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ORIGINAL PAPER

New pH-responsive linear and crosslinked functional copolymers of *N*-acryloyl-*N*′-phenyl piperazine with acrylic acid and hydroxyethyl methacrylate: synthesis, reactivity, and effect of steric hindrance on swelling

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Abstract New functional linear copolymers and crosslinked gels based on a disubstituted heterocyclic acrylamide, i.e., *N*-acryloyl-*N*′-phenyl piperazine (AcrNPhP) with acrylic acid (AA) and hydroxyethyl methacrylate (HEMA) were prepared by thermal free-radical polymerization. The composition of the linear copolymers was analyzed by infra-red spectral analysis and elemental analysis methods. The reactivity parameters of the monomers were determined by the Finemann-Ross and Kelen–Tüdös linearization methods. Using the values obtained from the Kelen–Tüdös linearization methods, the reactivity or resonance stabilization (Q) and polarity (e) of AcrNPhP with AA and HEMA were calculated (AcrNPhP–AA system $Q = 1.9$, $e = -0.6$, and AcrNPhP–HEMA system $Q = 2.5$, $e = -1.2$). Crosslinked copolymer hydrogels of AcrNPhP with AA and HEMA were prepared by bulk and solution polymerization methods. The method of preparation, the type of crosslinker and monomers showed a profound impact on the pH responsive swelling of the gels. The hydrogels were highly responsive to changes in external pH. The gels composed of AcrNPhP and AA swelled more than 1,200 % above the pK_a of acrylic acid. Interestingly, no significant swelling (about 1 %) was observed in solution of low pH (acidic) despite the presence of an ionizable tertiary amine function in the polymer network. This is attributed to the presence of a bulky phenyl group at the tertiary amine function of AcrNPhP which sterically hinders the protonation and thereby the final swelling of the gel. The gels composed of AcrNPhP and HEMA did not display a significant pH responsive behavior due to the same effect. The AcrNPhP–HEMA gel-containing 70 % AcrNPhP swelled to only 50 % despite the presence of a large fraction of the ionizable unit.

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Introduction

Emphasis on research in new polymeric materials in recent years is directed toward integrating multiple response functions into a single-polymeric materials for enhanced and targeted applications. "Stimuli"-responsive polymers are materials which can change their physical properties in response to certain external stimuli such as temperature, pH, ionic strength, illumination, magnetic field, etc. [1–6]. The response of the material to these external stimuli can be in the form of changes in phase, shape, volume, and optical properties. These advanced materials find applications in enhanced drug delivery systems, cosmetics, enzyme immobilization processes, chemical sensors, etc. [7–15].

Among the family of thermo-responsive polymers, poly(*N*-isopropyl acrylamide) PNIPAM is the most widely studied. This polymer is soluble in water below 32 °C and phase separates above this temperature. The temperature at which phase separation occurs is called the critical solution temperature (CST). This is because the polymer exhibits a first-order phase transition which is triggered by a small change in external environment. Polymers based on *N*-vinyl-2-pyrrolidone, vinyl pyridine, vinyl imidazole, dimethylamino ethyl methacrylate (DMAEMA), acrylic/methacrylic acid, itaconic acid, acryloyl propyl piperazine, etc., exhibit CST in response to changes in external pH of the medium [6–20]. These polymers that exhibit pH sensitivity are of considerable interest in polymer lithography, ultrafiltration, sorbents, carriers of bio-active compounds, etc.

The synthesis of new tailor-made functional polymers with desired properties is still an active area of research in the field of polymer chemistry. In order to design a functional copolymer system, for specific applications, the determination of reactivity parameters of the monomers involved is important. In line with our research interest, in understanding the properties of piperazine-based "stimuli-" responsive polymers [17–24] for targeted applications, in this article, we report the copolymerization behavior of an amido-amine monomer *N*-acryloyl-*N*′-phenyl piperazine (AcrNPhP) containing a bulky phenyl group at the tertiary amine function with two hydrophilic monomers such as AA and HEMA. The reactivity parameters of the two new copolymer systems were evaluated using the linearization methods.

Hydrogels based on these two new systems were prepared by chemically crosslinking the monomers with crosslinkers such as methylene bisacrylamide (MBA), and ethylene glycol dimethacrylate (EGDMA) both in bulk and solution. The pH responsive swelling behavior of these copolymer gels was studied to understand the influence of bulky groups on the swelling of piperazine-based hydrogels and is described in detail in this report. These results will be useful in the design of responsive gels with controlled swelling in terms of molecular architectures.

Experimental

Materials

Acryloyl chloride, ethylene glycol dimethacrylate (EGDMA), hydroxyethyl methacrylate (HEMA), and acrylic acid (AA) were purchased from Fluka, Switzerland. The monomers were purified by vacuum distillation. The free-radical initiator azobisisobutyronitrile (AIBN) was obtained from TCI, Japan, and was recrystallized in methanol. 1,1-dimethoxy-1-phenyl acetophenone (DMPA, Aldrich), and methylene bisacrylamide (MBA, Aldrich) were used as received. 1,4-Dioxane (Merck) was refluxed with metallic sodium for 2 h and distilled under nitrogen.

Synthesis of *N*-acryloyl *N*′-phenyl piperazine (AcrNPhP)

The monomer AcrNPhP was synthesized by the method described previously [25] as follows: *N*-phenyl piperazine (0.13 mol, 19.4 ml), and triethyl amine (0.13 mol, 17.7 ml) were dissolved in 300 ml of dry THF in a 1 l Claisen flask. The flask was cooled in an ice-bath and the content was stirred under dry nitrogen gas. Acryloyl chloride (0.13 mol, 10.3 ml) dissolved in 50 ml of dry THF was added drop-wise into the Claisen flask using a pressure equalizing funnel. After the addition of acryloyl chloride, the reaction mixture was allowed to equilibrate to room temperature. The precipitated triethyl amine hydrochloride salt was removed by filtration and the filtrate was concentrated on a rotary evaporator. The white solid product was purified by recrystallization in anhydrous *n*-heptane. Yield: 44 %. The reaction scheme is illustrated in Fig. 1A.

Synthesis of homopolymer (PAcrNPhP)

The homopolymer was prepared by solution polymerization method as follows: AcrNPhP (1 g) and AIBN (0.5 wt %) were dissolved in 20 ml of dry THF in a 50 ml round-bottom flask equipped with a glass vacuum tap. The reaction mixture was degassed three times by freeze–thaw cycle and the flask was sealed under vacuum. Polymerization reaction was carried out at 70 °C for 24 h. The reaction mixture was cooled to room temperature and poured into a beaker containing 300 ml of diethyl ether. The precipitated homopolymer was purified by re-precipitation in ether at least two times. The intrinsic viscosity of the homopolymer in chloroform was 0.10 dl g^{-1}.

Synthesis of linear copolymers

Linear statistical copolymers of AcrNPhP with either AA or HEMA with various monomer feed ratios were prepared by solution polymerization. The synthesis of the copolymer CPA-10-90 containing AcrNPhP and AA is described. AcrNPhP (0.15 g), AA (1.40 g), and AIBN (0.05 g) were dissolved in 20 ml of freshly distilled THF in a 50 ml round-bottom flask equipped with a glass vacuum tap. The reaction mixture was degassed three times by freeze–thaw cycle and the flask was

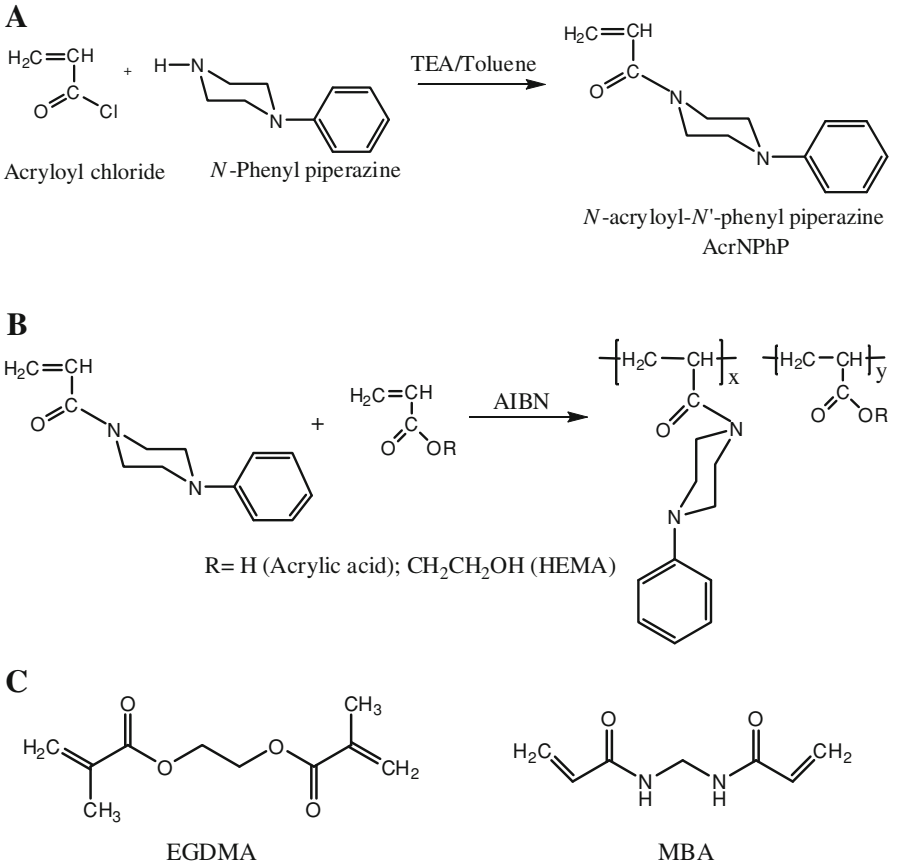

Fig. 1 **A** Schematic illustration of *N*-acryloyl-*N*′-phenyl piperazine AcrNPhP synthesis. **B** Schematic illustration of the linear copolymer synthesis by free-radical solution polymerization. **C** Chemical structure of the crosslinkers EGDMA and MBA

sealed under vacuum. Polymerization reaction was carried out at 75 °C for 40 min. The reaction mixture was cooled to room temperature and poured into 300 ml of diethyl ether to precipitate the copolymer. The copolymer was purified by re-precipitation (three times) and dried in vacuum at 50 °C for 1 day. The conversion of all the copolymers was limited between 10 and 20 %. The monomer feed ratios are presented in Tables 1 and 2 for AcrNPhP–AA and AcrNPhP–HEMA systems. The reaction scheme is illustrated in Fig. 1B.

Synthesis of crosslinked polymers (gels)

Chemically crosslinked gels of AcrNPhP with either AA or HEMA were prepared by bulk and solution polymerization methods using a photo-initiator.

Table 1 Composition of monomers in feed and in copolymer determined by FTIR peak analysis for the system AcrNPhP and AA

Copolymer	Feed (f) (mole fraction)		Conversion (%)	Copolymer (F) (mole fraction)	
	AcrNPhP (f_1)	AA (f_2)		AcrNPhP (F_1)	AA (F_2)
CPA95-05	0.8497	0.1503	10	0.856 ± 0.010	0.144 ± 0.010
CPA90-10	0.7435	0.2565	15	0.774 ± 0.008	0.226 ± 0.008
CPA80-20	0.5642	0.4358	12	0.724 ± 0.001	0.276 ± 0.001
CPA70-30	0.4368	0.5632	10	0.586 ± 0.002	0.414 ± 0.002
CPA60-40	0.3328	0.6672	15	0.515 ± 0.039	0.485 ± 0.039
CPA50-50	0.2499	0.7501	13	0.512 ± 0.040	0.488 ± 0.040
CPA40-60	0.1790	0.8210	15	0.427 ± 0.006	0.573 ± 0.006
CPA30-70	0.1264	0.8736	15	0.317 ± 0.004	0.683 ± 0.004
CPA20-80	0.0769	0.9231	15	0.277 ± 0.029	0.723 ± 0.029
CPA10-90	0.0347	0.9653	15	0.151 ± 0.014	0.849 ± 0.014

Table 2 Composition of monomers in feed and in copolymer determined by FTIR peak analysis for the system AcrNPhP and HEMA

Copolymer	Feed (f) (mole fraction)		Conversion (%)	Copolymer (F) (mole fraction)	
	AcrNPhP (f_1)	HEMA (f_2)		AcrNPhP (F_1)	HEMA (F_2)
CPH90-10	0.8408	0.1592	15	0.764 ± 0.000	0.236 ± 0.000
CPH80-20	0.7050	0.2950	12	0.624 ± 0.002	0.376 ± 0.002
CPH70-30	0.5827	0.4173	15	0.516 ± 0.006	0.484 ± 0.006
CPH60-40	0.4708	0.5292	10	0.385 ± 0.016	0.615 ± 0.016
CPH50-50	0.3742	0.6258	12	0.359 ± 0.019	0.641 ± 0.019
CPH40-60	0.2865	0.7135	15	0.259 ± 0.021	0.741 ± 0.021
CPH30-70	0.2037	0.7963	15	0.183 ± 0.004	0.817 ± 0.004
CPH20-80	0.1315	0.8685	12	0.125 ± 0.011	0.875 ± 0.011
CPH10-90	0.0622	0.9378	15	0.070 ± 0.001	0.930 ± 0.010

Bulk polymerization

The preparation of gel A7A3-B by bulk polymerization is described. AcrNPhP (0.71 g), AA (0.32 g), EGDMA (0.02 g), and DMPA (0.003 g) were mixed in a glass ampoule. The ampoule was placed in an ice-bath and the reaction mixture was purged with dry nitrogen gas for 30 min. The ampoule was then sealed using the flame. Polymerization was carried out by UV radiation ($\lambda < 300$ nm) for 30 min in a photochemical reactor (Rayonet). The resulting transparent polymer solid was washed by soxhlet extraction using ethanol to remove any unreacted components. The washed gel was cut into small disks of diameter (ca. 1.5 mm) and dried to constant weight in a vacuum oven at 50 °C. Gels of AcrNPhP–HEMA system were similarly prepared.

Solution polymerization

The preparation of gel A7A3-S by solution polymerization method is described. AcrNPhP (0.71 g), AA (0.32 g), EGDMA (0.02 g), DMPA (0.003 g) were in 5 ml of 1,4-dioxane in a glass ampoule. The ampoule was placed in an ice-bath and the reaction mixture was purged with dry nitrogen gas for 30 min. The ampoule was then sealed using the flame. Polymerization was carried out by UV radiation for 30 min (Rayonet photochemical reactor). The resulting transparent polymer solid was washed by soxhlet extraction using ethanol to remove the unreacted components. The washed gel was cut into small discs of diameter (ca. 1.5 mm) and dried to constant weight in a vacuum oven at 50 °C. Gel-containing AcrNPhP and HEMA were similarly prepared. The monomer feed compositions of the various gels prepared are summarized in Table 3.

Determination of molar absorptivity of AcrNPhP and reactivity ratios

The molar absorptivity of AcrNPhP was determined by infra-red spectral analysis. Samples in the form of thin polymer films were prepared as follows: calculated amount of poly(AcrNPhP) and PMMA were dissolved in minimum amount of dry chloroform. A small portion of the solution was placed on a clean sodium chloride window and the solvent was evaporated under vacuum. The FTIR spectrum of the resulting polymer films were recorded on a Perkin-Elmer (model 1725 X) FTIR spectrophotometer. The absorption of the phenyl ring (AcrNPhP) and the carbonyl group (PMMA) at wave numbers 700, and 1720 cm^{-1}, respectively, were recorded. Using these absorptions and the molar absorptivity of PMMA, the molar absorptivity of poly(AcrNPhP) was calculated. A value of 99 ± 13 dm^3 mol^{-1} cm^{-1} was obtained.

For the AcrNPhP/AA copolymers, the monomer reactivity parameters were determined by analyzing the relative intensities of the phenyl (AcrNPhP) and carbonyl absorptions (AA) of the two monomers. The ratio of monomer units in the copolymer was calculated from the following equation,

Table 3 Data on composition, appearance, time of gelation, and density of gels

Gel	AcrNPhP (g)	AA (g)	HEMA (g)	Appearance	Time (min)	Density (g ml^{-1})
A7AA3-B	0.71	0.32	–	Solid gel	20	1.26
A5AA5-B	0.50	0.51	–	Solid gel	20	1.26
A3AA7-B	0.32	0.71	–	Solid gel	20	1.27
A7AA3-S	0.71	0.33	–	Solid gel	35	1.27
A7HE3-B	0.70	–	0.31	Solid gel	20	1.15
A5HE5-B	0.50	–	0.50	Solid gel	20	1.16
A3HE7-B	0.31	–	0.72	Solid gel	20	1.16
A7HE3-S	0.70	–	0.30	Solid gel	30	1.17

$$\frac{[\mathrm{PAA}]}{[\mathrm{PAcrNPhP}]} = \frac{A_{1740\ \mathrm{cm}^{-1}}}{A_{700\ \mathrm{cm}^{-1}}} \times \frac{\varepsilon_{\mathrm{PAcrNPhP}}}{\varepsilon_{\mathrm{AA}}} \quad (1)$$

For the AcrNPhP/HEMA copolymers, the ratio of the monomer units in the copolymer was calculated using the following equation,

$$\frac{[\mathrm{PHEMA}]}{[\mathrm{PAcrNPhP}]} = \frac{A_{1720\ \mathrm{cm}^{-1}}}{A_{700\ \mathrm{cm}^{-1}}} \times \frac{\varepsilon_{\mathrm{PAcrNPhP}}}{\varepsilon_{\mathrm{PHEMA}}} \quad (2)$$

where A and ε are the absorbance and molar absorptivity, respectively, of the corresponding functional groups. The following values [21] for ε ($\mathrm{dm^3\ mol^{-1}\ cm^{-1}}$) were used in the calculations: $\varepsilon_{\mathrm{AcrNPhP}} = 99$, $\varepsilon_{\mathrm{AA}} = 353$, and $\varepsilon_{\mathrm{HEMA}} = 300$.

Equilibrium swelling studies

Gravimetric equilibrium swelling of the copolymer gels in buffer solutions of various pH was studied. The gels were cut into thin discs and immersed in water at 25 °C for 1 week. Each sample was then removed from the vial, tapped with a dampened Kimwipe towel to remove the excess surface water and weighed. The dry weights were measured after desiccating the gels for 3 days under vacuum at 40 °C. The weight swelling ratio (WSR) was calculated using the following equation,

$$\mathrm{WSR} = \left(\frac{W_\mathrm{t} - W_\mathrm{d}}{W_\mathrm{d}}\right) \quad (3)$$

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

Density measurements

The volume of the gel (V) in the dry or swollen state was determined by the buoyancy principle at 23 °C. The weight of the gel was measured in air and in a non-solvent (*n*-hexane) using a density kit (Mettler-Toledo). The volume of the gel was determined using the following expression,

$$V = \frac{W_\mathrm{air} - W_\mathrm{hexane}}{\rho_\mathrm{hexane}} \quad (4)$$

where W_air, W_hexane, and ρ_hexane are the weight of gel in air, *n*-hexane, and density of *n*-hexane, respectively.

Results and discussion

Composition of the copolymers

The reactivity parameters for the copolymerization reaction of the two new copolymer systems namely AcrNPhP–AA and AcrNPhP–HEMA were studied. The composition of the copolymer was conveniently determined using infra-red

spectroscopy and elemental analysis. The results obtained by these two methods are fairly in good agreement. The IR spectra of a few copolymers of AcrNPhP/AA and AcrNPhP/HEMA with various compositions are shown in Fig. 2A, B, respectively. From the phenyl and carbonyl absorptions of AcrNPhP and AA, respectively, the final composition of the copolymer was calculated using Eq. (1).

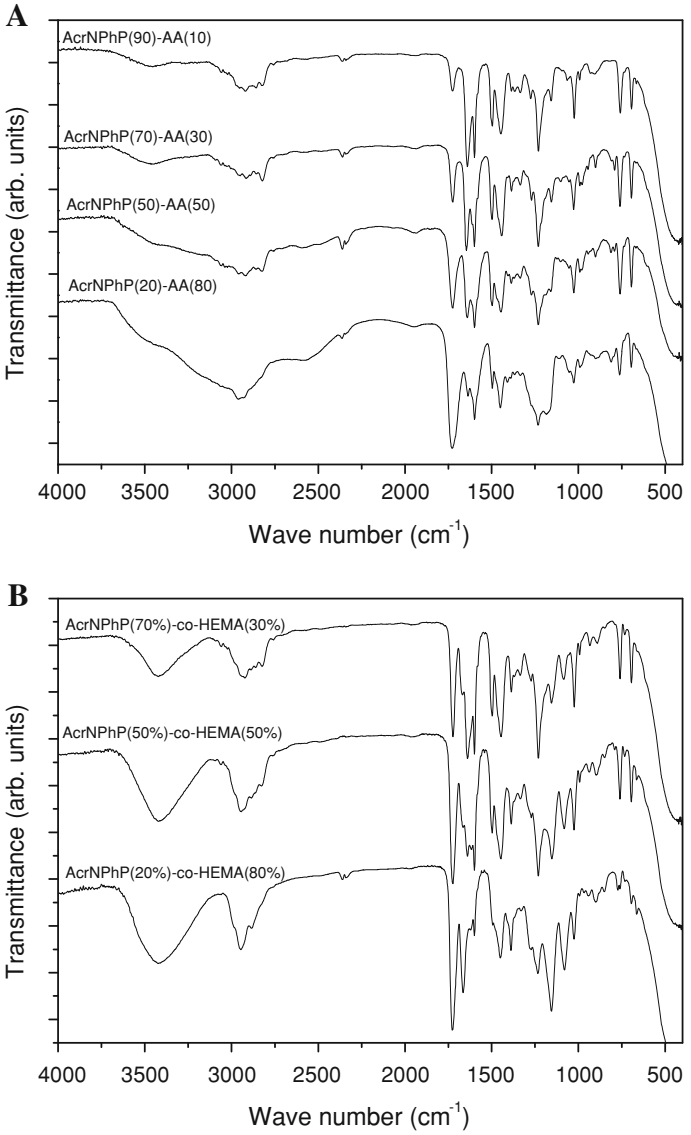

Fig. 2 **A** Infra-red spectra of the AcrNPhP–AA linear copolymers (film on NaCl window). **B** Infra-red spectra of the AcrNPhP–HEMA linear copolymers (film on NaCl window)

A composition plot of mole fraction (F_1) of AcrNPhP in the copolymer versus the mole fraction (f_1) of AcrNPhP in the feed determined by FTIR and elemental analysis methods for the systems AcrNPhP/AA and AcrNPhP/HEMA are shown in Fig. 3A, B, respectively, and the corresponding values are summarized in Tables 1 and 2. The data obtained in both cases, exhibits a significant deviation from the ideal copolymerization behavior (dashed line), and shows a tendency toward alternating (random) copolymer microstructure.

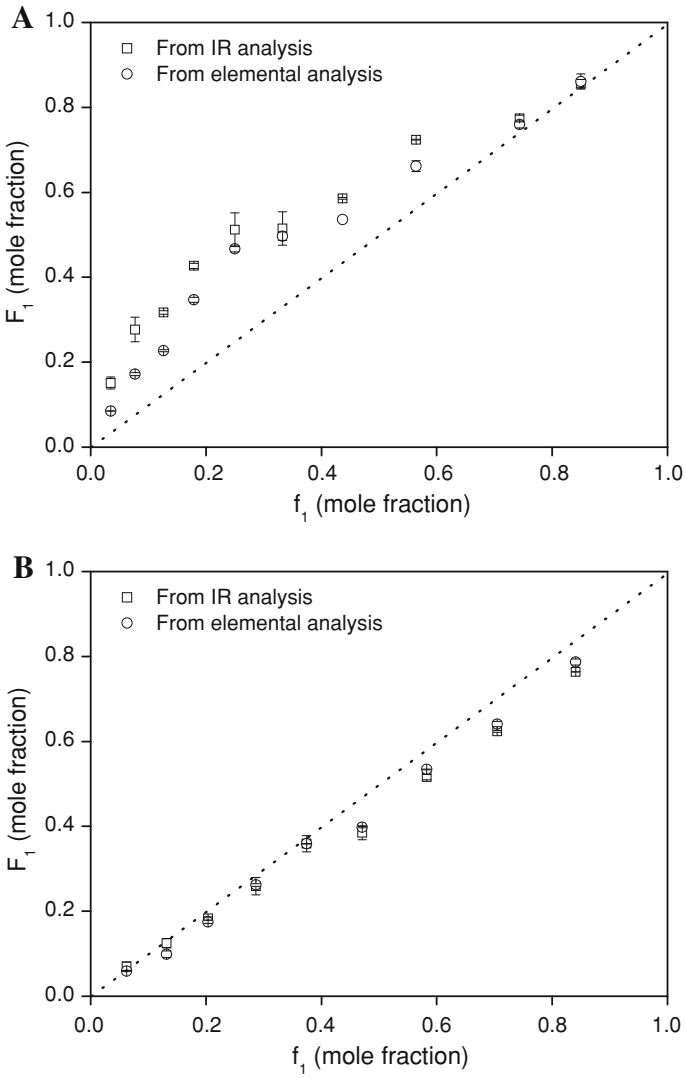

Fig. 3 **A** Composition profile for the linear AcrNPhP–AA copolymers. **B** Composition profile for the linear AcrNPhP–HEMA copolymers

Reactivity parameters

The reactivity ratio is a numerical expression of the relative reactivity of two monomers in a free radical copolymerization. Using the monomer feed ratios and the resultant copolymer compositions, the reactivity ratios of AcrNPhP–AA and AcrNPhP–HEMA were evaluated by the linearization methods of Finemann-Ross (FR) [26] and Kelen–Tüdös (K–T) [27]. The FR equation is given as,

$$\frac{f(F-1)}{F} = r_1\left(\frac{f^2}{F}\right) - r^2 \tag{5}$$

where $f = f_1/f_2$, $F = F_1/F_2$, and r_1, r_2 are the reactivity ratios of AcrNPhP and AA or HEMA, respectively. According to the equation, a plot $f\,(F-1)/F$ versus f^2/F, gives a linear distribution with r_1 and r_2 being the slope and the intercept of the linear fit, respectively. The least-square plot for the two copolymer system is shown in Fig. 4.

The second linearization method to calculate the monomer reactivity ratios is that of K–T according to the following equation

$$\eta = \left[r_1 + \left(\frac{r_2}{\alpha}\right)\right]\xi - \left[\frac{r_2}{\alpha}\right] \tag{6}$$

where η and ξ are functions of the molar ratios of the monomers in the copolymer and in the feed, respectively, α is any arbitrary denominator having any positive value, but so chosen as to give a more homogeneous distribution of data along the axis of η and ξ.

The values of r_1 and r_2 were calculated using a linear fit of η versus ξ data that is shown in Fig. 5. Thus the value of r_1 is the value of η when ξ is 1, and the intercept

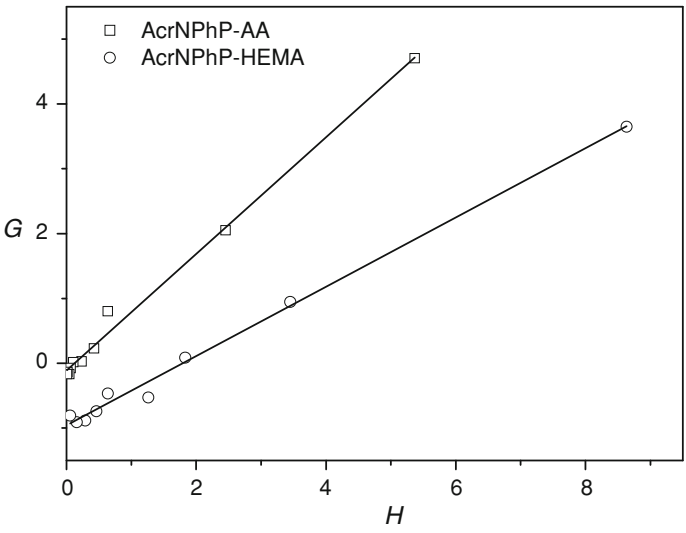

Fig. 4 FR plots for the copolymerization reactions (data evaluated from IR spectral analysis)

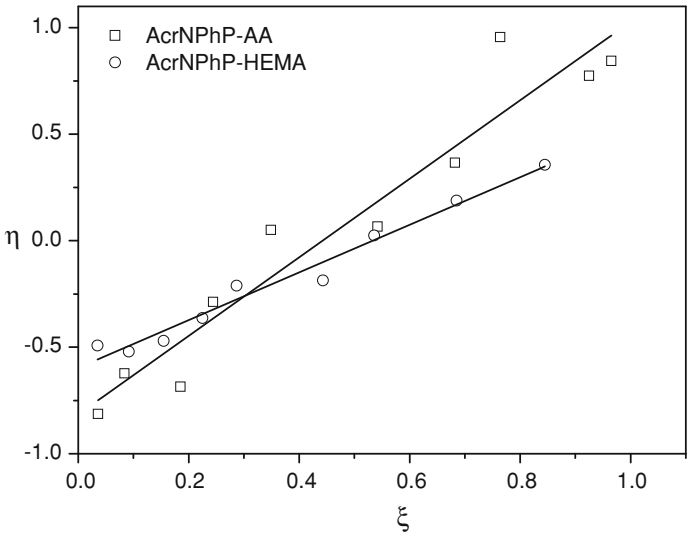

Fig. 5 KT plots for the copolymerization reactions (data evaluated from IR spectral analysis)

of the straight line $\eta = -r_2/\alpha$. The FR and KT parameters obtained for the copolymerization of AcrNPhP and AA (and HEMA) is summarized in Tables 4 and 5. The value of α was calculated as $\alpha = (H_{\min} \times H_{\max})^{0.5}$ by substituting the minimum and maximum value of H for an even distribution of the data points; H is defined as f^2/F. The results of the reactivity ratios obtained both by infra red analysis as well as by elemental analysis methods are presented in Table 6, and the results are in good agreement within the experimental error. Compared with the reactivity of AcrNPhP, both HEMA and AA show a higher reactivity which can be explained based on the availability of π electron and the stability of the free radical [28, 29].

The obtained value of $r_1 \times r_2$ for both the copolymer system is small (i.e., <0.25) which directly indicate that the copolymer has a lower content of AcrNPhP than in the reaction feed. This small value further suggests that the copolymers show some tendency toward alternating chain statistics. This tendency towards alternation was initially assumed to be the consequence of a hydrogen bonding mechanism between the amino group of AcrNPhP and the hydroxyl groups of HEMA and AA. However, the IR spectrum of the copolymers did not support any evidence for hydrogen bonding.

Determination of Q and e parameters

The reactivity or resonance stabilization Q, and the polarity e values provide a basis for the evaluation of the likelihood of two monomers undergoing a copolymerization reaction. The Q and e values for AcrNPhP for copolymerization with HEMA and AA were calculated from the monomer reactivity ratios evaluated by the KT method (from the IR spectral method) using the following Alfrey–Price equation [30].

Table 4 F–R and K–T parameters of the copolymers of AcrNPhP and AA derived from FTIR analysis

Copolymer	$F = F_1/F_2$	$f = f_1/f_2$	F–R parameters		K–T parameters	
			$H = f^2/F$	$G = f\,(F-1)/F$	$\xi = H/(+H)$	$\eta = G/(+H)$
CPA95-05	5.952	5.653	5.369	4.704	0.965	0.845
CPA90-10	3.424	2.899	2.454	2.052	0.925	0.774
CPA80-20	2.621	1.295	0.639	0.801	0.764	0.956
CPA70-30	1.416	0.776	0.425	0.228	0.682	0.366
CPA60-40	1.062	0.499	0.234	0.029	0.542	0.067
CPA50-50	1.049	0.333	0.106	0.016	0.349	0.051
CPA40-60	0.744	0.218	0.064	−0.075	0.244	−0.287
CPA30-70	0.465	0.145	0.045	−0.167	0.185	−0.686
CPA20-80	0.383	0.083	0.018	−0.135	0.084	0.623
CPA10-90	0.177	0.036	0.007	−0.167	0.036	−0.813

Table 5 F–R and K–T parameters of the copolymers of AcrNPhP and HEMA derived from FTIR analysis

Copolymer	$F = F_1/F_2$	$f = f_1/f_2$	F–R parameters		K–T parameters	
			$H = f^2/F$	$G = [f\,(F-1)]/F$	$\xi = H/(+H)$	$\eta = G/(+H)$
CPH90-10	3.321	5.282	8.633	3.647	0.845	0.357
CPH80-20	1.657	2.390	3.449	0.947	0.685	0.188
CPH70-30	1.066	1.397	1.830	0.086	0.536	0.025
CPH60-40	0.626	0.890	1.263	−0.531	0.443	−0.186
CPH50-50	0.561	0.598	0.638	−0.468	0.287	−0.211
CPH40-60	0.351	0.402	0.460	−0.743	0.225	−0.363
CPH30-70	0.224	0.256	0.292	−0.884	0.155	−0.471
CPH20-80	0.143	0.151	0.161	−0.910	0.092	−0.521
CPH10-90	0.076	0.066	0.058	−0.808	0.035	−0.492

Table 6 Reactivity parameters for the copolymerization reaction

Copolymer system	FR method			KT method		
	r_1	r_2	$r_1 \times r_2$	r_1	r_2	$r_1 \times r_2$
PAcrNPhP–AA	0.90 ± 0.02	0.11 ± 0.04	0.10	1.03 ± 0.28	0.16 ± 0.02	0.99
PAcrNPhP–HEMA	0.54 ± 0.02	0.96 ± 0.05	0.51	0.55 ± 0.13	0.99 ± 0.07	0.55

$$e_1 = e_2 \pm [-\ln r_1 r_2]^{0.5} \tag{7}$$

$$Q_1 = \left(\frac{Q_2}{r_2}\right) \exp\, -[e_2\,(e_2 - e_1)] \tag{8}$$

where Q and e are the reactivity and polarity of the monomer and r_1 and r_2 are the reactivity ratios. Using the reported values [31] of Q and e for HEMA and AA ($Q_{HEMA} = 1.78$, $e_{HEMA} = -0.39$; $Q_{AA} = 0.83$, $e_{AA} = 0.88$), the following values for AcrNPhP were calculated, (i) AcrNPhP–HEMA system $Q = 2.5$, $e = -1.2$, (ii) AcrNPhP–AA system $Q = 1.9$, $e = -0.6$.

Statistical microstructure

The distribution of monomer sequence along the copolymer chain was calculated on the basis of terminal copolymerization model [32]. In this method, the fractions of AcrNPhP–AcrNPhP (M_1–M_1), AA–AA (or HEMA–HEMA) (M_2–M_2), and AcrNPhP–AA (or HEMA) (M_1–M_2) units in the copolymer, as function of copolymer composition, and reactivity ratios was calculated statistically. Based on the triad fraction, the maximum tendency to alternation of the two copolymer systems AcrNPhP–AA and AcrNPhP–HEMA were at 65 and 70 mol %.

Swelling characteristic of the gels

Figure 6 shows the effect of pH on the swelling of AcrNPhP–AA gels prepared by bulk polymerization. The swelling is less significant in solutions of low pH and the gels remain in a shrunken state, while in solutions of high pH they swell significantly. The observed trend in swelling is a direct consequence of ionization of acrylic acid units present in the gels. The acid-ionization constant, pK_a of acrylic acid [33, 34] is around 4.3 above which, it dissociates to COO^- and H^+ ions. This leads to the formation of fixed electrical charges in the crosslinked network of the gels. The localized electric charges interact by electrostatic repulsion leading to differences in osmotic pressure between the gel interior and external solution (gel exterior). This difference in osmotic pressure leads to swelling and permits water diffusion into the gel (in solutions of pH $>$ 4.3). In solution of pH $<$ 4.3 the acrylic acid units in the gels do not dissociate and hence the gels do not show any appreciable swelling.

The effect AA content in the swelling of the gels can also be visualized in Fig. 6. The gel-containing 30 % AA (A7A3-B) exhibits a maximum swelling ratio of 3.2, while the gel containing 70 % AA (A3A7-B) swells almost five times to about 14.5. Increasing the amount of AA directly increases the fraction of ionisable group in the gel. As a result, the swelling of the gels increase with increase in AA. An interesting feature along the same line, is the shift in the onset of swelling (O_{SWR}) of the gels. The following values were deduced from Fig. 6: O_{SWR}: pH 6.0 (30 % AA); 4.7 (50 % AA); 4.2 (70 % AA). This clearly demonstrates that the pH responsive swelling of the AcrNPhP–AA gels can be tuned by varying the amount of AA in the gels.

Another interesting aspect of the AcrNPhP–AA gels is their insignificant swelling in solutions of low pH. The three gels shown in Fig. 6, exhibits a swelling ratio of $<$1 in solutions of low pH (acidic). These gels contain significant amount of AcrNPhP (30, 50, and 70 %) which has an ionizable tertiary amine functional group. Hence, these gels should also swell significantly in solutions of low pH. However, this was not observed. This insignificant swelling can be explained based

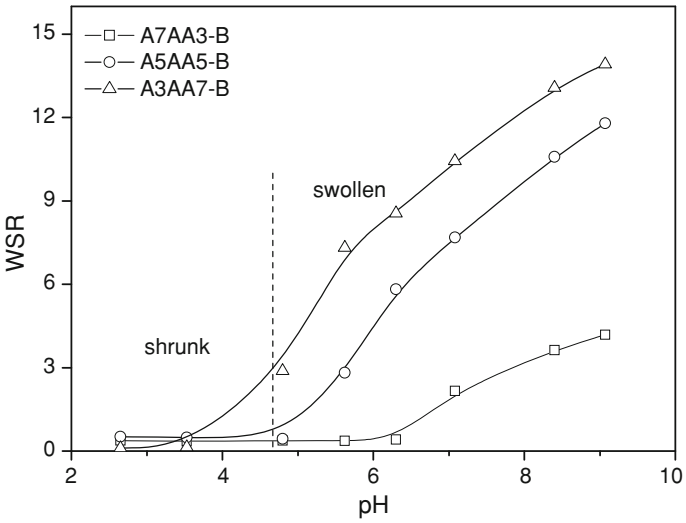

Fig. 6 Swelling profile of AcrNPhP–AA gels at 25 °C as function of solution pH

on weak protonation at the tertiary amine nitrogen of the AcrNPhP units. The phenyl group substitution at the tertiary amine moiety sterically hinders the protonation process due to its bulkiness. This leads to a weak or insignificant protonation at the tertiary amine nitrogen and hence to insignificant swelling of the gels. When the substitution is by less bulky groups such as methyl or ethyl, the protonation is more effective and the gels swell significantly in solutions of low pH [35, 36].

Another factor that can contribute to this observation is the additional physical crosslinking in the form of hydrogen bonds between the unionized carboxylic groups of AA. These observations suggest that apart from the density of ionizable groups, steric hindrance also plays a major role in controlling the magnitude of swelling in ionizable gels. These factors can be judiciously employed in the fabrication of gels with desired swelling degree for applications in drug delivery system.

The effect of synthesis method such as bulk and solution polymerization on the swelling of AcrNPhP–AA gels was also studied. Figure 7 shows the swelling profile of the gel A7AA3-B and A7AA3-S prepared by bulk and solution polymerization methods, respectively, as function of pH at 25 °C. The gel prepared by bulk polymerization shows a weight swelling ratio of 3, while the gel prepared by solution polymerization shows a swelling ratio of 30. An almost tenfold increase in swelling capacity of the gel is observed clearly demonstrating the impact of preparation method. Gels prepared by bulk polymerization are glass-like with a dense 3-D crosslink network. This high crosslink density constrains the elasticity of the network and leads to poor diffusion of solvent into the gel interior. In contrast, the gels prepared by solution polymerization are rubber-like and do not have additional physical crosslinks. This less dense network renders the gel elastic and the gel exhibits a higher swelling capacity.

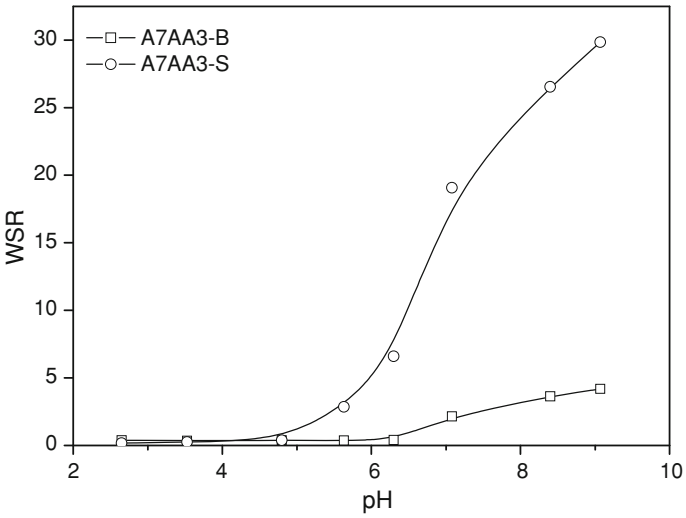

Fig. 7 Effect of preparation method on the swelling of AcrNPhP–AA gels at 25 °C as function of solution pH

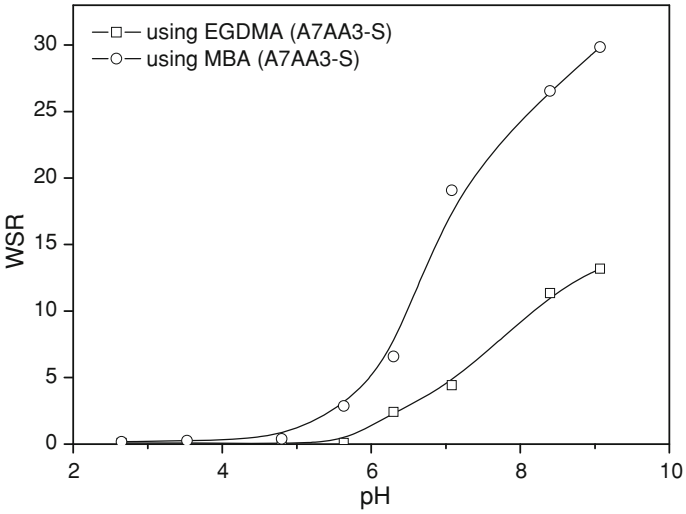

Fig. 8 Effect of crosslinker nature on the swelling of AcrNPhP–AA gels at 25 °C as function of solution pH

The effect of chemical nature of the crosslinker on the swelling AcrNPhP–AA gel A7AA30-S prepared by solution polymerization is shown in Fig. 8. Two types of di-functional chemical crosslinkers such as MBA and EGDMA were used. The gel containing MBA swells considerably (about three times), than the gel-containing EGDMA as the crosslinker. This difference in swelling behavior is attributed to the chemical structure of the crosslinker. MBA is more hydrophilic in nature than

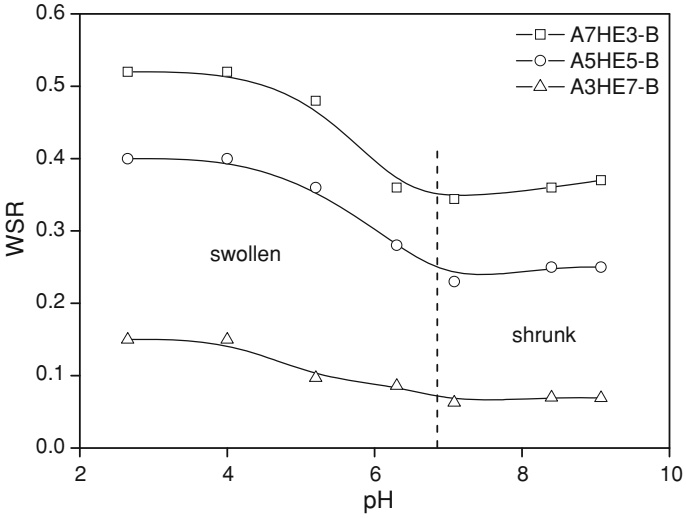

Fig. 9 Swelling profile of AcrNPhP/HEMA gels at 25 °C as function of solution pH

EGDMA, which allows the enhanced formation of hydrogen bonds with water thereby permitting higher water uptake of the gels [37].

To confirm that steric hindrance plays a vital role in controlling the swelling of tertiary amine-based ionizable gels, AA was replaced by a non-ionizable HEMA in the AcrNPhP gels. The effect of pH on the swelling of AcrNPhP–HEMA gels (by bulk polymerization) containing MBA as the crosslinker is shown in Fig. 9. Interestingly, the pattern in swelling is completely opposite to that observed for the AcrNPhP–AA gels. At a first look, it appears that the gels swell in solutions of low pH and shrink in solutions of high pH, and this swelling increase with increase in AcrNPhP content. Although the trend in swelling is expected, the magnitude of the weight swelling ratio is very small. The gel-containing 70 % AcrNPhP has a swelling ratio of 0.5 which is an insignificant swelling. Increasing the amount of AcrNPhP in the gel increases the amount of ionizable moieties, and in spite of this, the presence of the bulky phenyl group at the tertiary amine function sterically hinders the protonation process. This leads to poor swelling and poor water up-take of these gels. If the bulky phenyl group is replaced by a less bulky group viz. methyl, the swelling capacity increases significantly to about 5.5 [23]. These results demonstrates that the swelling of ionizable tertiary amine-based gels are dependent on various factors such as steric hindrance to protonation by bulky groups, method of preparation, type and amount of chemical crosslinker, and charge density of ionizable groups.

Network structure of gels

The swelling capacity of a gel depends on its network structure, hydrophilicity, crosslinking ratio, and the fraction of ionizable group. The number-average molecular weight between the crosslinks (M_c) is an important parameter which is

directly related to the crosslink density and controls the mechanical properties. In general, with increase in crosslink density, the M_c *o*f the gel will decrease with increase in pore density of the macromolecular network. The experimental M_c values of the AcrPhP–AA and AcrPhP–HEMA gels were determined using the Flory–Rehner equation [38] as given below,

$$M_c = -\frac{\left[\left(\frac{1-2}{\Phi}\right) V_1 \rho_2 \Phi_{2r}^{2/3} \Phi_{2m}^{1/3}\right]}{\ln(1-\Phi_{2m}+\Phi_{2m}+\chi\Phi_{2m}^2} \tag{9}$$

where V_1 is the molar volume of water = 18 ml mol^{-1}.

The values of Φ_{2r} and Φ_{2m} were calculated from the following respective equations,

$$\Phi_{2r} = \left[1 + \frac{\left(\frac{w_{as}}{w_d} - 1\right)\rho_2}{\rho_1}\right]^{-1} \tag{10}$$

$$\Phi_{2m} = \left[1 + \frac{\left(\frac{w_s}{w_d} - 1\right)\rho_2}{\rho_1}\right]^{-1} \tag{11}$$

where W_{as}, W_s, and W_d are the weight of gel after synthesis, swollen gel and dry gel, respectively.

The Flory–Huggins polymer–solvent interaction parameter χ was obtained from the following equation,

$$\chi = \frac{1}{2} + \frac{\Phi_{2m}}{\Phi} \tag{12}$$

where Φ is the functionality of the crosslinker, and for EGDMA and phantom network this value [31] is equal to 4.

The crosslink density of the gels were calculated as,

$$\rho_c = \frac{M_0}{M_c} \tag{13}$$

where M_0 is the average molar mass of repeat unit of the gel and is given as,

$$M_0 = \frac{m^{\text{AcrNPhP}} \times M_w^{\text{AcrNPhP}} + m^{\text{AA}} \times M_w^{\text{AA}}}{m^{\text{AcrNPhP}} + m^{\text{AA}}} \tag{14}$$

where m^{AcrNPhP} and m^{AA} are the masses of AcrNPhP and AA (or HEMA) monomers in the feed, respectively, M_w^{AcrNPhP} and M_w^{AA} are the respective molar masses of AcrNEP and AA (or HEMA).

From the molecular weight between cross-links, the number of links between two crosslinks, n was estimated as,

$$n = \frac{2M_c}{M_0} \tag{15}$$

Table 7 Characteristic network structural parameters of the gels in water at 25 °C

Gel	χ	M_c ($\times 10^{-4}$ g mol^{-1})	ρ_c ($\times 10^{-3}$)	ζ (Å)
A7AA3-B	0.520	3.63	1.88	100.32
A5AA5-B	0.513	3.98	1.07	110.01
A3AA7-B	0.502	3.67	0.92	115.34
A7HE3-B	0.532	4.17	1.89	120.12
A5HE5-B	0.521	4.32	1.65	114.10
A3HE7-B	0.518	4.63	1.03	111.36

The value of the root mean square end-to-end distance of the polymer chain in the freely jointed state was calculated as,

$$\left(\overline{r}^2\right)^{1/2} = l\sqrt{n} \tag{16}$$

where l is the carbon–carbon bond length (1.54 Å). The root mean squared end-to-end distance in unperturbed state was also calculated as,

$$\left(\overline{r}_0^2\right) = c_n^{0.5}\left(\overline{r}^2\right)^{1/2} \tag{17}$$

where is C_n is the Flory characteristic ratio or rigidity factor of the polymer (6.7). Using the above values, the mesh size of the polymer network, ξ, was determined from the following equation,

$$\xi = \Phi_{2m}^{-1/3}\left(\overline{r}_0^2\right)^{1/2} \tag{18}$$

The characteristic network parameters of the gels in water calculated using the above expressions are presented in Table 6. The polymer–solvent interaction parameter χ, decreases with increase in AA (and HEMA) content as a result of hydrophilicity of the gels. The average molar mass (M_c) increases with increase in both AA and HEMA content of the gel and the high values observed is attributed to ionization and fixed-charge interaction within the gel [39–41]. Further, the mess size of the gels increases with increase in the co-monomer content thus displaying that molecular heterogeneity plays a vital role in altering the swelling behavior which in turn can control the transport properties Table 7.

Conclusions

New functional copolymers based on *N*-acryloyl-*N*′-phenyl piperazine and acrylic acid and hydroxyl ethyl methacrylate were synthesized by free-radical solution polymerization. The compositions of the final copolymers were evaluated using FTIR and elemental analysis methods. The results obtained using these two methods were in good agreement. The reactivity ratios determined by linearization methods indicated that the copolymers were random in chain statistics with a high tendency toward alternating statistics. The AcrNPhP–AA gels swelled remarkably in solutions of high pH while the AcrNPhP–HEMA gels did not show any significant

swelling. Hence, steric hindrance on the protonation site plays a vital role in controlling the swelling behavior of disbustituted heterocyclic acrylamide gel systems. In addition, the swelling was greatly dependent on the method of preparation, the chemical nature of the crosslinker, and the amount, and type of monomer used in the fabrication of the gel. Thus by judiciously varying these parameters it will be possible to fabricate "Stimuli"-responsive gels with desired swelling capacity for targeted applications such as in enhanced drug delivery systems, contact lenses, chelating resins, super sorbent materials, etc. These gels are currently being study as sorbents for textile-waste water pollutants in our laboratory.

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