Influence of Amino Group pK_a on the Properties of Stimuli-Responsive Piperazine-Based Polymers and Hydrogels

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ABSTRACT: Linear homopolymers of N-acryloyl-N'-alkyl piperazine (N'-alkyl: methyl, ethyl, or propyl) and their corresponding crosslinked hydrogels were prepared. The polymers showed good responses to changes in the pH of the medium due to the presence of tertiary amine functions that could be protonated at a low pH. The nature of the N'-alkyl group attached to the piperazine amino nitrogen greatly affected the pK_a of the amino group. This in turn influenced the solution behavior of the polymers and was studied with light scattering, potentiometry, and viscosity measurements. The basicity of the polymers increased with an increase in the chain length of the N'-alkyl substituent. The intrinsic viscosity of the polymers in a good polar organic solvent such as dimethylformamide decreased slightly with increasing temperature because of decreased thermodynamic affinity (interaction) at high temperatures. The viscosity behavior of the polymers in sodium chloride solutions was similar to that of classical polyelectrolytes. The swelling property of the hydrogels was studied with water sorption measurements, and the swelling was by anomalous (non-Fickian) transport. The diffusion coefficient of the gels in solutions of pH 2.6 increased with increasing N'-alkyl chain length, whereas at neutral pH, the effect was reversed. This behavior was attributed to the increase in both the basicity and hydrophobicity of the gels with an increase in the chain length of the N'-alkyl groups. © 2007 Wiley Periodicals, Inc. J Appl Polym Sci 107: 1449–1458, 2008

Key words: gels; hydrogels; hydrophilic polymers; swelling

INTRODUCTION

Polymers that respond to external stimuli are termed smart, intelligent, stimuli-responsive, or environmentally sensitive polymers. Recent interest in intelligent polymeric systems has focused on aqueous solutions, interfaces, and hydrogels because of their potential applications in controlled drug delivery systems, skin care products, immobilization of enzymes, concentration of proteins, chemical sensors, and so forth.[1–4] These polymers exhibit the lower critical solution temperature (LCST) phenomenon in response to various physical, chemical, or biochemical stimuli in conjunction with thermal stimuli.[5] These polymers are soluble in water but undergo phase transitions in response to various physical, chemical, or biochemical stimuli such as pH, temperature, ionic strength, light, and magnetic field. The potential responses to these stimuli can be changes in the phase, shape, volume, optical properties, and so forth. Galaev[6] brilliantly reviewed various stimuli-responsive water-soluble polymers exhibiting LCST. A critical balance of hydrophilic and hydrophobic side groups

of the polymer system is a vital parameter for observing the LCST behavior.[6–9] The introduction of hydrophilic and hydrophobic comonomers can cause the LCST of the polymers either to increase or to decrease. The nature of the chemical structure of the polymer also plays a vital role in influencing the LCST, as pointed out by Taylor and Cerankowski.[4,10] The addition of one or two methylene groups to the monomer can convert the polymer from being totally soluble to one with LCST behavior. This is due to an entropy phenomenon, and the entropy change for the transfer of a methylene group into water has been reported to be $-20 \text{ J}^{-1} \text{ deg}^{-1} \text{ mol}$.

Of late, polymer systems that demonstrate a phase transition or response to more than one stimulus such as temperature and pH have received considerable research attention. The mutual influence of pH and temperature on the swelling of ionizable and thermosensitive hydrogels was demonstrated by Feil et al.[11] Later, Chen and Hoffman[3] studied graft copolymers that exhibited temperature-induced phase transitions over a wide range of pHs. Thermo- and chemomechanically responsive polymers were developed by Brazel and Peppas.[4] To prepare polymers that respond to more than one stimulus, monomers that are sensitive to certain stimuli have to be copolymerized.[11–14] In our continuous effort to develop

stimuli-responsive piperazine-based polymers[8,15,16] that can respond to various stimuli without the need of copolymerization with a second monomer, we report here the influence of an alkyl substituent on the tertiary amino nitrogen of the monomer that is the central part for protonation.

EXPERIMENTAL

Materials

Acryloyl chloride (Fluka), ethylene glycol dimethacrylate (EGDMA; Fluka), and methyl methacrylate (MMA; Merck, UK) were distilled under reduced pressure and stored in a refrigerator. Azobisisobutyronitrile (AIBN; TCI, Tokyo, Japan) was recrystallized in methanol. The photoinitiator 1,1-dimethoxy-1-phenyl acetophenone (DMPA; Aldrich) was used as received. N-Methyl piperazine and N-ethyl piperazine (Aldrich) were stored over molecular sieves (3 Å) before use. N-Propyl piperazine was extracted from N-propyl piperazine dihydrobromide (Acros). 1,4-Dioxane (Merck) and tetrahydrofuran (THF; Baker) were refluxed with metallic sodium for 5 h, and this was followed by distillation under nitrogen. All other materials were used as received. Buffer solutions of NaH_2PO_4–NaH_2PO_4 were prepared by the adjustment of a $0.1M$ NaH_2PO_4 solution with Na_2HPO_4 to the required pH.

Synthesis of N-acryloyl-N′-alkyl piperazine

The monomers N-acryloyl-N′-methyl piperazine (AcrNMP), N-acryloyl-N′-ethyl piperazine (AcrNEP), and N-acryloyl-N′-propyl piperazine (AcrNPP) were synthesized according to methods reported previously.[8,15,16]

Synthesis of the linear homopolymers

Linear homopolymers of AcrNMP, AcrNEP, and AcrNPP were prepared by thermally initiated free-radical solution polymerization, and the preparation of the first system is described.

Homopolymer of AcrNMP (PAcrNMP)

AcrNMP (8.74 mmol, 1.35 g) and the initiator AIBN (0.5 wt %, 0.02 g) were dissolved in 30 mL of freshly distilled dioxane in a 100-mL, round-bottom flask fitted with a vacuum tap. The contents of the flask were degassed three times by freeze–thaw cycles, and the flask was sealed under vacuum. Polymerization was carried out at 70°C for 24 h, and the polymer was isolated by precipitation in anhydrous ether (400 mL). The polymer was reprecipitated in diethyl ether at least three times and dried in vacuo at 45°C

for 24 h (yield = 90%, pale yellow, hygroscopic powder, glass-transition temperature = 102.8°C).

Homopolymers of AcrNEP (PAcrNEP) and AcrNPP (PAcrNPP)

AcrNEP (12.2 mmol, 2.04 g) and AcrNPP (5.6 mmol, 1.02 g) were polymerized in dioxane with AIBN as the initiator with a method similar to that described previously (PAcrNEP: yield = 75%, pale yellow, hygroscopic powder, glass-transition temperature = 101.3°C; PAcrNPP: yield = 65%, white powder, glass-transition temperature = 100°C).

Synthesis of the crosslinked polymers

Polymer networks were prepared by photopolymerization by the crosslinking of the monomers with a crosslinking agent, namely, EGDMA. The preparation of the crosslinked polymer of AcrNMP (CAcrNMP) can be described as follows, and the crosslinked polymers of AcrNEP (CAcrNEP) and AcrNPP (CAcrNPP) were prepared by a similar method. AcrNMP (9.7 mmol, 1.5 g), EGDMA (2 wt %, 0.03 g) as the crosslinking agent, and DMPA (0.3 wt %, 0.005 g) as the photoinitiator were mixed in a glass ampule. The contents of the ampule were purged with bubbling dry nitrogen for about 10 min, and the ampule was sealed. The sealed ampule was then sonicated for 5 min to expel any tiny air bubbles. Polymerization was carried out in a photochemical reactor by UV irradiation ($\lambda > 300$ nm) for 30 min. The clear, transparent polymer was recovered and was soaked in diethyl ether for 2 weeks to remove any unreacted monomers, with ether being replenished daily. The polymer was then cut into small rectangular slabs (ca. 1.5 cm, thickness ≈ 0.5 cm) and dried to a constant weight in vacuo. The basic structures of the polymers and the crosslinker are shown in Figure 1.

Light scattering measurements

The homopolymers were characterized by both static light scattering (SLS) and dynamic light scattering
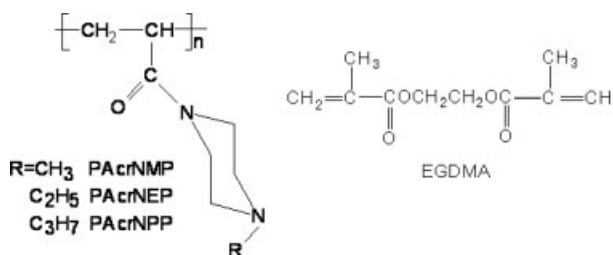

Figure 1 Chemical structures of the linear polymers and the crosslinking agent.

(DLS) techniques. A Brookhaven BI-200SM goniometer system equipped with a BI9000AT 532-channel digital multiple τ correlator was used. The light source was a power-adjustable, vertically polarized argon-ion laser with 400 mW of power operating at a wavelength of 488 nm. The temperature was controlled with a Science/Electronic water bath. The SLS measurements were evaluated according to the Zimm equation as follows:

$$\frac{KC}{R(q)} = \frac{1}{M_w}\left(1 + \frac{1}{3}\left\langle R_g{}^2\right\rangle_z \times q^2\right) + 2A_2 \times C \quad (1)$$

where M_w is the weight-average molar mass, $\langle R_g{}^2\rangle_z$ is the z-average mean-square radius of gyration, A_2 is the second virial coefficient, $K = 16\pi^2 \times n^2(dn/dc)^2/(\lambda_0{}^4 \times N_A)$, n is the refractive index of the solvent, λ_0 is the wavelength of the laser, dn/dc is the refractive-index increment, N_A is Avogadro's number, C is the weight concentration of the polymer, and $R(q)$ is the Rayleigh ratio at scattering vector q.

In DLS, a precise intensity–intensity time correlation function in the self-beating mode was measured. The REPES inverse Laplace transformation routine supplied with the GENDIST software package was used to analyze the correlation functions. The probability of rejection was always set to 0.5. The hydrodynamic radius (R_h) was calculated with the known Stokes–Einstein equation:

$$R_h = \frac{k_B T}{6\pi\eta D} \quad (2)$$

where k_B is the Boltzmann constant, T is the absolute temperature, η is the solvent viscosity, and D is the measured diffusion coefficient.

All the glassware was cleaned in a 20% nitric acid solution and thoroughly rinsed in deionized water before use. The sample solutions were filtered with a 0.2-μm filter (Whatman, UK) into cylindrical cuvettes, and the samples were allowed to equilibrate overnight before the measurements.

Potentiometric titrations

Potentiometric titrations were performed with an ABU93 triburette titration system (Radiometer, Copenhagen, Denmark). The instrument was integrated with a standard RS232C interface, and the titration was controlled with Aliquot titration software (Denmark). The electrode assembly consisted of an Origin pHg 201 glass electrode (Denmark) and an Orion REF 201 reference electrode (Denmark). The conductivity was measured with a CDM83 conductometer.

Viscosity measurements

The reduced viscosity of the polymers in dimethylformamide (DMF) and in aqueous sodium chloride solutions was measured at the desired temperatures with a Cannon-Ubbelohde dilution capillary viscometer in a water bath. The flow times of the pure solvent (t_0) and polymer solution (t) were recorded. The intrinsic viscosity ([η]) was obtained by extrapolation of both the reduced viscosity (η_{sp}/C) and the inherent viscosity (ln η_r/C) to infinite dilution according to the Huggins' and Kramer's relationships, respectively:

$$\frac{\eta_{sp}}{C} = [\eta] + k'[\eta]^2 C \quad (3)$$

$$\ln\frac{\eta_r}{C} = [\eta] + k''[\eta]^2 C \quad (4)$$

where $k' - k'' = \frac{1}{2}$.

Equilibrium swelling studies

The gravimetric equilibrium swelling of the gels was studied to determine their sensitivity to pH. For this study, sodium acetate/acetic acid (pH 2.6–5.6) and sodium hydrogen phosphate/disodium hydrogen phosphate (pH 6.3–9.1) buffer solutions were used. The gel slabs were immersed in respective buffer solutions in glass vials at 25°C for 1 week. Each sample was then removed from the respective vials, tapped with a dampened Kimwipe towel to remove the excess surface water, and weighed. The dry weights were measured after desiccation of the gels for 3 days under vacuum at 40°C until constant dry weights were recorded. All the swelling experiments were performed in duplicate for consistency, and the weight swelling ratio was calculated with the following expression:

$$\text{Swelling ratio} = \left(\frac{W_t - W_d}{W_d}\right) \quad (5)$$

where W_t and W_d are the wet and dry weights of the gel, respectively.

Water sorption studies

The gel slabs were accurately weighed and placed in glass vials with 10 mL of distilled water or a buffer solution of pH 2.6. The vials were placed in a thermostated water bath maintained at 25°C. The water uptake was calculated by the measurement of the weight gain of the sample at different times after careful wiping of the surface of gels for excess water. The water uptake, which is similar to the weight swelling ratio, was calculated with the previous equation.

TABLE I
SLS and DLS Results of Linear Polymers in THF Measured at 20°C

Polymer	$M_w \times 10^{-5}$ (g/mol)	R_g (nm)	R_h (nm)	$A_2 \times 10^4$ (cm³ mol/g²)	R_g/R_h
PAcrNMP	1.50	23.9	20.84	2.41	1.15
PAcrNEP	1.10	25.4	19.48	2.19	1.33
PAcrNPP	3.38	27.1	21.85	1.89	1.24

RESULTS AND DISCUSSION

Synthesis of the polymers and general observations

The linear homopolymers were prepared by thermally initiated free-radical solution polymerization with AIBN as the thermal free-radical initiator, whereas the crosslinked polymers were prepared by photoinitiated free-radical bulk polymerization with DMPA as the photoinitiator. DMPA was chosen as the photoinitiator because of its high rate of radical production at room temperature. The linear homopolymers, PAcrNMP and PAcrNEP, were completely water-soluble at all temperatures, whereas PAcrNPP showed the LCST phenomenon at 38°C, the details of which were reported earlier.[16]

Light scattering measurements

The usual characteristic molecular and thermodynamic parameters, determined by both SLS and DLS measurements, for the linear homopolymers in THF are summarized in Table I. The positive values of A_2 indicate that THF is a good solvent for the polymers when solvent–polymer interactions dominate. The DLS measurements in THF show a single decay mode for all the polymers. In accordance with the theory of dilute binary solutions, this mode is due to the translational diffusion of single polymer chains. THF being a good solvent for these polymers, no association of polymer chains was detected. Furthermore, with an increase in scattering vector q, the decay mode shifted to the left, indicating the diffusional behavior of the polymer chains. As the relaxation is caused by the diffusion of polymer chains, the decay time (τ) and q follow the relationship $\tau \propto 1/q^2$. The shape factor, defined as $\rho = R_g/R_h$ (R_g is the radius of gyration), is in the range of 1.2–1.3, which is predicted for flexible coils in a good solvent.[17]

The DLS results for the behavior of the polymers in Milli-Q water (pH 7) at 20°C are interesting. The decay time distributions for PAcrNPP in water measured at three different angles (60, 75, and 90°) are shown in Figure 2. The distribution is bimodal, and this is in stark contrast to the observed monomodal distribution in THF. The small first peak (τ_{fast}) appears at 82 μs, and the large second peak (τ_{slow}) appears at 695 μs, with the corresponding R_h values of 10.1 and 82 nm, respectively. The fast mode is attributed to single polymer chains (unimer), and the slow mode is attributed to aggregates of polymer chains as a result of association. Both decay modes exhibit a linear q^2 dependence, indicating that the diffusion is purely translational in nature. The observance of the fast mode is believed to be due to the association between the mild hydrophobic N'-propyl groups of PAcrNPP,[16] and the behavior resembles those of some associative polymers in aqueous solutions.[17]

These results indicate that PAcrNPP forms aggregates even below its LCST, and interestingly, we have observed similar aggregates below the LCST for 1 wt % poly(N,N-diethylacrylamide) aqueous solutions. For the solutions of the two lower analogues, PAcrNMP and PAcrNEP, only one relaxation decay mode corresponding to the translational diffusion of a single polymer chain was observed. These two polymers did not show any phase-transition behavior in the temperature range studied (5–90°C). The intensity correlation function and the corresponding relaxation time distribution for PAcrNEP in water at 20°C are shown in Figure 3. The hydrophobicity of the polymers increases with an increase in the alkyl chain length of the N'-substituted alkyl group. When the alkyl group contains three carbon atoms, the molecule becomes sufficiently hydrophobic to induce associations even below the transition temperature.
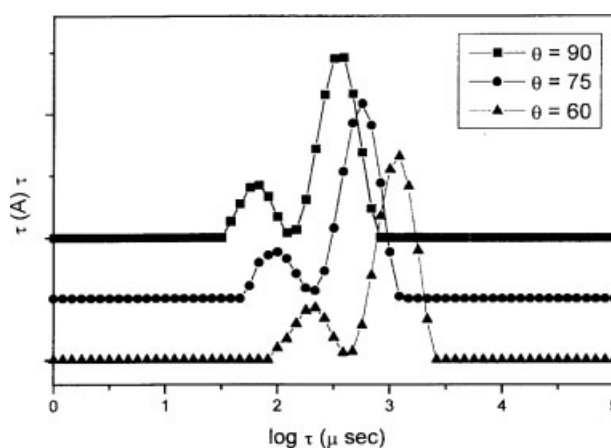

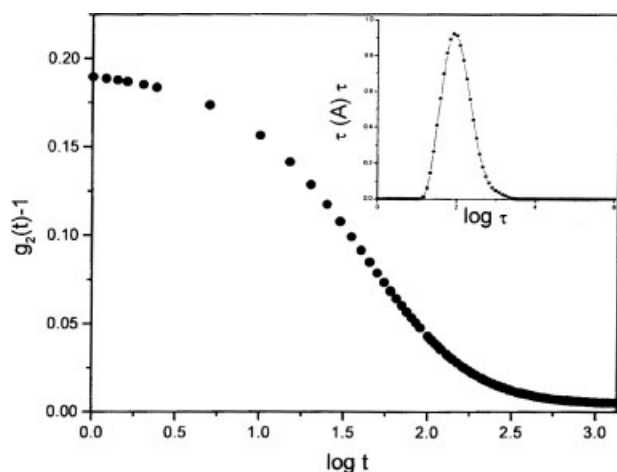**Figure 2** Relaxation time distribution for PAcrNPP in water (0.5 g/L) at 20°C.

Figure 3 Intensity autocorrelation function for PAcrNEP in water (0.5 g/L) at 20°C ($\theta = 90°$). The insert shows the relaxation time distribution.

Potentiometric titrations

Potentiometric titrations of the polymers were carried out to study the effect of charge on the phase separation. Titration curves were obtained by the titration of an aqueous polymer solution with 0.12M HCl without any added electrolyte. The apparent dissociation constant (pK_{ap}) of the copolymers was calculated from the titration curves with the following equation:

$$pK_{ap} = pH - \log \alpha/(1 - \alpha) \qquad (6)$$

where α is the degree of protonation [i.e., C_H/C_m, where C_H is the effective concentration of added HCl and C_m is the concentration of the polymer chains in terms of monomer units].[17] This definition of α implies that all H$^+$ added from HCl is assumed to have protonated the amine groups. The potentiometric data obtained with the equation are given in Table II. The pK_{ap} value increases slightly with an increasing N'-alkyl chain of the monomer unit. Thus, the pK_a of conjugate PAcrNMP is low, whereas that of conjugate PAcrNPP is high. This variation in the basicity is expected, as amines with ethyl groups are known to be more basic than amines with methyl groups.[18] Of the three polymers, only PAcrNPP exhibited the LCST phenomenon, and with the

TABLE II
Potentiometric Data of Linear Polymers Measured at 25°C

Polymer	α	pK_{ap}
PAcrNMP	0.0508	4.51
PAcrNEP	0.0853	4.58
PAcrNPP	0.0977	4.61

potentiometric data, the total amount of charged monomer units close to the LCST was estimated to be approximately 5.5–5.6 mol %. The basicity of PAcrNPP decreased slightly above its LCST because of the decreased dielectric constant of the environment.[10,19] This indicates that there is no phase separation until the number of charged groups on the polymer is reduced to a critical limit.[9,16,20]

Viscosity measurements in DMF

The viscosity behavior of the polymers was investigated in a good polar organic solvent, DMF, at three different temperatures. The reduced viscosity (η_{sp}/C_p) is linearly proportional to the polymer concentration, which is given by Huggins' equation as follows:

$$\eta_{sp}/C_p = [\eta] + k_H[\eta]^2 C_p \qquad (7)$$

where k_H is Huggins' constant. It can be observed that [η] of the polymers decreases slightly with increasing temperature. The effect of temperature on [η] of the polymers is shown in Figure 4. The plots are all linear with negative slopes. The negative slope indicates that the polymer coils are not swollen to a great extent in DMF. This is attributed to decreased thermodynamic affinity (interaction) between the solvent and polymer chains with an increase in temperature. Similar behavior has been reported for copolymers of MMA and acrylonitrile in DMF.[21] On the basis of the relative viscosity, the equivalent hydrodynamic volume (V_e) was calculated; it is a measure of the size of a solvated polymer molecule at infinite dilution.

The method described by Narang and Garg[22] to determine the shape of protein molecules was followed. This was done through the plotting of the fol-
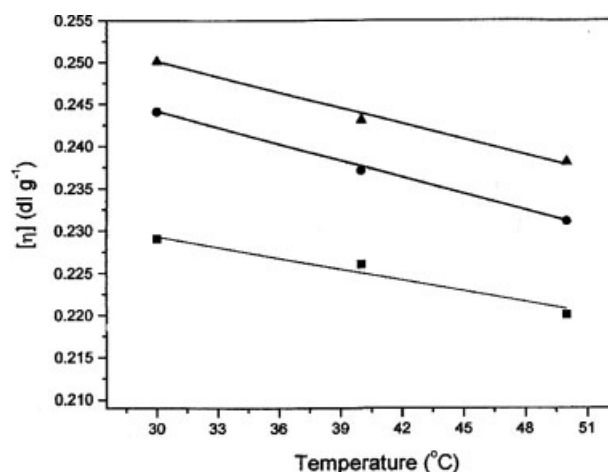

Figure 4 Effect of temperature on [η] of linear polymers in DMF: (■) PAcrNMP, (●) PAcrNEP, and (▲) PAcrNPP.
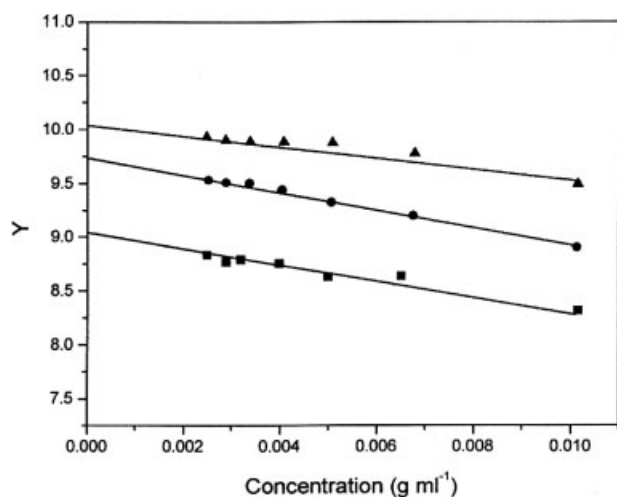
Figure 5 Plot of Y against the polymer concentration for linear polymers in DMF at 30°C: (■) PAcrNMP, (●) PAcrNEP, and (▲) PAcrNPP.

lowing expression against the polymer concentration and the extrapolation of C to 0 to obtain V_e:

$$Y = \frac{\left(\eta_r^{1/2} - 1\right)}{C\left(1.35\eta_r^{1/2} - 0.1\right)} \tag{8}$$

where V_e (mL/g) at infinite dilution is a measure of solvated polymer molecules and is dependent on temperature. Representative plots of Y versus the polymer concentration at 30°C, showing a decrease of V_e with an increase in temperature, are shown in Figure 5, and the values of the hydrodynamic volumes thus determined are given in Table III. The results indicate that solvation of a polymer decreases with increasing temperature. The shape factor (ν) was calculated by $[\eta] = \nu V_e$, where V_e is the hydrodynamic volume. The value of ν for all the polymers at 30, 40, and 50°C is around 2.55. This indicates that in the concentration range studied, the polymer molecules are roughly spherical in shape in this solvent.[21]

Viscosity measurements in NaCl solutions

The $[\eta]$ values of the polymers (1.0 g/L to 0.30 g/mL) in solutions of various NaCl concentrations (0.01–0.5M) of pH 7 are shown in Figure 6. This

TABLE III
Hydrodynamic Volume of Linear Polymers in DMF

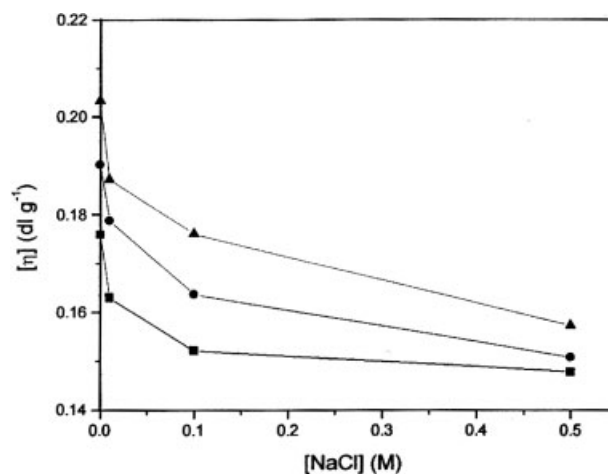| Polymer	V_e (mL/g)		
	30°C	40°C	50°C
PAcrNMP	8.92	8.16	7.79
PAcrNEP	9.74	9.01	8.98
PAcrNPP	10.14	9.56	9.25

Figure 6 Effect of NaCl on [η] of linear polymers at 25°C: (■) PAcrNMP, (●) PAcrNEP, and (▲) PAcrNPP.

measurement was performed to illustrate the effect of simple electrolytes such as NaCl on the viscosity of the polymers and also to demonstrate the polyelectrolyte nature of these polymers that belong to the class of poly(amido amines). When the concentration of NaCl was increased, the reduced viscosity decreased significantly because of the reduction in the coil size of the polymers. The trends of the viscosity curves are fairly similar, indicating that a change in the alkyl substituent (from methyl to propyl), which in turn affects the pK_a of the amino nitrogen, has little effect on the viscosity behavior. This behavior of viscosity reduction is similar to that of classical polyelectrolytes. Similar behavior has been reported for various polyelectrolyte and hydrophobically modified polyacrylate systems.[23] The impact of the molar mass (3.38 × 10⁵ g/mol) of PAcrNPP on its high [η] value could not be ruled out. However, in this measurement, we solely looked at the N'-alkyl substituent and its influence on the solution behavior of the polymers and hence did not investigate the effect of molar mass in detail. The Huggin's Constant (k_H) as a function of the NaCl concentration of PAcrNPP is shown in Figure 7. The values are greater than unity and are greatly dependent on the salt concentration. The observed high k_H values suggest the presence of polymer association in these salt solutions. This is consistent with the result that the LCST of PAcrNPP decreases in an almost linear relationship with an increase in the NaCl concentration. A small amount of NaCl (0.005M) was able to lower the LCST from 37.7 to 32.4°C.[16] Therefore, decreasing [η] with increasing k_H reflects a poor solvent condition.[24]

Swelling studies of the gels

The effect of pH on the swelling behavior of the gels was investigated. Figure 8 shows the equilibrium
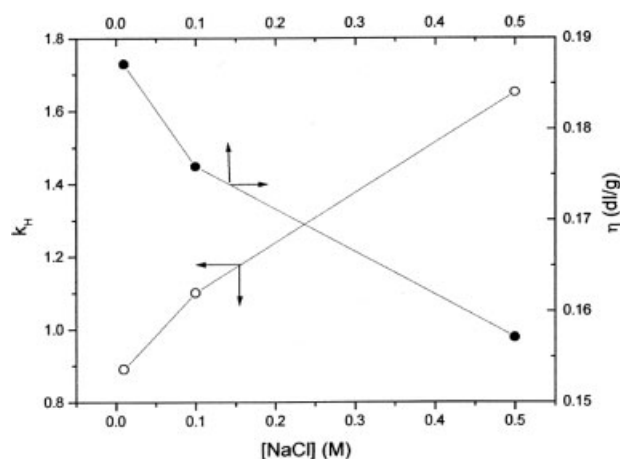
Figure 7 Effect of NaCl on $[\eta]$ and k_H for PAcrNPP at 25°C.

TABLE IV
Effect of the Buffer (pH 3.6) on the Swelling of Gels at 25°C

| | Weight swelling ratio | |
Gel	Citrate buffer	Phosphate buffer
CAcrNMP	3.74	8.12
CAcrNEP	4.13	10.16
CAcrNPP	5.65	12.10

weight swelling ratio versus pH at 25°C. The gels swelled in an acidic medium and deswelled in an alkaline medium. The swelling ratio reached a maximum of 12.9 for CAcrNPP at pH 2.6, whereas those of CAcrNEP and CAcrNMP were 11 and 8.6, respectively. At pH 9, the swelling ratio is about 3.1 for all the gels. This swelling ratio is considerably lower than that of the gels prepared in solution.[25] These gels were prepared in bulk, which imparted additional crosslinking in the form of physical entanglements. The pH-sensitive copolymer gels of N,N-dimethylaminoethyl methacrylate and n-butyl methacrylates prepared in bulk exhibited similar reduced swelling.[26] The lower swelling observed for the gels can thus be related directly to their network structure. Polymers prepared in bulk have high elastic constraint, which leads to lower swelling.

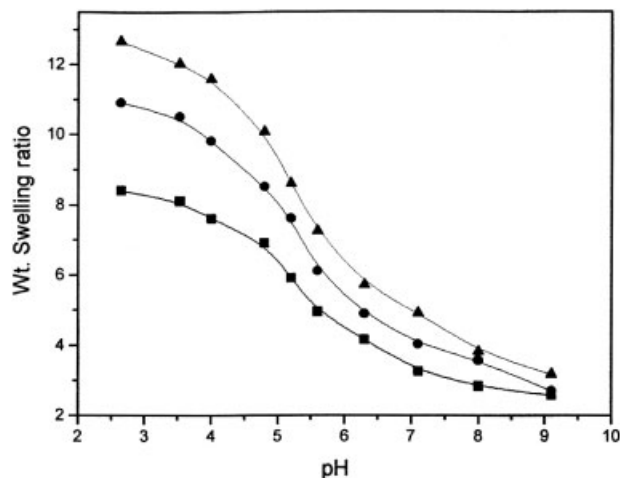The effect of the nature of the buffer on the swelling of the gels was also studied. The swelling ratios

of the gels in an acetate buffer and a citrate buffer of pH 3.6 at 25°C are summarized in Table IV. The effect of the nature of the buffer on the swelling of the gels is clearly evident. The swelling in the citrate buffer is lower than that in the phosphate buffer, and this can be explained on the basis of the shift in the charge on citrate counterions. The citrate buffer has three ionizable carboxylic acid groups with pK_1 3.15, pK_2 4.78, and pK_3 6.40. At a low pH, the citrate passes from being predominantly trianionic to being dianionic and finally to being monoionic. This explains the lower swelling in a multivalent counterion environment (citrate buffer).[27]

The swelling behavior of the gels in a simple electrolyte solution (NaCl) of pH 7 as a function of temperature was also investigated. Because of hydrophobicity and higher pK_a, CAcrNPP alone showed a significant change in the swelling behavior with increasing NaCl concentration and temperature, whereas the lower analogues hardly displayed any noticeable change. Figure 9 shows the effect of the NaCl concentration (pH 7) and temperature on the swelling of CAcrNPP gels. The observed drop in the swelling ratio with increasing NaCl concentration reflects a change in both the solubility and viscosity of the system. In general, increasing the simple electrolyte concentration decreases the solubility of the
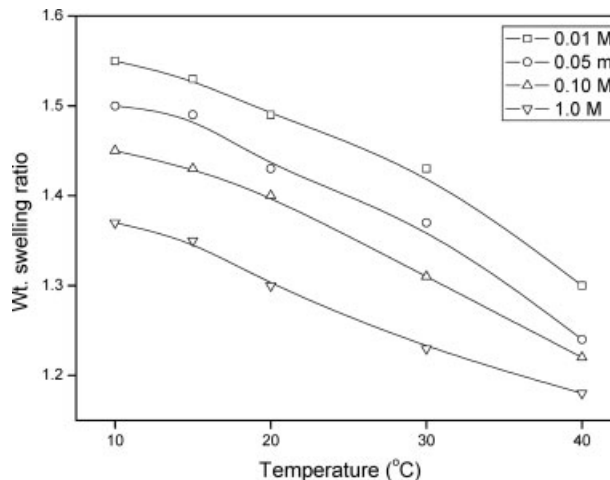

Figure 8 Effect of pH on the swelling of gels with 2 wt % EGDMA: (■) CAcrNMP, (●) CAcrNEP, and (▲) CAcrNPP.

Figure 9 Effect of NaCl and temperature on the swelling of CAcrNPP gel slabs (the lines are guides to the eye).
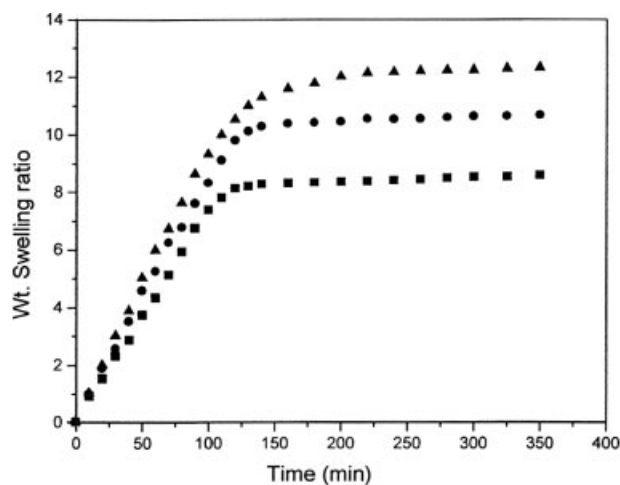
Figure 10 Water sorption of gels in buffer solutions of pH 2.6 at 25°C: (■) CAcrNMP, (●) CAcrNEP, and (▲) CAcrNPP.

polymer because of a salting-out effect. In agreement is the LCST behavior of linear PAcrNPP in simple salt solutions in water,[16] and similar behavior has also been reported for poly(N-isopropylacrylamide) in salt solutions.[22]

Water transport mechanism in gels

Water sorption isotherms of the gels (thin rectangular slabs: area = 1.5 cm, thickness = 0.5 cm) in buffer solutions of pH 2.6 at 25°C are shown in Figure 10. The water uptake increased steeply up to the first 100 min of swelling and leveled off thereafter. The swelling of CAcrNPP is highest with a swelling ratio of 12.5, and it is followed by the gels of CAcr-NEP and CAcrNMP. This trend is attributed to the size of the N'-alkyl substituent of the monomer unit and hence to the basicity of tertiary amine groups. The following equation prescribed by Ritger and Peppas[28] was fitted to the initial swelling of the sorption curves in the range of $M_t/M_\infty \leq 0.6$ (first 60% of fractional release):

$$\frac{M_t}{M_\infty} = kt^n \qquad (9)$$

where M_t and M_∞ are the weights of water taken up at time t and infinite time, respectively; k is a characteristic constant of the gel; and n is a characteristic diffusional exponent of the mode transport of the penetrate. This generalized expression couples both Fickian and non-Fickian mechanisms for a thin slab of polymer because many release processes fall between these limiting cases. The values of n and k were calculated from the slopes and intercepts of the plot of $\log(M_t/M_\infty)$ versus $\log t$. For Fickian kinetics in thin polymer films or slabs, in which the rate of

diffusion of the solvent is rate-limiting, n equals 0.5, whereas values between 0.5 and 1 indicate contributions from anomalous (non-Fickian) processes such as polymer relaxation.[28,29]

The collective diffusion coefficient (D) values of the gels were determined from the gradient of the plot of the initial sorption rate versus the square root of time (first 60% of fractional release) with the following equation, and the results are summarized in Table V:

$$\frac{M_t}{M_\infty} = \frac{4}{l}\left(\frac{Dt}{\pi}\right)^{1/2} = \frac{W_t}{W_\infty} \qquad (10)$$

where W_t and W_∞ are the weight swelling ratios at time t and infinite time, respectively, and l is the thickness of the dry gel. It has to be emphasized that this equation is strictly dependent on the geometry of the gel and is valid only for thin films or slabs.[28] The diffusional exponent (n) of the gels is within the limits of $0.50 < n < 1.00$ both in water and in a buffer solution of pH 2.6. This indicates that water diffusion in the gels follows an anomalous (non-Fickian) behavior that is attributed to polymer relaxations. Surprisingly, the values of n and D for the various gels in buffer solutions of pH 2.6 are in the ranges of 0.83–0.99 and 2.08–3.30 $\times$ 10^{-7} cm^2/s, respectively. These relatively high values are attributed to the hydrophilic nature of the gel network. As these gels are ionizable at the tertiary amine functions (N'-alkyl), more complications arise because both the solvent and ions must be transported into the gel to reach equilibrium. Therefore, under such conditions, in addition to solvent diffusion and polymer relaxation, other factors that contribute to swelling are believed to be ion diffusion and fixed charge group ionization.[26,27]

The swelling of the gel was further characterized by the method proposed by Schott:[30]

$$\frac{t}{W} = A + Bt \qquad (11)$$

where W is the water uptake at time t, $B = 1/W_\infty$ is the inverse of maximum swelling, and $A = 1/(dW/dt)_0$ is the reciprocal of the initial swelling rate. It

TABLE V
Water Sorption Characteristics of Gels at 25°C in Water

Gel	pH	n	k	$D \times 10^7$ (cm^2/s)
CAcrNMP	2.6	0.83	0.01	2.08
CAcrNMP	Water	0.52	0.07	7.20
CAcrNEP	2.6	0.94	0.01	2.78
CAcrNEP	Water	0.63	0.05	5.96
CAcrNPP	2.6	0.99	0.01	3.30
CAcrNPP	Water	0.83	0.03	5.00

was further demonstrated by Schott that eq. (11) implies second-order kinetics. Applying this equation to the swelling data gave straight lines with good correlation coefficients, as shown in Figure 11. The diffusion coefficients at pH 2.6 increased with increasing length of the N'-alkyl substituent, whereas at neutral pH in pure water, the trend was reversed. At pH 2.6, the extent of protonation was highest for CAcrNPP because it is the most basic gel among the three analogues, and this gives rise to the observed increased swelling and thus a high diffusion coefficient. At neutral pH, CAcrNPP is the most hydrophobic gel and thus swells the least, giving the lowest diffusion coefficient.

Further understanding of the swelling of hydrophilic gels in the form of thin slabs can be aided by the Siegel model,[26] which is pictorially described in Figure 12. The slab of gel that is immersed in the swelling medium at time $t = 0$ is in the glassy state. The swelling process is initiated by the diffusion of the solvent and ions into the gel matrix, during which the gel goes from its glassy state to the rubbery state and becomes soft. To initiate this transition, a certain threshold combination of the solvent and ions are needed, and as a result, a swelling front will appear, separating the glassy core from the rubbery periphery. The rigid core then constrains the swelling in the periphery, allowing swelling only in the direction that is normal to the front. This leads to the development of a differential swelling stress that drives the swelling front, and as a result of this, the two opposing faces will meet. At this point, the swelling constraint diminishes, whereby the differential swelling stress is released and swelling is permitted in all three dimensions. This leads to the observed acceleration in swelling of hydrophilic gels.
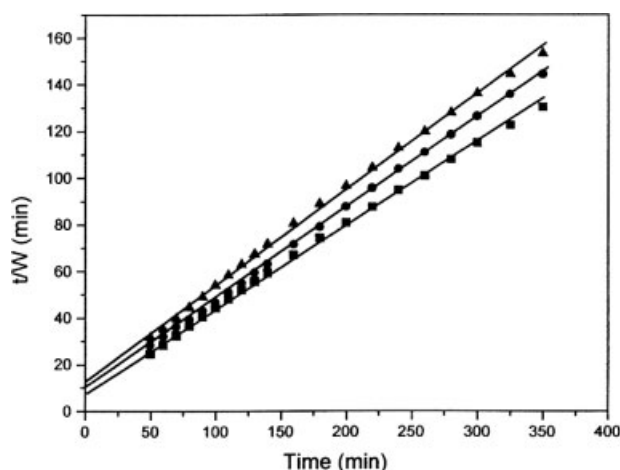

Figure 11 Plot of the reciprocal of the average swelling rate for various swelling times for gels in buffer solutions of pH 2.6 at 25°C: (■) CAcrNMP, (●) CAcrNEP, and (▲) CAcrNPP.
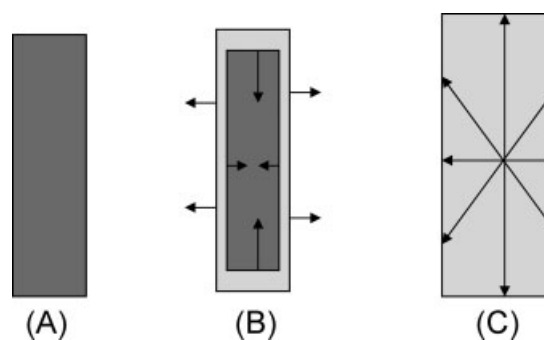

Figure 12 Schematic representation of swelling front and swelling of gels: (A) dry gel, (B) appearance of swelling front and expansion of gel, and (C) diminished swelling constraint followed by swelling in all directions.

CONCLUSIONS

Stimuli-responsive linear copolymers and cross-linked hydrogels of N-acryloyl-N'-alkyl piperazine were prepared. We observed that with an increase in the substituent alkyl chain length, the polymers went from a totally water-soluble system to a system that exhibited LCST. Because of the presence of tertiary amine functions, these polymers showed good responses to changes in the pH of the medium. At a low pH, the tertiary amines were protonated, leading to electrostatic repulsion between the charged chains, whereas at a high pH, they were deprotonated. The basicity of the polymers increased with an increase in the alkyl chain length of the N'-alkyl group. The effect of temperature on $[\eta]$ of the polymers indicated that the polymer coils did not swell to a great extent in DMF, and this was due to weak thermodynamic affinity at high temperatures. The viscosity measurements in sodium chloride solutions indicated that the N'-alkyl chain length had little effect, and the polymers behaved like classical polyelectrolytes. The water sorption kinetics of the gels followed an anomalous (non-Fickian) behavior due to polymer relaxation. The initial swelling in a solution of low pH was attributed to the development of a swelling front and therefore to a differential swelling stress. The effect of the N'-alkyl substituent in altering the properties of water-soluble polymers and gels has thus been demonstrated, and this is interesting in developing homopolymers/gels for specific applications that can respond to a variety of stimuli without the need of a second monomer.

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