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SHORT COMMUNICATION

# Preparation and characterization of pH- and temperature-responsive semi-IPN hydrogels of carboxymethyl chitosan with poly (*N*-isopropyl acrylamide) crosslinked by clay

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**Abstract** A new kind of pH- and temperature-responsive semi-interpenetrating polymer network hydrogel based on linear carboxymethylchitosan (CMCS) and poly (*N*-isopropylacrylamide) (PNIPA) crosslinked by inorganic clay was prepared. The pH-and temperature-responsive behaviors, the deswelling kinetics, and the mechanical properties of the hydrogel were investigated. The hydrogels exhibited a volume phase transition temperature around 33 °C with no significant deviation from the conventional PNIPA hydrogels. The results of the influence of pH value on the swelling behaviors showed that the minimum swelling ratios of the hydrogels appeared near the isoelectric point (IEP) of CMCS, and when pH deviated from the IEP, the hydrogels behaved as polycations or polyanions. The novel hydrogels had much higher response rate than the conventional CMCS/PNIPA hydrogels. Moreover, the semi-IPN hydrogels crosslinked by clay could be elongated to more than 800% and the elongation could be recovered almost completely and instantaneously.

**Keywords** Hydrogel · Carboxymethylchitosan · poly(*N*-isopropylacrylamide) · clay · pH/temperature-responsive

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## Introduction

Poly(*N*-isopropylacrylamide) (PNIPA) hydrogel is one of the most attractive thermo-responsive hydrogels that has a volume-phase-transition temperature (VPTT) around 33 °C in aqueous solution [1, 2]. Owing to this unique property, it has been used in many fields such as controlled drug release [3], molecular separation [4], enzyme immobilization [5], and chemical valves [6].

PNIPA hydrogels are commonly prepared using an organic crosslinker such as *N*, *N*′-methylenebisacrylamide (BIS). However, these gels often lose their transparency with the increase of the crosslinker content [7] and they are too weak and brittle to withstand high levels of stress and strain needed for various applications [8, 9]. Also, the deswelling rate is known to be very slow due to the formation of a dense and thick skin layer, which prevents water molecules from migrating out of the gel [10, 11]. These disadvantages mainly arise from restricted molecular motions of PNIPA chains caused by the random arrangement of a large number of crosslinks.

Recently, Haraguchi et al. [12–16] reported a novel nanocomposite hydrogel consisting of PNIPA and inorganic clay, which were prepared without using any organic crosslinker. This kind of nanocomposite hydrogel exhibits high transparency, fast deswelling rate, and extraordinary mechanical properties with high strength and elongation at break in excess of 1,000%. They considered that a unique organic/inorganic network structure was formed by in situ free radical polymerization, in which the inorganic clay platelets acted as multifunctional crosslinkers with the PNIPA chains linked on them. The process of forming the network structure was also studied through changes in viscosity, optical transparency, X-ray diffraction, and mechanical properties.

The initiator (KPS), which has a divalent anion, was closely associated with the clay surface through ionic interactions in the initial reaction solutions. In the subsequent reaction, free radical polymerization in the redox system was initiated on the clay surface and thus polymer chains were attached to clay platelets through ionic or polar interactions. It was also revealed that the unique network could only be formed by free-radical polymerization in the presence of inorganic clay and was not realized by the other procedures such as mixing clay and PNIPA solutions.

The interpenetrating polymer network (IPN) technology is a useful route to prepare temperature and pH responsive hydrogels. It was also reported that interpenetration of two networks might lead to higher swelling and deswelling rates as well as better mechanical properties. Zhang [17, 18] reported that semi-IPN hydrogels based on linear sodium alginate (SA) and crosslinked PNIPA exhibited pH/temperature-responsive behavior and the deswelling rate in response to temperature was improved significantly. Lee [19] reported that PNIPA/chitosan semi-IPN hydrogels have higher mechanical strength in comparison with the homopolymer network. In these semi-IPN hydrogels, PNIPA were always crosslinked by an organic crosslinker.

Chitosan is a unique polysaccharide derived from deacetylation of chitin, which has been used in a wide variety of applications in biomedical field [20, 21]. Carboxymethylchitosan (CMCS), a derivative of chitosan by introducing –$CH_2COOH$ groups onto –OH along chitosan molecular chain, is an amphoteric polyelectrolyte containing both cationic and anionic charges. Therefore, CMCS can be used as a hydrophilic polymer with pH responsivity to prepare the pH/temperature-responsive hydrogels with improved deswelling rate [22, 23].

In this paper, we intend to prepared a new kind of pH and temperature responsive semi-IPN hydrogels based on linear CMCS and PNIPA using inorganic clay as a multifunctional crosslinker in place of the conventional organic crosslinker. As expected, the novel hydrogels thus prepared possess fast deswelling rate and excellent toughness compared with the conventional PNIPA/CMCS hydrogel prepared by chemical crosslinking.

## Experimental part

### Materials

*N*-isopropylacrylamide (NIPA) (TCI, Tokyo, Japan) was purified by recrystallization from cyclohexane/toluene (60/40, v/v) to remove inhibitor before use. Ammonium persulfate (APS) (Shanghai Chemical, China) as an initiator was purified by recrystallization in methanol. *N*, N, N′, *N*′-tetramethylethylene diamine (TEMED) (Sigma) as an accelerator was used as received. Carboxymethylchitosan (CMCS) was purchased from Qingdao Haisheng Biological Technology. The IEP of CMCS estimated from spectrophotometric analysis was about 3.0. Inorganic clay, synthetic hectorite “Laponite XLG” ($[\mathrm{Mg}_{5.34}\mathrm{Li}_{0.66}\mathrm{Si}_8\mathrm{O}_{20}\text{-}(\mathrm{OH})_4]\mathrm{Na}_{0.66}$, layer size=20–30 nm$\Phi\times1$ nm, cation exchange capacity=104 mequiv/100 g) was purchased from Rockwood Additives, Cheshire, UK. *N*, *N*′-methylenebisacrylamide (BIS) was purchased from Fluka Chemical and was used without further purification. Deionized water used for all experiments was bubbled with $N_2$ gas for more than 3 h before use.

### Preparation of hydrogels

In preparation of the semi-IPN hydrogels crosslinked by clay, the initial solution consisting of monomer NIPA (1.04 g), deionized water (8 ml) and various ratios of clay was stirring in an iced-water bath for 1 h to prepare a transparent aqueous solution. Then TEMED (40 µl) and various ratios of CMCS (dissolved in $H_2O$ 3.5 ml) were added with stirring. Finally, initiator APS (0.0208 in $H_2O$ 1.0 ml) was added to the solution. The free-radical polymerization was carried out in a water bath at 20 °C for 24 h. The hydrogel crosslinked by clay is expressed as CMCS*m*/PNIPA/Clay*n* hydrogel. The letters *m* and *n* correspond to the weight percent of CMCS and clay against NIPA monomer, respectively. The hydrogel crosslinked by clay but without CMCS is expressed as PNIPA/Clay*n* hydrogel.

The conventional CMCS/PNIPA semi-IPN hydrogel crosslinked by BIS was also prepared for comparison and expressed as CMCS*m*/PNIPA hydrogel. In the preparation, 2 wt% BIS based on the monomer NIPA was used and the contents of other components were the same as those in CMCS*m*/PNIPA/Clay*n* hydrogel.

After gelation was completed, the gel was cut into disks 10 mm in diameter and 2 mm in thickness, and then immersed in an excess of deionized water for 4 days to remove the residual unreacted monomer. For FTIR analyses, the swollen hydrogels were dried at room temperature for 2 days and further dried at 40 °C under vacuum for 48 h before characterization.

### FT-IR analyses

FTIR measurements were carried out using dried hydrogels with various compositions or clay itself. The samples were directly analyzed using a Fourier transform infrared spectroscope (FT-IR, Nicolet NEXUS-670) in a KBr flake.

### TEM observation

To investigate the dispersion of clays in the hydrogel, TEM micrographs of dried hydrogels were obtained on a JEM-2010EXII transmission electron microscope (JEOL, Tokyo, Japan) with an acceleration voltage of 120 kV. Ultrathin sections about 100 nm thick were cut with a LKB-5 microtome (LKB , Uppsala, Sweden) equipped with a diamond knife and placed in a 200-mesh copper grid.

### VPTT determination

The VPTT of hydrogel was determined using a differential scanning calorimeter (DSC) (Mettler Toledo 822). All hydrogels were immersed in deionized water at room temperature and allowed to swell for at least 48 h to reach equilibrium state. The DSC analyses of the swollen hydrogels were performed from 20 to 45 °C at a heating rate of 3 °C/min under a nitrogen atmosphere with a ?ow rate of 40 ml/min. Deionized water was used as the reference in the DSC analyses.

### Measurement of swelling ratio

The swelling ratios of hydrogel were measured in the temperature range of 25 to 45 °C or in the pH range of 1.2 to 9.2 using a gravimetric method. The compositions of the buffers employed were as follows: pH 1.0, 0.1 M HCl; pH 3.0, 15.89 ml of 0.1 M citric acid mixed with 4.11 ml of 0.2 M $Na_2HPO_4$; pH 4.0, 12.29 ml of 0.1 M citric acid mixed with 7.71 ml of 0.2 M $Na_2HPO_4$; pH 6.8, 49.5 ml of 0.2 M $Na_2HPO_4$ mixed with 51.0 ml of 0.2 M $NaH_2PO_4$; pH 7.4, PBS (phosphate buffer solution); pH 9.2, 8.0 ml of 0.05 M borax mixed with 2.0 ml of 0.2 M $H_2BO_3$. Under each particular condition, hydrogel samples were incubated in the medium for at least 48 h and weighed after the excess water on the surface removed. The swelling ratio is defined as:

$$\text{Swelling ratio} = (W_\mathrm{s} - W_\mathrm{d})/W_\mathrm{d},$$

where $W_\mathrm{s}$ is the weight of the swollen hydrogel at different conditions and $W_\mathrm{d}$ is the dry weight of hydrogel.

### Deswelling behavior of hydrogels

The deswelling behavior of the hydrogel was studied by recording the weight of water in the hydrogels. Water retention (WR) was calculated as

$$\mathrm{WR} = (W_t - W_\mathrm{d})/(W_\mathrm{s} - W_\mathrm{d}),$$

where $W_t$ is the weight of the hydrogels at a given time interval during the course of deswelling after the swollen hydrogels at 25 °C had been quickly transferred into hot water at 45 °C.

### Measurement of mechanical properties

Tension was measured for hydrogels with the same size [6 mm in diameter, 20 mm in crosshead length) and the same water/PNIPA ratio (12.5/1 (w/w)] using a Dejie DXLL-20000. All hydrogel specimens in the form of rods were used after gelation to keep them the same water/PNIPA ratio. The specimens were clamped between jaws maintained at a fixed distance (20 mm) and the tensile forces developed were measured utilizing a load cell (capacity 100 N) connected to the jaws. The tensile properties of the hydrogels were obtained under the following conditions: test temperature 25 °C and crosshead speed 50 mm/min. Each test is repeated three times to calculate the mean value and standard deviation. The initial cross-section (28.26 mm$^2$) was used to calculate the tensile strength. The tensile modulus was calculated from the increase in load detected between elongation of 100 and 200%.

## Results and discussion

### Preparation and structure of the hydrogels

Uniform hydrogels were prepared by in situ free-radical polymerization in solutions containing different contents of clay and CMCS. The PNIPA hydrogels crosslinked by clay exhibit good transparency regardless of clay content; however, when CMCS was introduced into the network, the hydrogels become opaque as the aqueous solution of CMCS is turbid.

The FTIR spectra of the clay and the dried hydrogels are shown in Fig. 1. A band at 1,005 cm$^{-1}$ attributed to a Si–O stretching vibration can be found in the spectrum of the clay. The spectrum of CMCS10/PNIPA hydrogel shows a

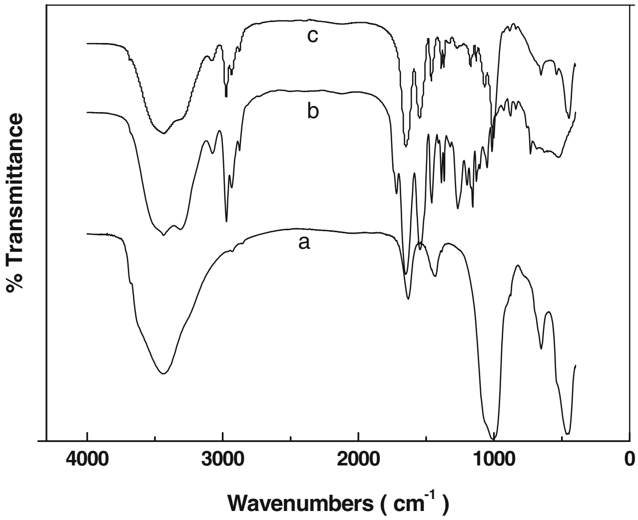

**Fig. 1** FTIR spectra of clay and hydrogels: **a** clay; **b** CMCS10/PNIPA; **c** CMCS10/PNIPA/Clay20

C–H stretching vibration (2,972; 2,933 cm$^{-1}$) and typical double peaks at amide I band (1,650 cm$^{-1}$) and amide II band (1,550 cm$^{-1}$) of PNIPA. As the sample was immersed in the buffer solution (pH 9.2) before drying, the clear peaks at 1,604 and 1,416 cm$^{-1}$ attributed to the asymmetric and symmetric stretching vibration of $-CO_2^-$ can be observed as a consequence of the ionization of –COOH to $-CO_2^-$. The FTIR spectrum of CMCS10/PNIPA/Clay20 hydrogel shows the characteristic absorptions of both CMCS/PNIPA gel and clay, indicating that all of them are present in the hydrogel network.

The dispersion of clay in the polymer matrix is shown in Fig. 2 for CMCS5/PNIPA/Clay20 hydrogel. The silicate layers are substantially intercalated by the polymer matrix and dispersed homogeneously in the hydrogel. Some of them are agglomerated with a size level of about 20 nm; some are exfoliated in single layer. According to the mechanism suggested by Haraguchi, PNIPA chains in hydrogel were attached to the surface of clay sheets, which acted as effective multifunctional crosslinkers during in situ polymerization through ionic or polar interactions. Was CMCS also crosslinked by clay or did it exist in the form of linear chains?

To find the answer, a mixture of the aqueous solution of clay and CMCS with same composition was prepared and remained in a water bath at 20 °C for 24 h. It was seen that a turbid gel-like material was formed; however, as it remained immersed in water, it turned into a turbid solution. Therefore, it could be inferred that CMCS was not crosslinked by clay but existed as linear chains incorporated into the hydrogels just like that in the conventional CMCS/PNIPA hydrogel reported previously [24].

## VPTT of the hydrogels

The DSC thermograms of semi-IPN hydrogels are shown in Fig. 3. The temperature at the onset point of the DSC endotherm is referred to the VPTT of the hydrogel [25]. At the VPTT, water in the hydrogels separated from the system, leading to a smaller heat capacity. It can be noted from Fig. 3 that all the hydrogels exhibit a similar VPTT around 33 °C, and there is no significant deviation from the VPTT of the conventional PNIPA hydrogel, indicating that in the semi-IPN system, the PNIPA network retains its own property because there is no chemical bond between CMCS and PNIPA network. On the other hand, it can also be concluded that the phase-transition temperature of the hydrogel network is independent of the type and content of the crosslinker used in this study.

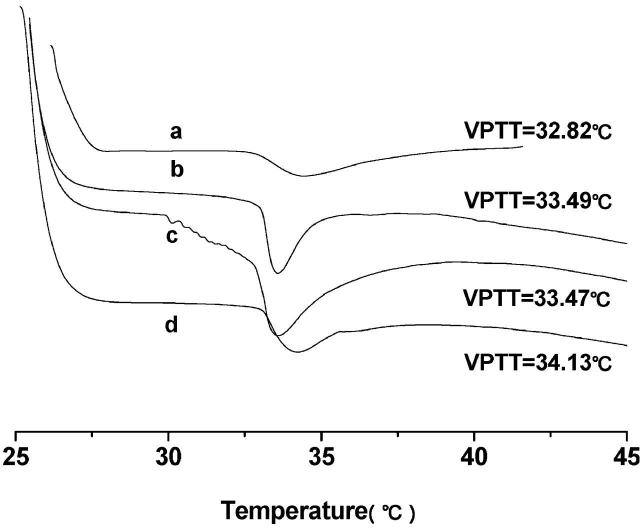

**Fig. 3** DSC thermograms of the semi_IPN hydrogels: **a** CMCS10/PNIPA; **b** CMCS5/PNIPA/Clay20; **c** CMCS10/PNIPA/Clay20; **d** CMCS10/PNIPA/Clay33

## Temperature dependence of the hydrogels

The effect of temperature on the equilibrium swelling ratio of hydrogels in phosphate buffer solution (pH 7.4) is shown in Fig. 4. In general, an abrupt decrease of swelling ratio can be observed around VPTT for all samples, which is

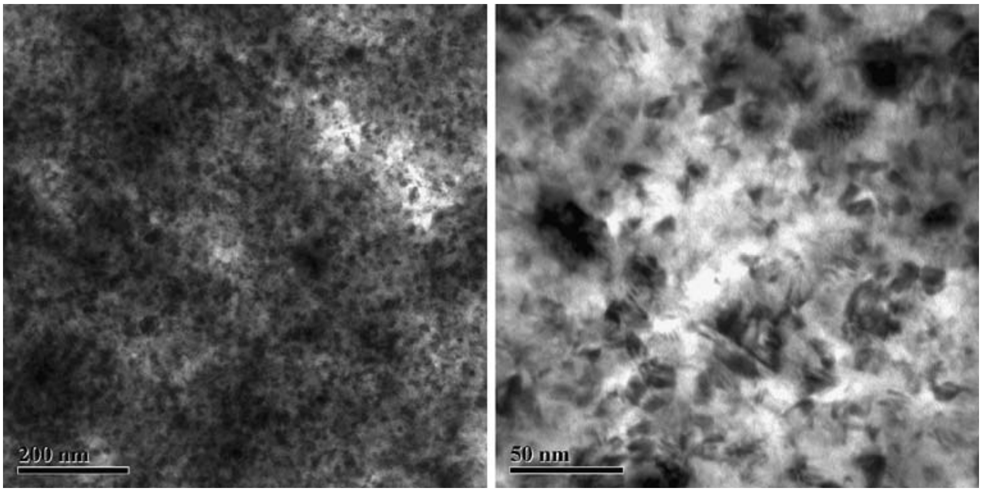

**Fig. 2** Transmission electron micrograph of dried CMC5/PNIPA/Clay20 at different magnifications

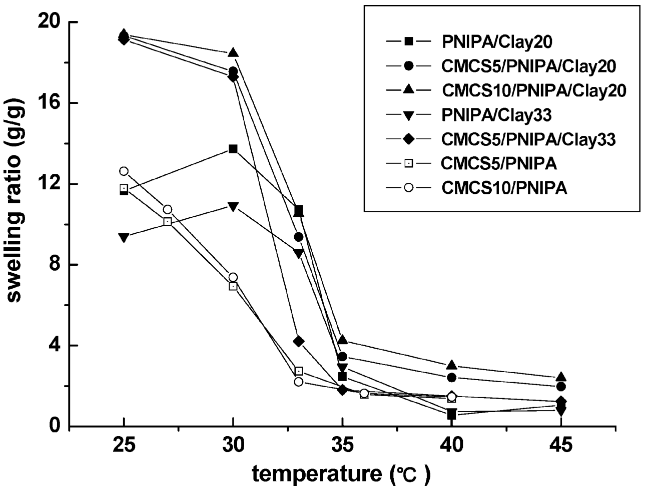

**Fig. 4** Swelling ratios of hydrogels as a function of temperature in buffer solution, pH 7.4

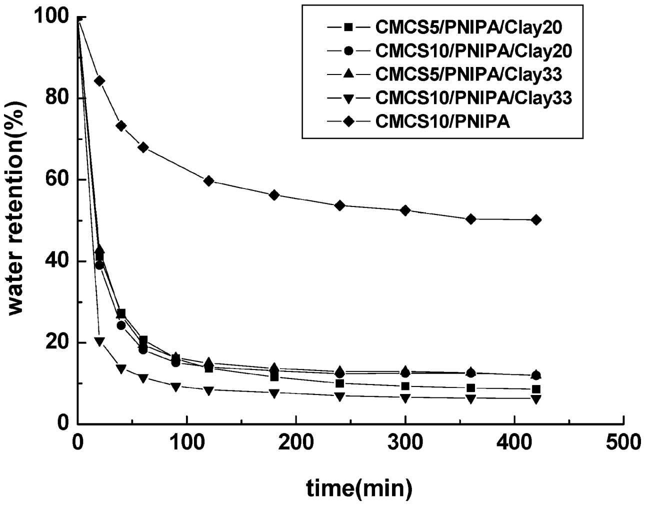

**Fig. 6** Deswelling behavior of hydrogels at 45 °C (pH 7.4)

attributed to the coil-globular transition of PNIPA. The swelling ratios of CMCS/PNIPA/clay hydrogels below VPTT are much larger than those of conventional CMCS/PNIPA hydrogels crosslinked by BIS. It was theoretically evaluated by Haraguchi [13] that the polymer chain between the crosslinking points in hydrogels crosslinked by clay were long and flexible, and the distribution of chain lengths was fairly narrow.

Therefore, it is reasonable to infer that the hydrogels crosslinked by clay have lower crosslink density than those of conventional CMCS/PNIPA hydrogels crosslinked by BIS. As a result, the swelling ratio is higher. However, when the temperature is above the VPTT, the difference between the swelling ratios of the two hydrogels tend to be less significant.

It was also found that for the PNIPA/Clay hydrogels, the introduction of CMCS leads to a remarkable increase in the swelling ratio, which could be attributed to the hydrophilicity of CMCS. CMCS is a hydrophilic polymer with water absorbing groups on the molecular chain, which might improve the swelling ratio of the hydrogel. As to the effect of clay content, the changes of swelling ratio at VPTT for the PNIPA/clay hydrogels were inclined to decrease with the increase of clay contents. However, these changes for CMCS/PNIPA/clay systems were inconspicuous.

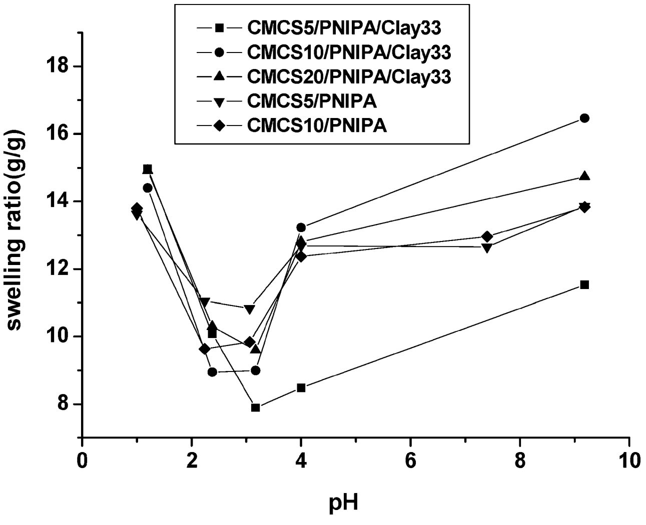

**Fig. 5** Swelling ratios of hydrogels as a function of pH value of the medium at 25 °C

## pH dependence of the hydrogels

CMCS is a kind of natural amphoteric polyelectrolyte, which has both –COOH and –$NH_2$ groups in its molecular chain, and the IEP of CMCS was near 3.0 as estimated by spectrophotometric analysis. To investigate the influence of pH value of the medium on the swelling ratios of the hydrogels, the pH range is selected from 1.2 to 9.2 in this study. As shown in Fig. 5, the swelling behaviors of CMCS/PNIPA/clay hydrogels are quite similar to tho conventional CMCS/PNIPA hydrogels, and the minimum swelling ratios of all the hydrogels appeared near the IEP. When the pH of the external solution deviates from the IEP, the hydrogels behave as polycations or polyanions and the swelling ratios increase.

According to the Donnan equilibrium [26], the driving force for the swelling and shrinking of polyelectrolyte gel is the difference between the concentration of free ions inside and outside of the gel. At the IEP, the numbers of –$COO^-$

**Table 1** Mechanical property of CMCS/PNIPA/clay hydrogel

| Hydrogel | Mechanical strength, kPa | Tensile modulus, kPa | Elongation at break, % |
|---|---|---|---|
| CMCS5/PNIPA /Clay20 | 31.7±4.5 | 3.2±0.5 | 1443.8±58.9 |
| CMCS5/PNIPA /Clay33 | 38.2±4.1 | 7.6±0.6 | 1120.6±37.2 |
| CMCS5/PNIPA /Clay46 | 41.6±9.5 | 11.3±1.3 | 812.9±41.2 |

and $–NH_3^+$ groups are equal and the intraionic attraction between opposite charges results in the lowest mobile ionic concentration in the hydrogel. As a result, the osmotic pressure in the surrounding bath causes the hydrogel to shrink to a minimum equilibrium volume. When the pH deviates from the IEP, the amount of residual ionic concentration in the hydrogel increases gradually with the increase or decrease of pH, which leads to the increase of the swelling ratios [27].

### Deswelling behavior of hydrogels in response to temperature change

The deswelling behavior of hydrogels after a temperature jump from the equilibrium-swollen state at 25 °C (below the VPTT) to the deionized water at 45 °C (above the VPTT) is shown in Fig. 6. It can be seen that the CMCS/PNIPA/clay hydrogels have much higher response rates than the conventional CMCS/PNIPA hydrogels. For instance, CMCS10/PNIPA/Clay33 loses about 80% water within 20 min, whereas the CMCS10/PNIPA takes 2 h to lose only 40% water.

### Mechanical properties of CMCS/PNIPA/clay hydrogels

The hydrogels prepared by two different crosslinkers differ markedly as regards their mechanical properties. The conventional CMCS/PNIPA hydrogels were so weak and brittle that it was difficult to perform a normal tensile test on them. In contrast, the CMCS/PNIPA/clay hydrogels were very tough and could be elongated to more than 800% as shown in Table 1. Furthermore, if the samples were elongated to 800% and then released the stress, the recovery of the CMCS/PNIPA/clay hydrogel from elongation was almost complete and instantaneous.

For example, about 93% recovery occurred within 1 min for CMCS5/PNIPA/Clay33 hydrogel. This is because the polymer chains between the clay sheets are long and flexible enough to be deformed to a large extent on macroscopic deformation. Also, the complete and instantaneous recovery on release of stress is consistent with extension and contraction of the flexible polymer chains [13].

## Conclusions

In this study, pH- and temperature-responsive CMCS/PNIPA/clay semi-IPN hydrogels were prepared by introducing linear CMCS into the inorganic clay-crosslinked PNIPA hydrogels network. The novel hydrogels exhibit the same VPTT around 33 °C as that of the conventional PNIPA hydrogel. The swelling ratios of CMCS/PNIPA/clay hydrogels below VPTT are much larger than those of conventional CMCS/PNIPA hydrogels crosslinked by BIS, which may associate with the lower crosslink density.

At the IEP of CMCS, the semi-IPN hydrogels shrink most and show a minimum swelling ratio. When pH deviates from the IEP, the hydrogels behave as polycations or polyanions and the swelling ratios increase. Moreover, the CMCS/PNIPA/clay hydrogel has a much higher response rate than the conventional CMCS/PNIPA hydrogels. It was also found that this novel hydrogel could be elongated to more than 800% and the elongation could be recovered almost completely and instantaneously.

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