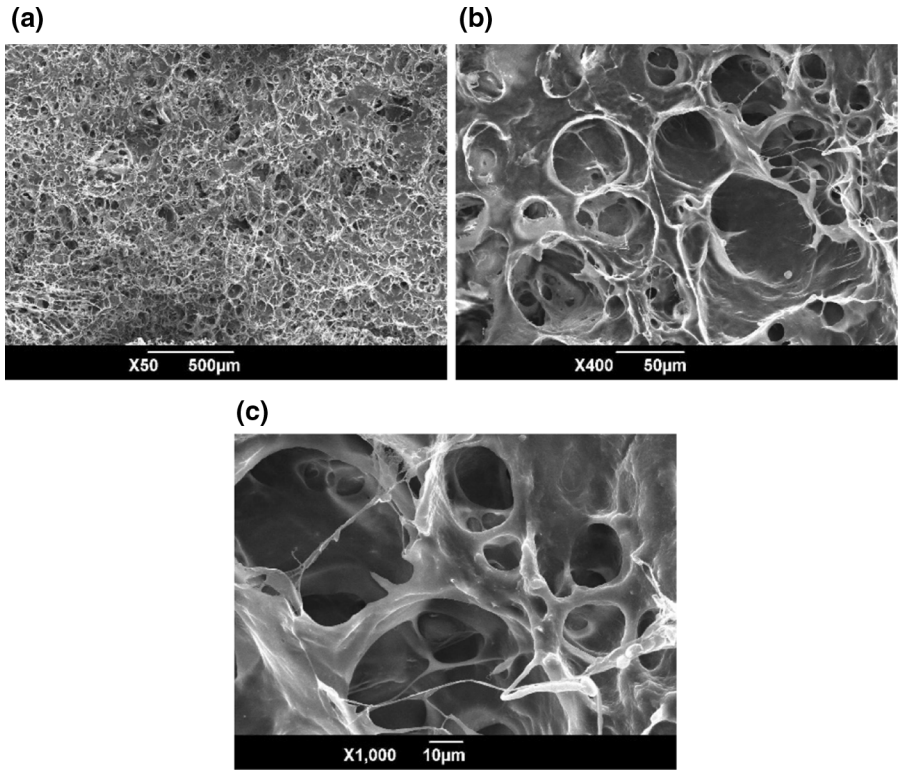


Fig. 3 SEM images of the CMXN2 hydrogel dried in a freeze dryer after swelling at 25 °C (**a** × 50; **b** × 400; **c** × 1000)

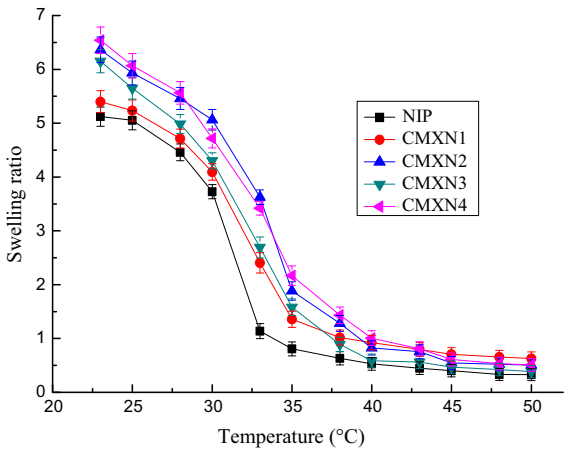


Fig. 4 The equilibrium swelling ratios of the CMX–PNIPAm hydrogels at different temperatures

temperature sensitivity. Compared to the pure PNIPAm hydrogel, the transition temperature of the CMX–PNIPAm hydrogels shifted to higher temperature. Upon increasing the CMX content, the shrinkage time of the hydrogels prolonged, suggesting that the composition of hydrogels played an important role in the phase transition behaviors of hydrogels.

It is well-known that the temperature sensitivity of PNIPAm hydrogel is attributed to the pendant groups, the amide (hydrophilic group) and iso-propyl (hydrophobic group) in the NIPAm unit, with a special hydrophilic and hydrophobic balance (Hirokawa and Tanaka 1984). At low temperature (below the LCST), hydrogen bonds formed between water molecules and hydrophilic groups on the polymer chain, leading to a great deal of water up-taking into the temperature sensitive hydrogel network. When the temperature increased (above the LCST), the hydrogen bonds became weakened, and hydrophobic interactions of the polymer chains became a leading role, and the polymer chains in hydrogels aggregated with each other through hydrophobic interactions among hydrophobic regions, and a great amount of water molecules absorbed in the network were supplanted, resulting in the volume phase transition and dramatic decrease of equilibrium swelling ratio. If the balance is broken by the change of the interactions between the hydrophilic or hydrophobic groups, the temperature of

the dehydration would fluctuate, giving rise to the shift of LCST of the hydrogels (Inomata et al. 1990; Shibayama et al. 1996). As CMX is more hydrophilic, the equilibrium swelling ratio of the CMX–PNIPAm hydrogels was relatively higher compared with PNIPAm hydrogel. Addition of the CMX broke the original balance between hydrophilic and hydrophobic groups, and the increase of the hydrophilicity enhanced hydrogen bond interactions; therefore, the transition temperature of the CMX–PNIPAm hydrogels increased with an increase in the CMX content. The phase transition behavior of the synthesized hydrogels was further studied by DSC test.

LCST of the CMX–PNIPAm hydrogels

According to Nemethy–Scheraga hydrophobic interaction theory, the thermodynamic properties of the free water in the hydrogel network can be characterized by DSC test. At the temperature below its LCST, the hydrophilic groups in hydrogels interact with water molecules through hydrogen bonds, and the enthalpy change ΔH of the swelling process is negative because of the formation of the hydrogen bonds. Meanwhile, these hydrogen bonds behave cooperatively around the hydrophobic groups to form a stable and orderly shell; therefore, the entropy ΔS becomes negative. From the formula $\Delta G_{water} = \Delta H_{water} - T\Delta S_{water}$, we can know that when the T rises up to Tv which make $\Delta G_{water} = 0$, the phase transition will occur with a continue increase in temperature (Liu et al. 2004). In this process, the absorbed water and hydrogel polymer are separated, and this is an endothermic process because of the destruction of a part of hydrogen bonds and the collapse of the shell, and this was reflected in the DSC curves in which an endothermic peak was present. LCST is determined as the intersecting point of two tangent lines from the baseline and slope of the endothermic peak, which corresponds to the phase transition temperature (Zhang et al. 2009).

The LCST of the CMX–PNIPAm hydrogels were determined by DSC as shown in Fig. 5. Compared to the xylan-PNIPAm hydrogel, the LCST of the CMX–PNIPAm hydrogels increased obviously, demonstrating that CMX is more hydrophilic than xylan and proving once again that the carboxymethylation of xylan was achieved. The LCST of the CMX–PNIPAm hydrogels were higher than PNIPAm hydrogel, and

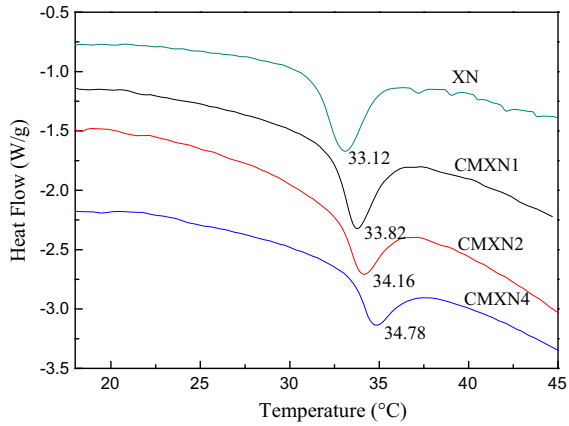


Fig. 5 DSC curves of the XN and CMXN hydrogels

the LCST increased in the order of CMNX1 < CMNX2 < CMNX4 with increasing CMX content in the hydrogels. Such a result is analogous to that observed by swelling ratio measurement as above. Because of the introduction of the hydrophilic groups, the coordination of hydrogen bonds within the polymer network strengthened and the bound water shell around hydrophobic groups was more stable, causing an increase in the enthalpy change ΔH and a decrease in the entropy ΔS during the swelling process (Liu et al. 2004), and the final performance showed an increase in the LCST.

pH-Sensitivity of the hydrogel

The equilibrium swelling ratios of the prepared hydrogels at different pH are shown in Fig. 6a, and the CMX–PNIPAm hydrogel had a relatively higher pH sensitivity compared with PNIPAm hydrogel, and the swelling ratio of the PNIPAm hydrogel only increased from 5.3 to 6.6 with increasing pH value from 1.5 to 12; however, the swelling ratio of the CMX–PNIPAm hydrogel increased from 4.7 to 6.7 with increasing pH value from 1.5 to 12. This phenomenon can be explained according to the descriptions of Ma et al. (2007) and Lee and Chen (2001), and –COOH groups of CMX can form hydrogen bonds with both the –OH groups in the CMX and the –NHCO in PNIPAm in acidic solution, and a large amount of hydrogen bonds between the inter- and intra-molecules could make the CMX–PNIPAm hydrogel shrink. In the higher pH solution, –COOH groups were negatively charged, and the

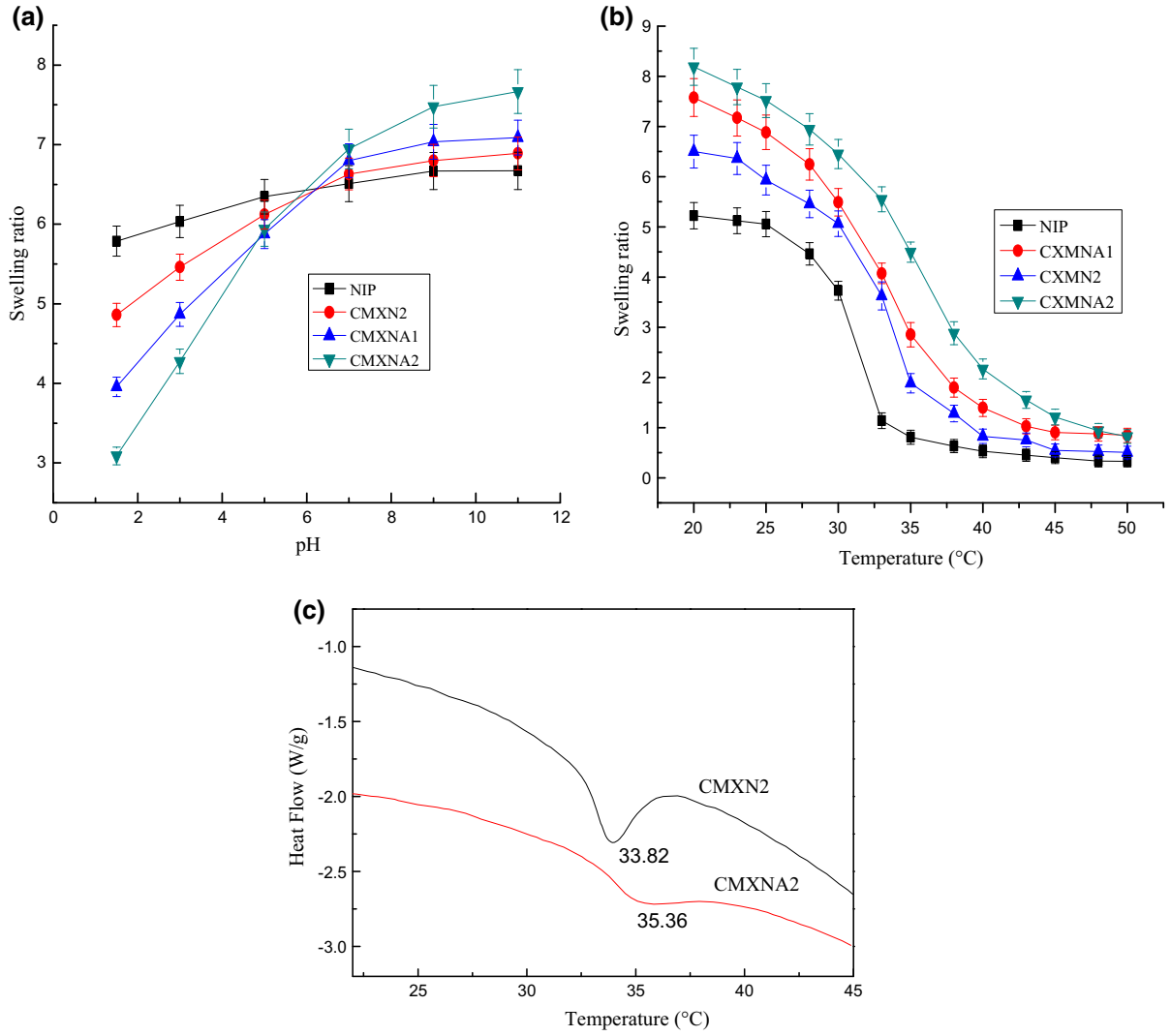


Fig. 6 The temperature/pH responsive behaviors of the CMXN hydrogel and CMXNA hydrogel. **a** Swelling ratios in different pH solutions; **b** swelling ratios at different temperatures; **c** DSC curves of the CMXN2 and CMXNA2 hydrogels)

hydrogen bonds in the network were dissociated, and the electrostatic repulsion between the $–COO^-$ groups made the hydrogels swell. It is well-known that the hydrophilic and ionic groups in polymer network have significant impact on the swelling behavior and play an important role in the swelling (Kim and Park 2004). In order to improve the pH sensitivity of the CMX–PNIPAm hydrogel, AAc was added, mixing with CMX and NIPAm, during the preparation of the hydrogels. As shown in Fig. 6a, the swelling ratio of the CMXNA2 hydrogel increased from 3.0 to 7.6 with increasing pH value from 1.5 to 12. The CMX–PNIPAm/AAc hydrogel was more sensitive to pH because of the formations of more hydrogen bonds at low pH and stronger electrostatic repulsion at high pH. Figure 6b shows the equilibrium swelling ratios of the CMX–PNIPAm/AAc hydrogels at different temperatures, and the swelling ratios of the hydrogels appeared a relatively increase at low temperature because of the presence of the ionizable –COOH group. With increasing the AAc content in the hydrogels, the phase transition temperature shifted to higher temperature and the transition region became broad, and the temperature sensitivity slightly decreased. The same conclusion was acquired from the DSC test of the CMX–PNIPAm/AAc hydrogels, as shown in Fig. 6c.

The addition of the hydrophilic AAc broke the balance between hydrophilic and hydrophobic groups, and the hydrophilic –COOH groups made the coordination of hydrogen bonds within the hydrogel enhance and the water shell around the hydrophobic groups became denser at low temperature. Therefore, the enthalpy change ΔH during the swelling process increased and the entropy change ΔS decreased, and then the LCST increased when the movement of the polymer chains tended to shrink and twist with increasing temperature. Dual sensitivities on the pH and temperature give the hydrogels wider applications, especially suitable for the applications in gastro-intestinal drug delivery.

Swelling behavior

The swelling behavior of the CMX–PNIPAm hydrogels with different CMX/NIPAm ratios at 20 °C are shown in Fig. 7. According to the previous study (Dang et al. 2011), it is known that the swelling process of hydrogels is controlled by three consecutive steps: the diffusion of water molecule into the polymer system, the relaxation of the hydrated polymer chains, and the expansion of the polymer network into aqueous solution. Strong inter/intra molecular interactions would greatly constrain the relaxation of the polymer chains, leading to the slower swelling rate for that hydrogel (Dang et al. 2011; Zhang et al. 2004a). The inter/intra molecular interactions in the CMX–PNIPAm hydrogels were stronger than that in the PNIPAm hydrogel, resulting in the lower swelling rate. The interactions in the polymeric network would be strengthened further from CMXN1 to CMXN2 because of an increase in CMX content; however, the swelling ratio of the CMX–PNIPAm hydrogels increased when the content of the CMX in the hydrogels increased to 23.1 wt%, and this phenomenon is consistent with the results of temperature sensitive hemicellulose-based hydrogels studied by Yang et al. (2011), and the result may be due to the minimum levels of CMX additions in CMXN1 and CMXN2 hydrogels. The swelling behavior is complexly controlled by the synergistic effect of the several factors, mainly including the interactions among the polymer in the hydrogels (Jeong et al. 2002; Dang et al. 2011), the pore size that influenced by the method of drying sample (Yang et al. 2011), and the chemical structure (Zhang et al. 2009; Kaneko et al. 1995). Owing to an increase in the hydrophilic CMX content, more hydrogen bonds with water molecules generated, leading to an expanded configuration of the hydrogel (Yin et al. 2007), thus a faster water uptake rate appeared (Yang et al. 2011). The superior hydrophilicity of the CMX and the interconnected pore structure within the network made the swelling ratio increase with increasing the CMX content.

De-swelling behavior

Figure 8 shows the de-swelling behaviors of the prepared hydrogels from the equilibrated swollen state at 20 °C to the shrunken state at 40 °C. All

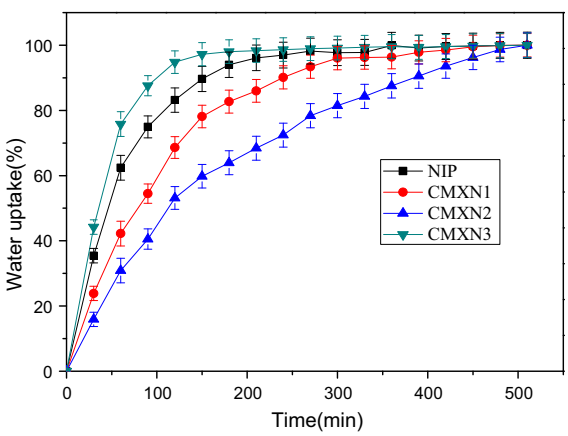


Fig. 7 Swelling behaviors of the CMX–PNIPAm hydrogels in distilled water at 20 °C

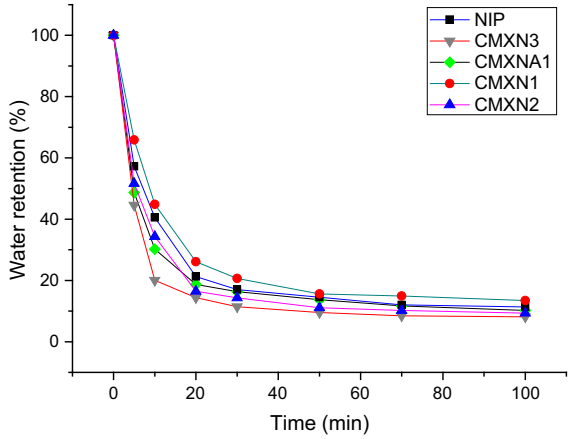


Fig. 8 De-swelling behaviors of the hydrogels in distilled water at 40 °C measured from the equilibrium swelling state at 20 °C

prepared hydrogels had fast de-swelling rates, and the de-swelling rate of the CMX–PNIPAm hydrogel (CMXN3) was higher than that of PNIPAm hydrogel; however, the de-swelling rate of the CMX–PNIPAm/AAc hydrogel was lower than that of the CMX–PNIPAm hydrogel (CMXN3) because of the incorporation of the non-thermo-responsive specie AAc into the hydrogels (Yang et al. 2011). Zhang and coworkers' study found that the de-swelling rate of the dextran–NIPAAm hydrogel was controlled by two opposite factors, weaken skin layer and dilution with the incorporation of the non-thermo-responsive species (Zhang et al. 2004b). When the CMX–PNIPAm hydrogels were immersed in water at 40 °C, the absorbed water in the outmost region of the hydrogel was extruded firstly and the hydrophobic interactions in this region became stronger, resulting in a rapid shrinkage of the outmost surface (Kim and Park 2004). The formation of a dense skin layer in PNIPAm hydrogel would limit the diffusion out of free water in the hydrogel network, and this lead to a slower de-swelling rate (Zhang and Zhou 2000). In contrast, the introduction of the hydrophilic CMX polymer into hydrogel networks could inhibit the formation of the dense skin layer, and such hydrophilic chains also would facilitate water molecule permeating from the gel interior (Lee and Chen 2001; Kim and Park 2004; Zhang et al. 2005b). As the same effect of the pore structure on the swelling process, the pore structure of the CMX–PNIPAm hydrogels provided channels for water diffusing out, and heat transfer from the hot water into the innermost of the hydrogel occurred rapidly because of the existence of the pores (Lee and Chen 2001), which resulted in a rapid phase separation.

Temperature-dependent swelling reversibility of the CMX–PNIPAm hydrogels

The oscillatory swelling experiments were conducted by alternately immersing swollen hydrogels in distilled water at 40 °C and 20 °C. The temperature-dependent swelling reversibility of the CMX–PNIPAm hydrogels is shown in Fig. 9, demonstrating that the hydrogels were evidently in response to the alternating temperature change between 40 °C (above the LCST) and 20 °C (below the LCST). When the swollen CMX–PNIPAm hydrogels at 20 °C were placed in distilled water at 40 °C, the hydrogels

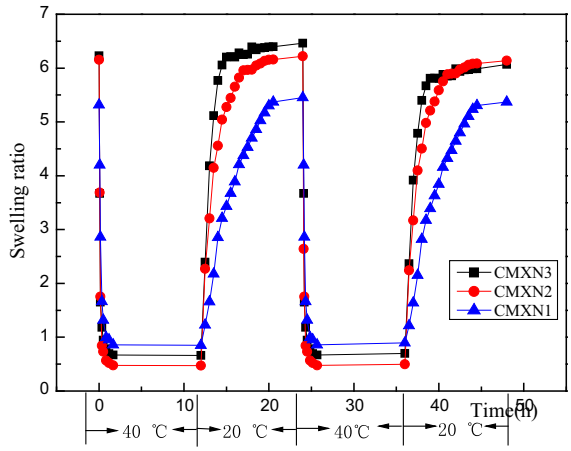


Fig. 9 The temperature-dependent swelling reversibility of the CMX–PNIPAm hydrogels at different times and temperatures

rapidly dewatered in the next time interval. It is obvious that water uptake and de-watering behaviors changed alternately, which would be due to CMX that facilitated water diffusion in the semi-IPN hydrogel (Ma et al. 2007). The above results showed that the synthesized CMX–PNIPAm hydrogels possessed a good reversible response to the change of temperature with an excellent reproduction. Thanks to its temperature responsiveness and reversibility, the CMX–PNIPAm hydrogels are expected to be an intelligent material for controlled drug release. Xylan-based temperature/pH sensitive hydrogel has been studied for drug release, and the drug encapsulation efficiency of the hydrogel reached to 97.60% and the cumulative release rate of acetylsalicylic acid was 90.12% and 26.35% in the intestinal and gastric fluid, respectively (Gao et al. 2016).

Conclusions

A pH/temperature dual-responsive semi-interpenetrating hydrogel was synthesized using CMX and PNIPAm in this study, and xylan was extracted from wheat straw and modified by carboxymethylation. The chemical structure and morphology of the synthesized hydrogels were studied by FT-IR and SEM, respectively. Compared to the pure PNIPAm hydrogel, the transition temperature of the CMX–PNIPAm hydrogels shifted to higher temperature. The lower critical solution temperature of the prepared hydrogels increased and the shrink-age extended with an

increase in CMX content. The superior hydrophilicity of the CMX and the interconnected pore structure within the network improved the swelling, and the CMX–PNIPAm hydrogels also had a high de-swelling rate. Addition of AAc in the hydrogels improved pH sensitivity but decreased temperature sensitivity. The hydrogels possessed a good reversible response to the change of temperature with an excellent reproduction. Attributing to temperature/pH responsiveness and reversibility, the synthesized CMX–PNIPAm hydrogel is expected to be used in biomedical fields as an intelligent material.

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