Synthesis and Aqueous Solution Properties of Novel Thermoresponsive Graft Copolymers Based on a Carboxymethylcellulose Backbone

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ABSTRACT: The synthesis of thermoresponsive graft copolymers based on a carboxymethylcellulose (CMC) backbone is reported. Thermal responsive properties are introduced by grafting the CMC sample with amino-terminated poly(*N*-isopropylacrylamide) (PNIPAM) side chains of a relatively low molecular weight. Turbidity measurements in dilute copolymer solutions showed that, due to the hydrophilic CMC backbone, macroscopic phase separation by increasing temperature above the lower critical solution temperature (LCST) of PNIPAM is not allowed for pH ≥ 3. Pyrene fluorescence probing studies in aqueous solutions revealed the formation of hydrophobic microdomains above the LCST of PNIPAM. In semidilute solution these microdomains interconnect the polymer chains, leading to the thermally induced formation of a physical network. The macroscopic result is the observation in semidilute solutions of a pronounced thermally induced viscosity enhancement. This thermothickening phenomenon is almost irrespective of pH, and it remains very important even at pH values as low as 3.

Introduction

Materials exhibiting thermally induced thickening (thermothickening) or gelling properties in aqueous solution, i.e., presenting a substantial viscosity increase upon heating, are rather exceptional, as most fluids are characterized by the well-known Arrhenius thermothinning behavior. In most of cases where thermothickening properties are observed in aqueous solutions, polymers with lower critical solution temperature (LCST) behavior in water are involved. Because of a delicate balance between hydrophilic and hydrophobic interactions, these thermosensitive polymers separate out from water upon heating, although they are well soluble at low temperature. Poly(ethylene oxide) (PEO) and oligomers of poly(propylene oxide),[1] poly(*N*-isopropylacrylamide) (PNIPAM),[2,3] and nonionic cellulose ethers[4] are the most representative examples. A significant viscosification or gelation has been observed upon heating concentrated aqueous solutions of some nonionic cellulose ethers[4] or their aqueous mixtures with sodium dodecyl sulfate.[5−8] An analogous case is the mixtures of hydrophobically modified sodium polyacrylate with PNIPAM or copolymers based on *N*-isopropylacrylamide (NIPAM).[9,10]

Copolymers containing both hydrophilic sequences and thermosensitive ones are another class of materials with potential thermothickening properties in water. Triblock poly(ethylene oxide)−poly(propylene oxide)−poly(ethylene oxide) copolymers are such a case.[11] However, grafting of LCST chains onto a hydrophilic backbone seems to be a more flexible approach in designing thermothickening materials.[12−21] In their works, Hourdet and co-workers[14−16,18−21] have developed a whole family of thermoassociative graft copolymers, by grafting side chains, like PEO, PNIPAM, ethylene oxide−propylene oxide copolymers, or NIPAM-based copolymers, onto a hydrophilic backbone based on sodium acrylate. The onset of the viscosity increase was observed at an association temperature (T_{ass}) well compared with the LCST of the corresponding side chain. At temperatures higher than T_{ass}, the highly hydrophilic character of the backbone does not allow macroscopic phase separation of the side chains. As a result, the side chains are organized in hydrophobic microdomains, as was revealed by small-angle neutron scattering studies,[18] promoting efficiently the physical connectivity between the polymer chains.

In the present paper we report on the synthesis and solution behavior of graft copolymers based on a carboxymethylcellulose (CMC) backbone bearing thermosensitive PNIPAM side chains, CMC-*g*-PNIPAM. Following a variety of the synthetic procedure described by Hourdet, amino-terminated PNIPAM chains were grafted onto the CMC backbone in water (Scheme 1). Amino-terminated PNIPAM chains were prepared by using an amine-containing chain transfer agent during polymerization of NIPAM.

CMC is a chemically modified cellulose derivative with large water solubility, broadly used due to its low cost, lack of toxicity, and biodegradability. Food industry, cosmetics, pharmaceuticals, suspension agents, tablet excipients, viscosity increasing agents, formulation agent in controlled release of drugs and pesticides, paper and paper products, adhesives, and ceramics provide a small compilation of the numerous applications where CMC is used in the acid or in the sodium salt form.[22,23] Grafting of PNIPAM side chains onto the hydrophilic CMC backbone is expected to provide CMC with new, thermosensitive properties in solution. The reversibility of the phase transition of PNIPAM, occurring at an easily accessible temperature (∼33 °C) close to the body temperature, is of great interest for uses in biomedical applications, like isolation and purification

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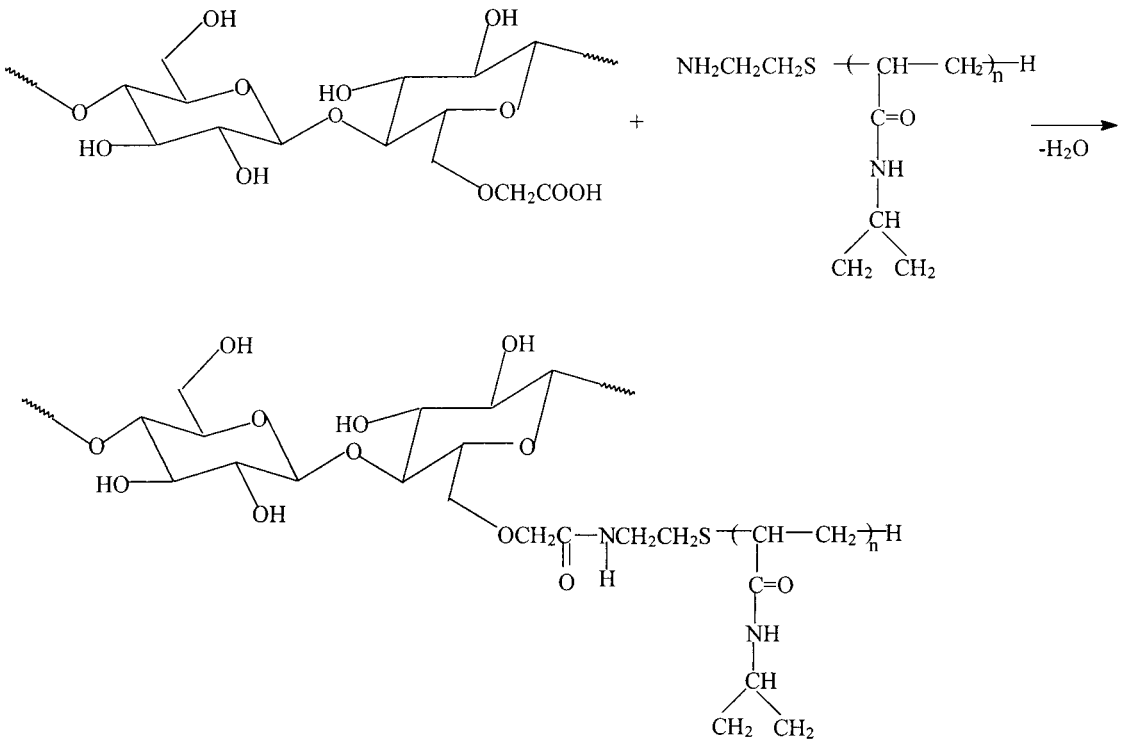
Scheme 1



of biologically active substances.[3,24,25] Furthermore, graft copolymers with NIPAM-based side chains, for example onto a dextran[26,27] or sodium polyacrylate (PAA)[28,29] backbone, have been proposed as starting materials for the preparation of modulated drug release systems.

Another reason for choosing CMC as a backbone is to avoid drawbacks from hydrogen-bonding interaction of the side chains with the backbone at low pH. Because of hydrogen-bonding association between PNIPAM and PAA,[30] the graft copolymers PAA-*g*-PNIPAM are insoluble at room temperature for pH values lower than 4,[28,29,31] limiting their performance as thermothickeners in the alkaline or neutral pH region. In contrast, no such interaction has been reported between PNIPAM and CMC, and it is expected that possible thermothickening properties will be significant even at much lower pH. To our knowledge, only a case of such pH-independent thermothickening behavior has been recently reported by grafting PNIPAM side chains onto a nonionic backbone.[32,33]

In this study, we focus on the influence of pH and temperature on the properties of aqueous dilute and semidilute solutions of graft CMC-*g*-PNIPAM copolymers. In semidilute solutions pronounced thermothickening phenomena are observed, while the study in dilute solutions provides essential information for a deeper understanding of the thermoresponsive properties of these new, water-soluble materials.

Experimental Section

Materials. Sodium carboxymethylcellulose (CMC) was a product of Polyscience. Its molecular weight was of a nominal value $M_w = 8.2 \times 10^4$ g/mol. The content of the carboxyl groups was determined by titration of the acid form with 0.1 M NaOH and was found to be 0.78 carboxyl groups per anhydroglycose unit.

N-Isopropylacrylamide (NIPAM, Aldrich), ammonium persulfate (APS, Serva) of analytical grade, 2-aminoethanethiol hydrochloride (AET, Aldrich), 1-(3-(dimethylamino)propyl)-3-ethyl-carbodiimide hydrochloride (EDC, Aldrich), and $LiNO_3$ (Sigma) were used. Water was purified by means of a Seralpur Pro 90C apparatus combined with a USF Elga laboratory unit.

Amino-terminated PNIPAM was prepared by radical polymerization in aqueous solution by using the redox couple APS/AET as initiator.[19] The monomer was dissolved in water (0.1 mol in 80 mL of water), and the solution was deaerated with nitrogen bubbling. The temperature was adjusted at 29 °C by using a water bath. The initiators (1.1 mmol of APS and 2.2 mmol of AET·HCl) were dissolved separately in 10 mL of water and added after about 1 h to the monomer solution. The reaction time was 3 h. The product was purified by dialysis against water through a membrane (cutoff ~12 000 Da, Sigma) and freeze-dried.

The CMC-*g*-PNIPAM copolymers were prepared by a coupling reaction between CMC and PNIPAM using EDC as condensing agent. As an example, the synthesis conditions of the copolymer containing 27 mol % NIPAM units is described: 2.7 g of CMC and 1.35 g of PNIPAM were dissolved under stirring for 12 h in 160 and 35 mL of water, respectively. The two solutions were mixed, and their pH was adjusted to 8 by adding some drops of 2 M NaOH solution. 0.20 g of EDC dissolved in 5 mL of water was added into the mixture at room temperature. After 8 h the reaction mixture was dialyzed against water and freeze-dried. The product obtained was extracted for 8 h with chloroform to remove unreacted PNIPAM chains.

Characterization. The composition of the graft copolymers has been assessed by IR, ^{1}H NMR spectroscopy, and elemental analysis: The IR spectra of the graft copolymers, measured on a Perkin-Elmer 577 instrument, with the samples being incorporated in KBr tablets, showed not only the characteristic absorption bands of CMC but also the characteristic bands of −CONH− (1650 cm^{-1}), indicating that they contain PNIPAM. The ^{1}H NMR spectra were recorded by a Bruker AVANCE DRX 400 MHz spectrometer in D_2O solutions. Elemental analysis was carried out on a Carlo-Erba CHNS-O elemental analyzer EA1108.

Size exclusion chromatography (SEC) was used to detect any unreacted PNIPAM chains. Analyses were carried out with a Waters 501 HPLC pump equipped with two Shodex OH-pak

Table 1. Characterization of CMC, PNIPAM, and the CMC-*g*-PNIPAM Samples

sample	notation	$[\eta]$ (mL/g)	$M_v \times 10^{-4}$ (g/mol)	wt % of NIPAM units in the graft copolymer: ^{1}H NMR	wt % of NIPAM units in the graft copolymer: elemental analysis
carboxymethylcellulose	CMC	186[a]	8.2[c]		
poly(*N*-isopropylacrylamide)	PNIPAM	31.5[b]	4.3[d]		
carboxymethylcellulose-*g*-poly(*N*-isopropylacrylamide)	CMC-*g*-PNIPAM27	165		28	26
carboxymethylcellulose-*g*-poly(*N*-isopropylacrylamide)	CMC-*g*-PNIPAM47	107		49	45

[a] 25 °C in 0.2 M NaCl aqueous solution. [b] 20 °C in 0.5 M $LiNO_3$ aqueous solution. [c] Determined from the intrinsic viscosity bu using the relation[46] $[\eta] = 4.3 \times 10^{-2} M_v^{0.74}$. [d] Determined from the intrinsic viscosity bu using the relation[47] $[\eta] = 0.047 M_v^{0.61}$.

columns, B804 and B805, equilibrated at room temperature in 0.5 M $LiNO_3$ in a 1 mL/min flow rate. The samples were injected into the columns in concentration 2×10^{-3} g/mL. The results obtained showed the presence of a small residual quantity of PNIPAM in the reaction product and its complete removal after extraction with $CHCl_3$.

The thermal behavior of the graft copolymer was investigated by thermogravimetric analysis. The thermogravimetric and differential thermogravimetric (TG/DTG) curves were recorded on a Paulik-Paulik-Erdey derivatograph, MOM-Budapest, in air flow of 30 mL/min, with sample mass of 30 mg. Differential scanning calorimetry (DSC) curves were recorded on a Metller DSC 12E at a heating rate of 10 °C/min and nitrogen flow of 30 mL/min. To eliminate the water and to ensure the reproducibility of the results, at least three or four successive runs have been made. Indium was used as standard.

Turbidimetry. The change in absorbance of the aqueous solutions of the polymers was monitored as a function of temperature at a fixed wavelength of 490 nm by means of a Hitachi spectrophotometer model U 2001, equipped with a circulating water bath.

Viscometry. Reduced viscosity measurements were carried out with an automated viscosity measuring system (Schott-Gerate AVS 300, Germany) equipped with a micro-Oswald-type viscometer, while for the intrinsic viscosity ($[\eta]$) measurements an Ubbelhode-type viscometer was used. Temperature was controlled within a precision of ±0.02 °C, and flow times were measured with an accuracy of ±0.1 s. Kinetic energy and dilution corrections have been applied. The reduced viscosity has been calculated as the ratio $(t - t_0)/(t_0 c)$, where t_0 and t are respectively the flow times of the solvent of the polymer solution of a concentration c. The intrinsic viscosity $[\eta]$ has been determined from the extrapolation of the reduced viscosity curve at zero concentration.

Fluorescence Probing. Steady-state fluorescence spectra were recorded on a Perkin-Elmer LS50B luminescence spectrometer equipped with a circulating water bath in order to control the temperature of the measuring cell. Pyrene, from an ethanolic stock solution 1×10^{-3} M, was used as a micropolarity sensitive probe in a final concentration 6×10^{-7} M. The excitation wavelength was 334 nm. The change in the intensity ratio (I_1/I_3) of the first and the third vibronic band, namely 373 and 384 nm (I_1 and I_3, respectively), in emission spectra was used to detect hydrophobic microdomains.

Rheology. Steady-state shear viscosity measurements of 5×10^{-2} g/mL polymer solutions were performed on a Rheometrics SR-200 controlled-stress rheometer by using a cone−plate geometry (diameter = 25 mm, angle = 2°).

Sample Preparation. Polymer solutions were prepared by dissolving under gently stirring for 24 h the appropriate amount of polymer in pure water or in buffer solutions. Citrate−phosphate buffers in 0.1 M NaCl were used. The ionic strength of the solution is estimated to be 0.15−0.17 M.

Results and Discussion

Synthesis and Characterization. Both reaction steps were conducted in water and at a temperature lower than 30 °C to avoid phase separation of PNIPAM chains and to ensure that the reaction mixture is homogeneous. However, this severe temperature constrain seems not to limit significantly the conversion of the grafting reaction. This is evidenced in Table 1, where the most important characteristics of the obtained polymers are summarized. The composition of the graft copolymers is close to that used in the reaction mixture. Moreover, their intrinsic viscosity is close to the additive value, evaluated as the weight average of the values of the two pure components. They will be referred to as CMC-*g*-PNIPAM27 and CMC-*g*-PNIPAM47, according to their weight percentage content in NIPAM units. On the basis of their composition and the molar masses of the two components, it is roughly estimated that each CMC chain is grafted with one or two PNIPAM chains, for CMC-*g*-PNIPAM27 or CMC-*g*-PNIPAM47, respectively.

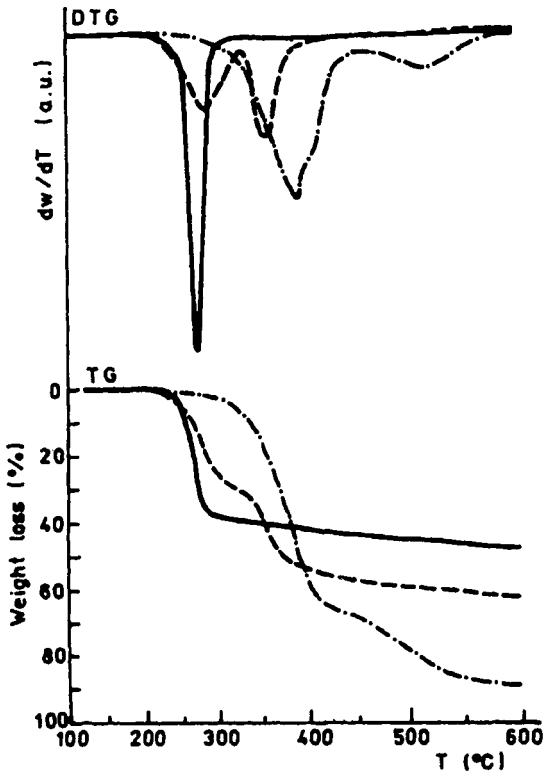


Figure 1. TG/DTG curves for the thermal degradation of the polymers: CMC (—), PNIPAM (— · —), and CMC-*g*-PNIPAM27 (- - -).

The TG/DTG curves for the thermal degradation of CMC, PNIPAM, and CMC-*g*-PNIPAM27 are shown in Figure 1. CMC, presenting a single thermogravimetric step, decomposes in the 200−310 °C temperature range with a mass loss of 36 wt %. Between 250 and 450 °C, PNIPAM exhibits a degradative step with a mass loss of 63 wt %. The thermal degradation of the graft copolymer occurs in two stages. The first TG stage

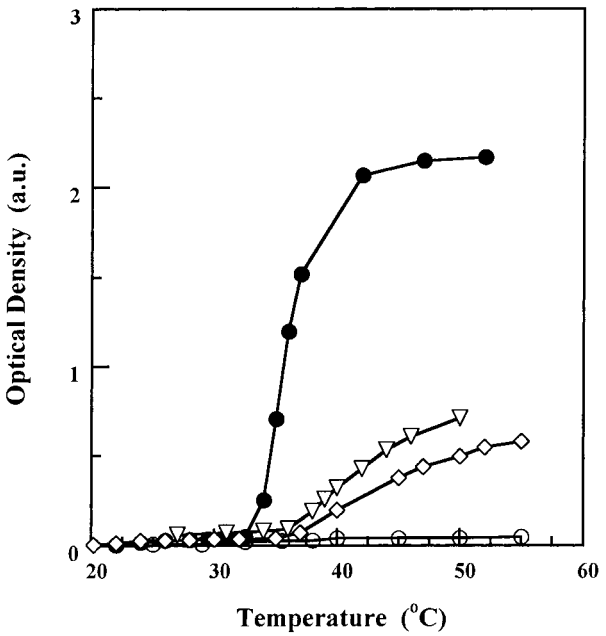


Figure 2. Turbidimetric curves of PNIPAM (●), CMC (○), CMC-*g*-PNIPAM27 (◊), and CMC-*g*-PNIPAM47 (▽) in buffer solution of pH = 2. The polymer concentration is 2 mg/mL.

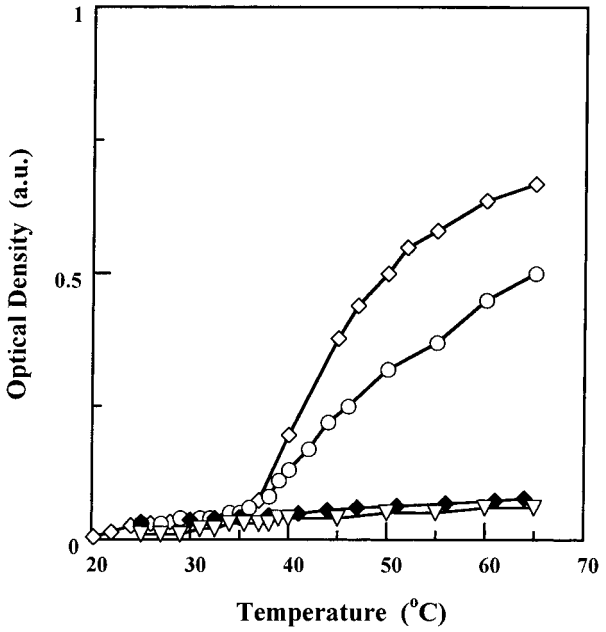


Figure 3. Turbidimetric curves of CMC-*g*-PNIPAM27 in buffer solutions of pH = 7 (▽), pH = 3 (♦), pH = 2.5 (○), and pH = 2 (◊). The polymer concentration is 2 mg/mL.

referring mainly to degradation of the CMC main chain takes place in the 280−330 °C temperature range, with a mass loss of 25%. The second TG stage occurring in the 325−420 °C temperature range with a mass loss of 25 wt % could be ascribed to the decomposition of the PNIPAM side chains. The first DTG peak is shifted to higher temperature than that of CMC while the second DTG peak is shifted to lower temperature with respect to the corresponding peak of PNIPAM. Therefore, the decomposition of the main chain and the grafts do not occur independently. DSC measurements confirmed that microphase separation occurs at the solid state, as two transition temperatures, 75.5 and 140 °C, were observed for CMC-*g*-PNIPAM27, close to the T_g's of the pure components, i.e., 77 °C for CMC and 140 °C for PNIPAM.

Study in Dilute Aqueous Solution. a. Turbidity Measurements. The turbidity behavior of the two parent polymers, PNIPAM and CMC, and the two graft copolymers, CMC-*g*-PNIPAM27 and CMC-*g*-PNIPAM47, at pH = 2 is presented as a function of temperature in Figure 2. As expected, the aqueous CMC solution is transparent in the whole temperature range studied, as CMC is hydrophilic. On the other hand, the well-known thermal sensitivity of the PNIPAM aqueous solution is revealed by an abrupt increase in absorbance at about 33 °C, because PNIPAM phase-separates from the aqueous solution at this temperature. The aqueous solutions of the two graft copolymers present also a turbidity increase at roughly the same temperature. Nevertheless, the change is now much more gradual, and absorbance remains at values lower than 0.75 even when temperature reaches 55 °C. On the contrary, the absorbance of the PNIPAM solution has reached a plateau value of around 2 already at 40 °C. Therefore, attaching the PNIPAM chains to a rather stiff and hydrophilic backbone as that of CMC perturbs the phase separation mechanism, leading to the formation of less or smaller PNIPAM aggregates. Nevertheless, increasing the PNIPAM content of the graft copolymer seems to facilitate phase separation, as the solution of CMC-*g*-PNIPAM47 is slightly more turbid than that of CMC-*g*-PNIPAM27.

In Figure 3 the turbidity curves of CMC-*g*-PNIPAM27 for several pH values are presented. In fact, for pH = 3 or higher, polymer solutions appear transparent in the whole temperature range studied, and no significant change of their optical density is observed. The solutions start to turn significantly turbid with temperature only when pH is as low as 2.5. This turbidity increase becomes more pronounced when pH decreases to 2. Because of neutralization at high pH or dissociation of the weak carboxylic units in the acid pH region, the CMC backbone bears a significant content of charged carboxylate units. These charges stabilize efficiently the copolymer at high temperatures, and macroscopic phase separation of the PNIPAM side chains is inhibited. Only at very low pH, where the dissociation of carboxylic units is sufficiently depressed, the polymer can be considered practically uncharged and macroscopic phase separation can take place. Nevertheless, even in this case the hydrophilic CMC backbone does not allow the full collapse of the PNIPAM side chains, and turbidity is maintained at low levels, compared to the turbidity of the PNIPAM solutions in the same conditions, as shown in Figure 2. Finally, note that the similar PAA-*g*-PNIPAM graft copolymers phase-separate already at pH = 4 even at room temperature,[28,29,31] due to hydrogen-bonding interaction between PNIPAM side chains and the PAA backbone. In contrast, such an interaction is not important in the CMC-*g*-PNIPAM graft copolymers, leading to a good water solubility in a much larger pH range.

b. Viscometry. In Figure 4 we report the temperature dependence of the reduced viscosity of the graft copolymer CMC-*g*-PNIPAM27 in water and in buffer solutions of various pH. The corresponding curves of PNIPAM and CMC in pure water are also plotted. In all cases, the polymer concentration is 2×10^{-3} g/mL. The reduced viscosity of CMC either in pure water or at pH = 7 decreases only slightly with increasing temperature, because CMC is hydrophilic and not

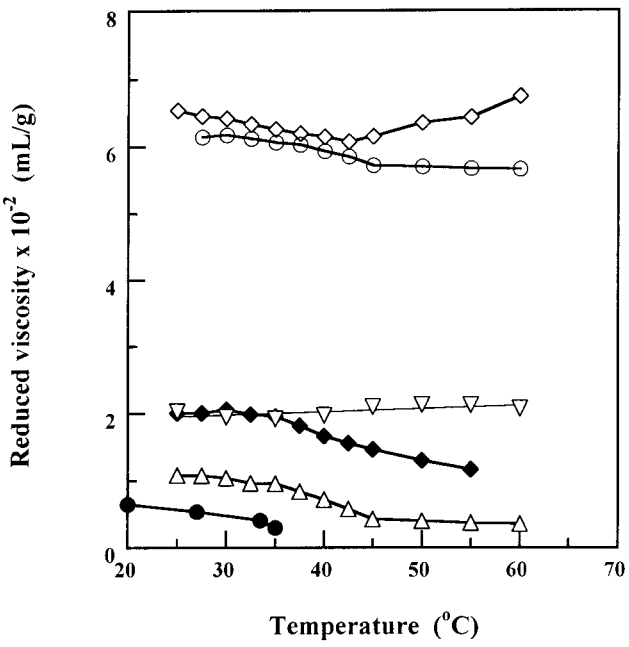


Figure 4. Variation of the reduced viscosity as a function of temperature for the homopolymers PNIPAM (●) and CMC (○) in pure water and for the graft copolymer CMC-*g*-PNIPAM27 in pure water (◇) and in buffer solutions of pH = 2 (△), pH = 3 (◆), and pH = 7 (▽). The polymer concentration is 2 mg/mL.

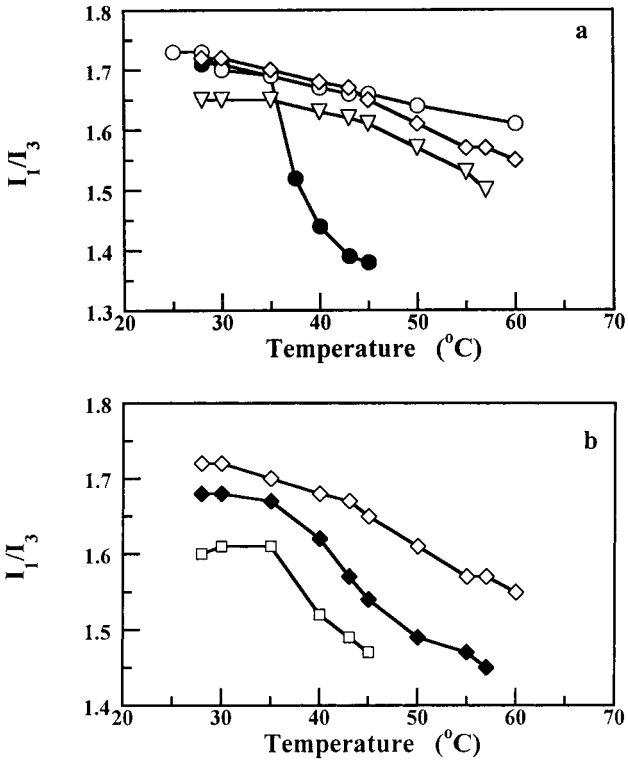


Figure 5. (a) Variation of the ratio I_1/I_3 as a function of temperature for PNIPAM (●), CMC (○), CMC-*g*-PNIPAM27 (◇), and CMC-*g*-PNIPAM47 (▽) in pure water. The polymer concentration is 2 mg/mL. (b) Variation of the ratio I_1/I_3 as a function of temperature for the copolymer CMC-*g*-PNIPAM27 in pure water (◇) and in buffer solutions of pH = 3.5 (◆) or pH = 2 (□). The polymer concentration is 2 mg/mL.

especially thermosensitive. On the contrary, the thermosensitive character of PNIPAM is revealed by an important decrease of the reduced viscosity when temperature approaches LCST, and the polymer chains collapse before phase separation takes place.[34−36] The behavior of the graft copolymer at pH = 2 is similar to that of PNIPAM, as a decrease of the reduced viscosity is observed at a temperature region close to the LCST of PNIPAM. Nevertheless, the transition is now less abrupt, and it is completed within a temperature range of about 10 °C. The change in reduced viscosity becomes even smoother for pH = 3, while for pH = 7 the reduced viscosity of the copolymer remains practically constant. Obviously at pH = 2, where the backbone is uncharged, the hydrophobic interactions between the PNIPAM side chains lead to the shrinkage of the polymer chain at high temperature and eventually to phase separation. By increasing pH, the number of charged carboxylate groups on the CMC backbone increases, making more and more difficult the polymer chain shrinkage.

In pure water the ionic strength is low, and there is not any considerable charge shielding, contrary to what happens in the buffer solutions, where the ionic strength is estimated to be about 0.15−0.2 M. The reduced viscosity of CMC-*g*-PNIPAM27 is much higher in pure water, as compared to the corresponding results in buffer solution of pH = 7, although the pH of pure water polymer solution is also around 7. As a result, the polymer chains are considerably expanded due to electrostatic repulsions between the carboxylate groups of the CMC backbone of the copolymer. Under these conditions, smooth interpolymer physical cross-links through the PNIPAM side chains can be formed at high temperature. This could probably explain the gradual increase of the reduced viscosity of CMC-*g*-PNIPAM27 for temperatures higher than 45 °C.

c. Fluorescence Probing Study. The formation of hydrophobic microdomains with increasing temperature in the CMC-*g*-PNIPAM graft copolymers has been detected from the changes of the fluorescence emission spectrum of pyrene, which is known to be sensitive to the polarity of the microenvironment that this probe experiences. As known, high values of the intensity ratio of the first over the third vibronic peak of the pyrene spectrum, I_1/I_3, reveals an aqueous polar environment, while low values are characteristic of a low-polarity microenvironment, where the hydrophobic pyrene molecules are preferentially solubilized.[37]

Figure 5a presents the variation of the ratio I_1/I_3 with temperature for dilute solutions of PNIPAM, CMC, and the two graft copolymers, CMC-*g*-PNIPAM27 and CMC-*g*-PNIPAM47, in pure water. For the homopolymer PNIPAM, the well-known[38] abrupt decrease of the ratio I_1/I_3 is observed at a temperature close to the LCST of the polymer, revealing the formation of hydrophobic microdomains at this temperature. On the other hand, for CMC the ratio I_1/I_3 takes high values in the whole temperature range studied, revealing that no hydrophobic domains exist in this case, as expected. In this case, the smooth decrease of the ratio I_1/I_3 with temperature reflects the behavior of pure pyrene solutions.[39] The curve for CMC-*g*-PNIPAM27 starts to deviate to lower values at ∼45 °C, a temperature close to the temperature where the onset of the reduced viscosity increase was observed in Figure 4. We should note, however, that the decrease of the ratio I_1/I_3 is not very important in pure water. This must be attributed to the formation of either less or looser (less hydrophobic) microdomains under these conditions. A more important decrease is, in contrast, observed with the copolymer CMC-*g*-PNIPAM47 bearing a substantially higher PNIPAM content.

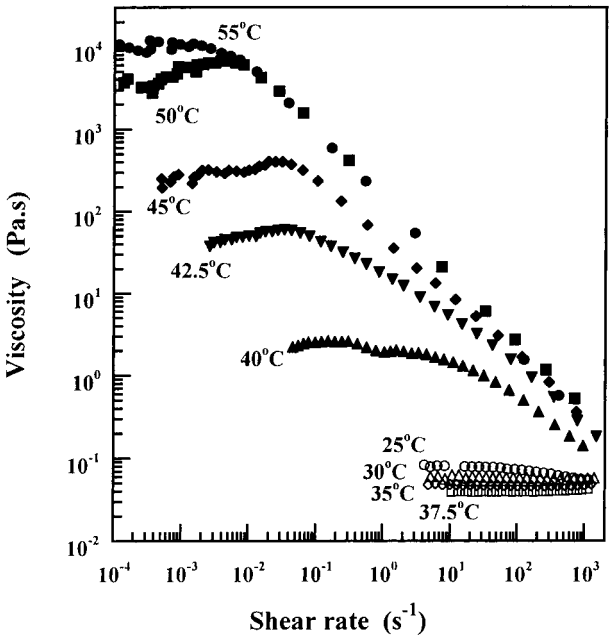


Figure 6. Viscosity−shear rate profiles for the PNIPAM-*g*-CMC27 sample in pure water at various temperatures. The polymer concentration is 5×10^{-2} g/mL.

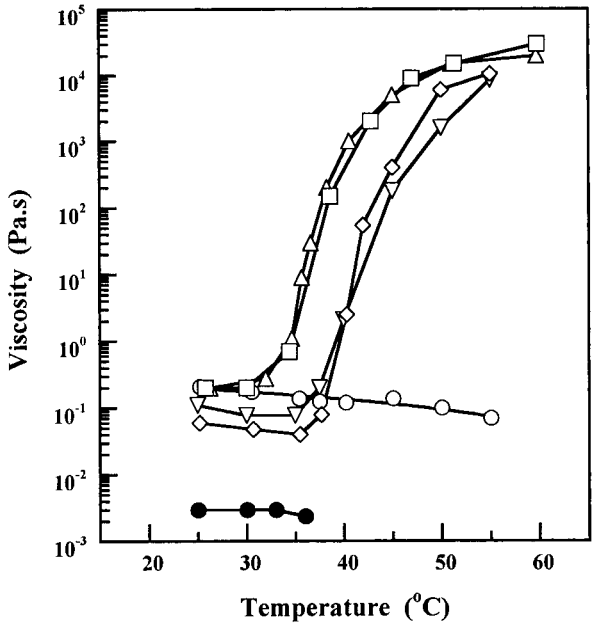


Figure 7. Variation of the zero-shear viscosity as a function of temperature for PNIPAM (●), CMC (○), CMC-*g*-PNIPAM27 (◇), and CMC-*g*-PNIPAM47 (▽) in pure water. Results for CMC-*g*-PIPAM27 in buffer solutions of pH = 3 (□) and pH = 7 (△) are also shown. The polymer concentration is 5×10^{-2} g/mL.

By decreasing pH, the number of carboxylate groups on the CMC backbone decreases, and the formation of better organized, more hydrophobic microdomains is facilitated, as is shown in Figure 5b. At pH = 2 or pH = 3.5, the value of the ratio I_1/I_3 at high temperatures is close to that observed for PNIPAM solutions above the LCST. However, for CMC-*g*-PNIPAM27 the I_1/I_3 decrease is more gradual, taking place at a large temperature region of 15−20 °C, whereas for PNIPAM it is completed within a few degrees. These results are qualitatively in agreement with the respective reduced viscosity changes discussed in Figure 4.

Thermothickening Properties in Semidilute Solution. The viscosity profiles of CMC-*g*-PNIPAM27 in pure water are presented in Figure 6 as a function of shear rate for various temperatures *T*, ranging from room temperature, 25 °C, up to 55 °C. The polymer concentration is 5×10^{-2} g/mL. The reversibility of the obtained curves has been assesssed by repeated measurements. When *T* is lower than 35 °C, viscosity is low and Newtonian even for very high shear rates. Moreover, in this temperature region, viscosity decreases slightly, following the usual Arrhenius-type behavior of most fluids. In contrast, for higher temperatures, the behavior is completely different. A spectacular viscosity increase is observed upon heating, while the solution is not Newtonian anymore. Newtonian behavior is limited to low shear rate, while for higher shear rates the polymer solution exhibits a pronounced shear thinning behavior. In some cases, a weak shear thickening is observed just before the shear thinning part, similarly to the behavior reported for other associating systems.[40,41] Moreover, the shear rate limit for Newtonian behavior is displaced to lower values upon heating, i.e., as the solution viscosity increases. This behavior is characteristic not only of thermothickening systems[13,16,19] but also of most reversible hydrophobically associating systems,[42−45] and it is the result of the destruction of the physical cross-links when shear is applied.

The viscosity at the Newtonian plateaus of PNIPAM, CMC, CMC-*g*-PNIPAM27, and CMC-*g*-PNIPAM47 in water is plotted in Figure 7 as a function of temperature. For CMC-*g*-PNIPAM27 the corresponding viscosity curves in buffer solutions of pH = 3 and pH = 7 are also presented. The polymer concentration in any case is 5×10^{-2} g/mL. Both CMC and PNIPAM show the usual slight thermothinning behavior with increasing temperature. This regular viscosity decrease is verified for CMC in the whole temperature range studied, while for PNIPAM phase separation at ∼35 °C did not allow measurements at higher temperatures. The two graft copolymers, on the other hand, show a spectacular thermothickening behavior. As temperature increases from ∼35 up to 50 °C, a viscosity enhancement of about 5 orders of magnitude is observed. The threshold temperature to observe thermothickening, i.e., the so-called T_{ass},[19] defined as the intersection point of the lower plateau with the tangent at the inflection point of the rheology curve, is 37 °C, slightly higher than the cloud point of a 2×10^{-2} g/mL PNIPAM water solution, determined to be 35 °C. As temperature increases above T_{ass}, PNIPAM side chains aggregate to form hydrophobic microdomains which cross-link physically the polymer chains, leading to the formation of a high-viscosity reversible network. In buffer solutions of pH = 7 and pH = 3, due to their ionic strength, T_{ass} is displaced to 33 °C, in agreement with the depression of the cloud point of PNIPAM[3] and of T_{ass} by adding salt or other ionic cosolutes.[20] Contrary to the behavior in dilute solutions, where only in pure water a slight increase in the copolymer viscosity with temperature was observed, the high PNIPAM concentration and the increased chain entanglement in semidilute solutions favor the formation of interchain hydrophobic PNIPAM cross-links and the appearance of thermothickening properties even at low-pH solutions. Furthermore, we have to point out that, in contrast to the similar PAA-*g*-PNIPAM graft copolymers that are not soluble at low pH,[28,29,31] the thermothickening properties of CMC-*g*-PNIPAM27 are pronounced and comparable to those

exhibited in pure water, even in the very difficult environment of pH = 3.

Conclusion

The CMC-*g*-PNIPAM graft copolymers, prepared by grafting amino-terminated poly(*N*-isopropylacrylamide) (PNIPAM) chains of a relatively low molecular weight onto a carboxymethylcellulose (CMC) backbone, present a convenient combination of the hydrophilic character of CMC with the hydrophobic one of PNIPAM. The covalent bonding of PNIPAM chains onto the hydrophilic CMC backbone does not allow the macroscopic phase separation of the side chains at high temperature, unless pH is sufficiently low to depress any dissociation of the carboxylic groups of CMC. Nevertheless, pyrene emission fluorescence data show that microphase separation takes place as hydrophobic aggregates are detected by increasing temperature. These aggregates between PNIPAM side chains of the graft copolymer form a thermally induced physical network in semidilute solution, leading to pronounced thermothickening properties.

The high biodegradability of the CMC backbone makes these derivatives attractive environmental friendly candidates for industrial applications where effective thermothickening properties in aqueous formulations are needed. Moreover, they offer a larger range of possible applications, as thermothickening properties are effective in a very large pH region, ranging from alkaline solutions down to pH = 3. They could, also, be useful in pharmaceutical applications when thermally controlled formation of hydrophobic microdomains is demanded. The natural origin of CMC and its good biocompatability is an important advantage for such applications.

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References and Notes

(1) Molyneux, P. *Water-Soluble Synthetic Polymers: Properties and Behavior*; CRC Press: Boca Raton, FL, 1987; Vol. I, Chapter 2.
(2) Heskins, M.; Guillet, J. E. *J. Macromol. Sci., Chem.* **1968**, *A2* (8), 1441.
(3) Schild, H. G. *Prog. Polym. Sci.* **1992**, *17*, 163.
(4) Klug, E. D. *J. Polym. Sci., Part C* **1971**, *36*, 491.
(5) Carlsson, A.; Karlstrom, G.; Lindman, B. *Colloids Surf.* **1990**, *47*, 147.
(6) Nystrom, B.; Lindman, B. *Macromolecules* **1995**, *28*, 967.
(7) Nystrom, B.; Kjoniksen, A.-L.; Lindman, B. *Langmuir* **1996**, *12*, 3233.
(8) Wang, G.; Lindell, K.; Olofsson, G. *Macromolecules* **1997**, *30*, 105.
(9) Bokias, G.; Hourdet, D.; Iliopoulos, I.; Staikos, G.; Audebert, R. *Macromolecules* **1997**, *30*, 8293.
(10) Bokias, G.; Mylonas, Y. *Macromolecules* **2001**, *34*, 885.
(11) Brown, W.; Schillen, K.; Almgren, M.; Hvidt, S.; Bahadur, P. *J. Phys. Chem.* **1991**, *95*, 1850.
(12) Vos, S.; Moller, M. *Macromol. Chem., Macromol. Symp.* **1993**, *75*, 223.
(13) Vos, S.; Moller, M.; Visscher, K.; Mijnleieff, P. F. *Polymer* **1994**, *35*, 2644.
(14) Hourdet, D.; L'Alloret, F.; Audebert, R. *Polymer* **1994**, *35*, 2624.
(15) L'Alloret, F.; Hourdet, D.; Audebert, R. *Colloid Polym. Sci.* **1995**, *273*, 1995.
(16) Hourdet, D.; L'Alloret, F.; Audebert, R. *Polymer* **1997**, *38*, 2535.
(17) Bromberg, L. *J. Phys. Chem. B* **1998**, *102*, 1956.
(18) Hourdet, D.; L'Alloret, F.; Durand, A.; Lafuma, F.; Audebert, R.; Cotton, J. P. *Macromolecules* **1998**, *31*, 5323.
(19) Durand, A.; Hourdet, D. *Polymer* **1999**, *40*, 4941.
(20) Durand, A.; Hourdet, D. *Polymer* **2000**, *41*, 545.
(21) Durand, A.; Hourdet, D. *Macromol. Chem. Phys.* **2000**, *201*, 858.
(22) Just, E. K.; Majewicz, T. G. Cellulose Ethers. In *Encyclopedia of Polymer Science and Engineering*, 2nd ed.; Mark, H. F., Bikales, N. M., Overberger, C. G., Menges, G., Kroschwitz, J. I., Eds.; John Wiley & Sons: New York, 1985.
(23) *Hercules Incorporated Catalogue*; Merck Index, XI Edition Centennial Edition; Merck and Company Inc.: Rahway, 1989.
(24) Hoffman, A. S. *Macromol. Symp.* **1995**, *98*, 645.
(25) *Biorelated Polymers and Gels*; Okano, T., Ed.; Academic Press: New York, 1998.
(26) Kurisawa, M.; Yui, N. *Macromol. Chem. Phys.* **1998**, *199*, 2613.
(27) Huh, K. M.; Hashi, J.; Oooya, T.; Yui, N. *Macromol. Chem. Phys.* **2000**, *20*, 613.
(28) Chen, G.; Hoffman, A. S. *Nature*, **1995**, *373*, 49.
(29) Chen, G.; Hoffman, A. S. *Macromol. Rapid Commun.* **1995**, *16*, 175.
(30) Staikos, G.; Karayanni, K.; Mylonas, Y. *Macromol. Chem. Phys.* **1997**, *198*, 2905.
(31) Durand, A. Thesis, Université Paris VI, 1998.
(32) Violy, J.-L.; Hourdet, D.; Sudor, J. French Patent No. 98 16 676.
(33) Sudor, J.; Barbier, V.; Thirot, S.; Godfrin, D.; Hourdet, D.; Millequant, M.; Blanchard, J.; Violy, J.-L. *Electrophoresis* **2001**, *22*, 720.
(34) Ricka, J.; Meewes, M.; Nyffenegger, R.; Binkert, T. *Phys. Rev. Lett.* **1990**, *65*, 657.
(35) Meewes, M.; Ricka, J.; de Silva, M.; Nyffenegger, R.; Binkert, T. *Macromolecules* **1991**, *24*, 5811.
(36) Wu, C.; Zhou, S. *Macromolecules* **1995**, *28*, 8381.
(37) Zana, R. In *Surfactant Solutions: New Methods of Investigation*; Zana, R., Ed.; Surfactant Science Series Vol. 22; Marcel Dekker: New York, 1987.
(38) Schild, H. G. *ACS Symp. Ser.* **1991**, *No. 467*; Chapter 16.
(39) Winnik, F. M. *J. Phys. Chem.* **1989**, *93*, 7452.
(40) Biggs, S.; Selb, J.; Candau, F. *Polymer* **1993**, *34*, 580.
(41) Chang, Y.; McKormick, C. L. *Polymer* **1994**, *35*, 3503.
(42) Wang, K. T.; Iliopoulos, I.; Audebert, R. *Polym. Bull.* **1998**, *20*, 577.
(43) Hill, A.; Candau, F.; Selb, J. *Macromolecules* **1993**, *26*, 4521.
(44) Yekta, A.; Xu, B.; Duhamel, J.; Adiwidjadja, H.; Winnik, M. A. *Macromolecules* **1995**, *28*, 956.
(45) Volpert, E.; Selb, J.; Candau, F. *Macromolecules* **1996**, *29*, 1452.
(46) *Polymer Handbook*, 3rd ed.; Brandrup, J., Immergut, E. H., Eds.; Wiley-Interscience: New York, 1989; p VII-32.
(47) Bokias, G.; Durand, A.; Hourdet, D. *Macromol. Chem. Phys.* **1998**, *199*, 1387.

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