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ORIGINAL PAPER

New functional copolymers of *N*-acryloyl-*N*′-methyl piperazine and 2-hydroxyethyl methacrylate: synthesis, determination of reactivity ratios and swelling characteristics of gels

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Abstract Copolymers of *N*-acryloyl-*N*′-methylpiperazine (AcrNMP) and 2-hydroxyethyl methacrylate (HEMA) were synthesized by free radical solution polymerization in dioxane at 70 ± 1 °C, using 2,2′-azobisisobutyronitrile (AIBN) as initiator. The copolymer compositions were analyzed by the methods of FTIR spectroscopy and elemental analysis. Both the method of analysis yielded results that agreed reasonably well. The monomer reactivity ratios of the copolymerization were determined by the linearization methods of Finemann–Ross (FR) and Kelen–Tüdös (KT). The reactivity parameter results derived using FTIR analysis showed that the copolymerization yielded mainly alternating structure with reactivity ratios, r_1(AcrNMP) = 0.263 ± 0.011 and r_2(HEMA) = 0.615 ± 0.097 by F–R method and r_1 = 0.227 ± 0.074 and r_2 = 0.53 ± 0.15 by KT method. Microstructure data calculated by the method of Igarashi also supports the alternating structure (tendency) of the copolymer. Crosslinked polymer gels of this system exhibited remarkably high swelling of more than 500% in water at ambient temperature.

Keywords *N*-acryloyl-*N*′-methyl piperazine · 2-Hydroxyethyl methacrylate · Gels · Reactivity ratio · Finemann–Ross · Kelen–Tüdös

Introduction

In recent years, research emphasis is directed more towards developing new functional polymeric materials exhibiting hydrophilic properties. These materials are interesting owing to their potential applications in the development of controlled drug delivery systems, skin care products, enzyme immobilizations, contact lenses,

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etc. [1–5]. A wide range of functional hydrophilic polymers (both homopolymers and copolymers) with interesting properties have been studied. Most of these polymers are soluble or swell in water and this property of solubility can be tuned by varying the type of constituent monomers in them.

Functional polymers based on 2-hydroxyethyl methacrylate (HEMA) [6, 7] monomer are an interesting class of materials because of their excellent biomedical properties such as biocompatibility, optical clarity, oxygen permeability, mechanical strength, stability, etc. Functional polymers based on HEMA with various other comonomers such as vinyl alcohol, acrylic acid, malic acid, vinyl pyridine, collagen, etc. has been widely reported [8–12]. In order to design a functional copolymer system for specific applications the determination of reactivity parameters of the reacting monomers is important [13]. There exist a vast number of literatures on these parameters for various functional copolymer systems [14–16].

In this article, we report a new functional copolymer based on HEMA and an amido-amine viz. *N*-acryloyl-*N*′-methyl piperazine (AcrNMP). The synthesis of the new functional polymer, the reactivity of the two monomers, and the swelling behavior of their crosslinked networks are described in detail. It is expected that the presence of hydroxyl groups (from HEMA) and piperazine ring (from AcrNMP) in the functional material will lead to higher hydrophilicity which can manifest in certain interesting and desired properties.

Experimental

Materials

Acryloyl chloride, ethylene glycol dimethacrylate (EGDMA) and HEMA purchased from Fluka, Switzerland were distilled at reduced pressure under nitrogen and stored in a refrigerator before use. 1,4-Dioxane (Merck) was freshly distilled under nitrogen over metallic sodium. AIBN (TCI, Japan) was purified by recrystallization from methanol.

Preparation of linear copolymers

AcrNMP was synthesized by the method described previously [17]. For copolymerization, the monomers AcrNMP and HEMA in various proportions but with the total weight maintained at $\sim$3 g, and the initiator AIBN (0.5 wt% based on the total weight of the monomers) were dissolved in 25 mL of freshly distilled dioxane. The contents of the flask was degassed three times by freeze–thaw cycles and sealed under vacuum. Polymerizations were carried out at 70 $\pm$ 1 °C for periods ranging from 30 min to 1 h. Each polymer was recovered by precipitation in diethyl ether and filtered through a sintered glass. After washing several times with diethyl ether, the copolymer was dried in vacuum at 75 °C for 24 h. For the determinations of reactivity ratios, the polymer conversions were always maintained at less than 10% except in two cases where they were slightly higher than about 15%.

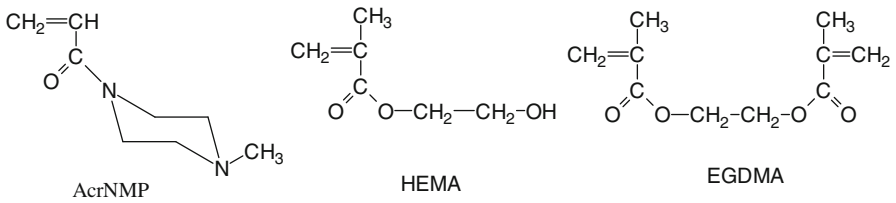

Fig. 1 Chemical structure of monomers (AcrNMP, HEMA) and crosslinker (EGDMA)

Preparation of crosslinked polymer networks (gels)

Chemically crosslinked gels of AcrNMP and HEMA using various percentage of EGDMA as the crosslinker was prepared by thermally initiated bulk polymerization. The preparation of a gel containing 1 wt% of the crosslinker is described as follows: AcrNMP and HEMA (50/50 mol %), EGDMA (0.5 wt% based on the total weight of the monomers), and AIBN (0.3 wt%) were were mixed in a glass ampoule at room temperature. The mixture was purged with dry nitrogen gas for 15 min to expel the dissolved oxygen and the ampoule was flame sealed. Polymerization was conducted at 70 °C for 2.5 h. The resulting transparent, solid polymer gel was recovered by breaking the ampoule. The gel was purified by soxhlet extraction using methanol for 2 days. Gels containing crosslinker content of 1, 2, and 4 wt% were prepared by the similar method.

The chemical structure of AcrNMP, HEMA, and EGDMA are illustrated in Fig. 1.

FTIR measurements

Infrared spectra were recorded using a Perkin-Elmer 1725-X Fourier transform infrared (FTIR) spectrometer. The copolymer sample was dissolved in a minimum amount of methanol and the solution was cast on a clean sodium chloride window. The solvent was allowed to evaporate completely under vacuum and the IR spectrum of the film was recorded. To obtain the monomer ratio in each copolymer sample, at least three determinations with different film thickness were recorded and the average value was used.

Elemental analysis

Elemental analysis of the copolymers were measured using a LECO CHNS 932 elemental analyzer. All the samples were dried for at least 2 h in a vacuum oven at 70 °C and then cooled to room temperature in a vacuum desiccator prior to the measurements.

Equilibrium swelling studies

Gravimetric equilibrium swelling of the copolymer gels in pure water 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 Kim-wipe 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 until constant dry weights were maintained. The weight swelling ratio (WSR) was calculated using the following equation:

$$\mathrm{WSR} = \left(\frac{W_t - W_d}{W_d}\right) \quad (1)$$

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

Results and discussion

Compositional study by FTIR analysis

Due to the hydrophilic nature of both monomers, all the copolymers were soluble in water and methanol. They were also soluble in dimethyl formamide (DMF), but not in chloroform as in the case of poly(AcrNMP-co-MMA) [9]. The compositions of the copolymer could be conveniently determined from their IR spectra. The IR spectra of three copolymers are shown in Fig. 2. It can be seen that the two carbonyl absorptions at 1724 and 1635 cm^{-1} for the two monomer units, HEMA and AcrNMP, respectively, were fairly well separated. Hence, the compositions of the copolymers were determined by analyzing the relative intensities of the carbonyl absorptions of the two monomers. The molar extinction coefficient of the carbonyl absorption at 1635 cm^{-1} for AcrNMP has previously been determined to be $\varepsilon_{1635} = 330 \pm 13$ dm^3 mol^{-1} cm^{-1} [3, 17]. The molar extinction coefficient of the carbonyl absorption at 1724 cm^{-1} for HEMA was assumed to be the same as that for MMA which is $\varepsilon_{1724} = 300 \pm 19$ dm^3 mol^{-1} cm^{-1}. This assumption is deemed

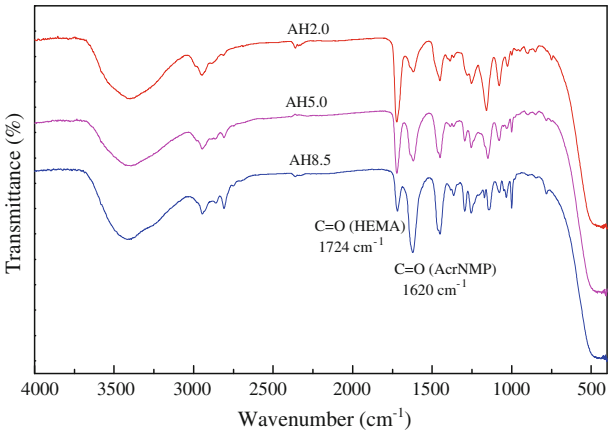

Fig. 2 Infra-red spectra of the copolymers (film on NaCl window)

reasonable as both the HEMA and MMA have the same ester linkage and should have very similar ε values for the corresponding carbonyl absorptions.

The reason that ε for the carbonyl absorption of HEMA was not determined in this study was due to the difficulty in finding a suitable solvent for poly(HEMA) which has no absorption interference in the 1720 cm^{-1} region. Using the above molar extinction coefficients, the ratio of the monomer units in the copolymer were calculated from the intensities of the absorptions, using Eq. 2:

$$\frac{[\text{HEMA}]}{[\text{AcrNMP}]} = \left(\frac{A_{1724}}{A_{1635}}\right) \times \left(\frac{\varepsilon_{1635}}{\varepsilon_{1724}}\right). \tag{2}$$

In the cases where there was slight overlapping of the two absorptions, deconvolution treatment was first performed using Perkin-Elmer FTIR software. The composition of the copolymers determined using Eq. 2 is given in Table 1.

The composition of monomer units in the copolymer was also determined from elemental analysis. Three determinations were performed for each copolymer sample and the results are presented in Table 2. The results obtained by the two different method of analysis are fairly good agreement validating both the methods of evaluation.

A composition plot of mole fraction (F_1) of AcrNMP in the copolymer versus the mole fraction (f_1) of AcrNMP in the feed determined by FTIR and elemental analysis methods is shown in Fig. 3. The obtained data exhibits a significant deviation from the ideal copolymerization behavior (dashed line), and shows a tendency towards alternating microstructure. The azeotropic point occurred at approximately 40% of AcrNMP in the feed. Similar copolymerization behaviors have also been reported for several other water soluble copolymer systems [3, 17–21].

Table 1 Composition of monomers in feed and in copolymer determined by FTIR peak analysis

Copolymer	Feed (f) (mole fraction)		Conversion (%)	Copolymer (F) (mole fraction)	
	AcrNMP (f_1)	HEMA (f_2)		AcrNMP (F_1)	HEMA (F_2)
AH1.0	0.105 ± 0.011	0.895 ± 0.017	4.5	0.268 ± 0.017	0.732 ± 0.017
AH2.0	0.203 ± 0.011	0.797 ± 0.015	5.9	0.221 ± 0.008	0.779 ± 0.008
AH3.0	0.303 ± 0.011	0.697 ± 0.014	5.0	0.396 ± 0.013	0.604 ± 0.013
AH4.0	0.401 ± 0.012	0.599 ± 0.013	4.1	0.444 ± 0.007	0.556 ± 0.007
AH5.0	0.502 ± 0.013	0.498 ± 0.013	6.1	0.401 ± 0.007	0.599 ± 0.007
AH6.0	0.574 ± 0.013	0.426 ± 0.011	6.4	0.456 ± 0.012	0.544 ± 0.012
AH6.5	0.649 ± .0014	0.351 ± 0.011	7.0	0.497 ± 0.010	0.504 ± 0.010
AH7.0	0.696 ± 0.014	0.304 ± 0.011	7.3	0.554 ± 0.007	0.446 ± 0.007
AH7.5	0.750 ± 0.015	0.250 ± 0.011	8.3	0.578 ± 0.004	0.422 ± 0.004
AH8.0	0.779 ± 0.015	0.221 ± 0.010	7.2	0.627 ± 0.009	0.373 ± 0.009
AH8.5	0.841 ± 0.016	0.159 ± 0.010	13.6	0.684 ± 0.004	0.316 ± 0.004
AH9.0	0.900 ± 0.017	0.100 ± 0.010	15.1	0.761 ± 0.028	0.239 ± 0.028

Table 2 Composition of monomers in feed and in copolymer determined by elemental analysis

Copolymer	Nitrogen content in copolymer (%)	Mole fraction of monomers in copolymer	
		F_1 (AcrNMP)	F_2 (HEMA)
AH2.0	3.49	0.167 ± 0.038	0.833 ± 0.038
AH3.0	7.23	0.358 ± 0.047	0.642 ± 0.047
AH4.0	7.69	0.382 ± 0.018	0.618 ± 0.018
AH6.0	7.92	0.395 ± 0.013	0.606 ± 0.013
AH6.5	9.15	0.461 ± 0.007	0.539 ± 0.007
AH7.0	11.11	0.571 ± 0.073	0.429 ± 0.073
AH7.5	12.07	0.626 ± 0.075	0.374 ± 0.075
AH8.0	11.71	0.605 ± 0.063	0.395 ± 0.063
AH8.5	13.16	0.689 ± 0.065	0.311 ± 0.065
AH9.0	14.36	0.761 ± 0.020	0.239 ± 0.020

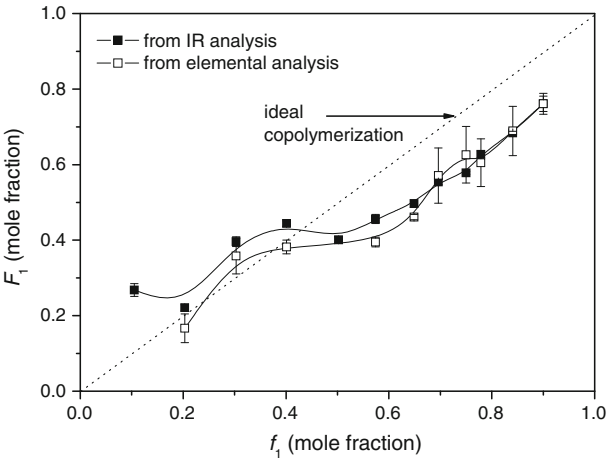

Fig. 3 Composition diagram for the copolymerization reaction

Reactivity ratio studies by FTIR and elemental analysis

The reactivity ratio is a numerical expression of the relative reactivities of two monomers in a free radical copolymerization. Using the monomer feed ratios and the resultant copolymer compositions, the reactivity ratios of AcrNMP and HEMA were evaluated by the linearization methods of Finemann–Ross (FR) [22] and Kelen–Tüdös (KT) [23]. The FR equation is given as

$$\frac{f(F-1)}{F} = r_1\left(\frac{f^2}{F}\right) - r^2 \tag{3}$$

where $f = f_1/f_2$, $F = F_1/F_2$ and r_1, r_2 are the reactivity ratios of AcrNMP and HEMA, respectively. The FR plots can be made is two ways. In the first method

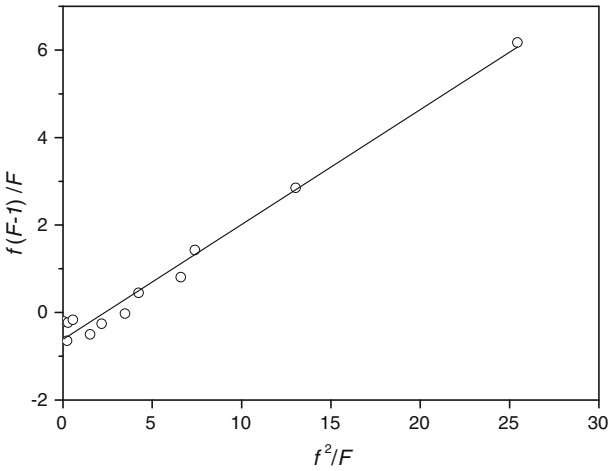

Fig. 4 F-R plot for the copolymerization reaction (data from IR spectral analysis)

called the FR1 method, $f(F-1)/F$ is plotted versus f^2/F, with r_1 and r_2 being the slope and the intercept of the straight line respectively. In the second method called the FR2 method, $(2F-1)(1-f_1)/(1-F_1)f_1$ is plotted versus $(1-f_1)^2F_1/(1-F_1)f^2$, with $-r_2$ and r_1 being the slope and intercept of the straight line respectively. However, the FR2 method is not often applied and therefore we do not put any special emphasis on this [17, 24]. The least-square plots of FR1 method is shown in Fig. 4 and the reactivity ratios r_1 and r_2 obtained from the plot were 0.26 ± 0.01 and 0.62 ± 0.10 respectively.

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

$$\eta = \left[r_1 + \left(\frac{r_2}{\alpha}\right)\right]\xi - \left[\frac{r_2}{\alpha}\right] \tag{4}$$

where η and ξ are functions of the molar ratios of the monomers in the copolymer and in the feed, respectively, and 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 of the straight line $\eta = -r_2/\alpha$. The FR and KT parameters obtained for the copolymerization of AcrNMP and HEMA are given in Table 3. 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. Thus, $(0.228 \times 25.44)^{0.5}$ gave a value of 2.408 for α. The KT plot is shown in Fig. 5 from which the reactivity ratios, r_1(AcrNMP) $= 0.23 \pm 0.07$ and r_2(MMA) $= 0.53 \pm 0.15$ were obtained. The results of the reactivity ratios obtained both by infra red analysis as well as by elemental analysis methods are summarized in Table 4, and the results are in fairly good agreement. Compared with AcrNMP, HEMA shows a

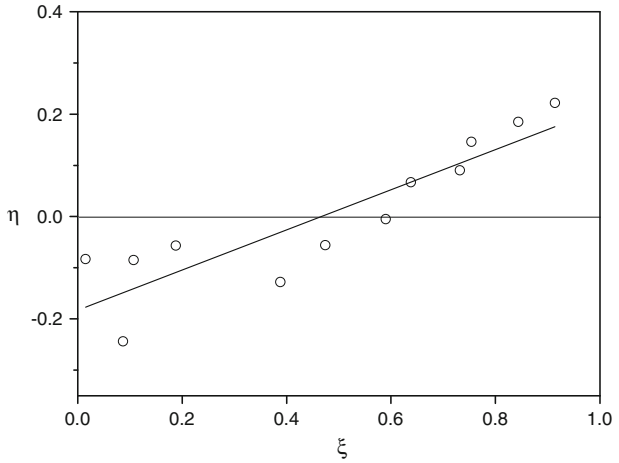

Fig. 5 K-T plot for the copolymerization reaction (data from IR spectral analysis)

Table 3 F-R and K-T parameters of the copolymers derived from FTIR analysis

$F = F_1/F_2$	$f = f_1/f_2$	F-R parameters		K-T parameters	
		$H = f^2/F$	$G = [f(F-1)]/F$	$\xi = H/(\alpha + H)$	$\eta = G/(\alpha + H)$
0.366	0.117	0.037	−0.203	0.015	−0.083
0.283	0.254	0.228	−0.644	0.087	−0.244
0.655	0.434	0.288	−0.229	0.107	−0.085
0.799	0.668	0.559	−0.168	0.188	−0.057
0.668	1.009	1.524	−0.501	0.388	−0.128
0.840	1.349	2.166	−0.257	0.474	−0.056
0.986	1.849	3.467	−0.026	0.590	−0.005
1.242	2.294	4.237	0.447	0.638	0.067
1.368	3.003	6.592	0.808	0.732	0.090
1.682	3.525	7.387	1.429	0.754	0.146
2.161	5.305	13.023	2.850	0.844	0.185
3.184	9.000	25.440	6.173	0.914	0.222

higher reactivity which can be explained based on the availability of π electron and the stability of the free radical [16, 25].

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

Table 4 Reactivity parameters for the copolymerization reaction

Methods	IR analysis		Elemental analysis	
	r_1	r_2	r_1	r_2
FR	0.26 ± 0.01	0.62 ± 0.10	0.28 ± 0.02	0.85 ± 0.19
KT	0.23 ± 0.07	0.53 ± 0.15	0.26 ± 0.11	0.78 ± 0.24

Comparison of calculated and experimental composition curves

Using the values of r_1 and r_2 obtained from KT method ($r_1 = 0.23$) and ($r_2 = 0.53$), the composition diagram was obtained from the following 'instantaneous copolymer composition' equation

$$F_1 = \frac{\left(r_1 f_1^2 + f_1 f_2\right)}{\left(r_1 f_1^2 + r_2 f_2^2 + 2 f_1 f_2\right)} \tag{5}$$

The calculated composition curve is plotted along with the experimental data and is shown in Fig. 6. The calculated theoretical values and the experimental data are in fairly good agreement.

Statistical microstructure

The distribution of monomer sequences along the copolymer chain was calculated on the basis of terminal copolymerization model of Igarashi [26]. This method calculates statistically the fractions of AcrNMP-AcrNMP (M_1–M_1), HEMA-HEMA (M_2–M_2), and AcrNMP-HEMA (M_1–M_2) units in the copolymer as function of reactivity ratios and composition. The analysis procedure can be described in detail

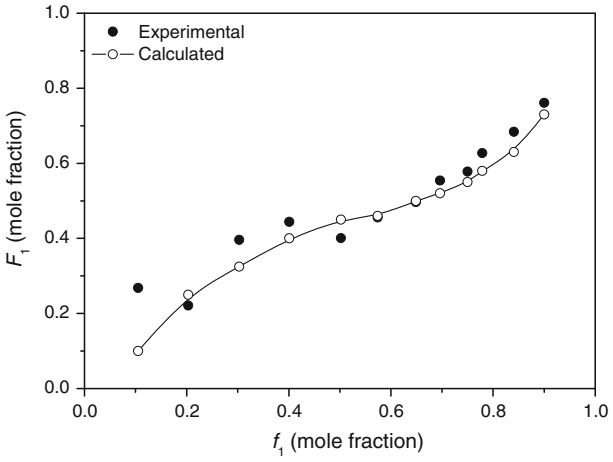

Fig. 6 Instantaneous copolymer composition curve

as follows. If x, y, and z are functions of M_1–M_1, M_2–M_2, and M_1–M_2 units in the copolymer then,

$$x = \frac{a_1}{(a_1 + a_2 + a_3)} \tag{6}$$

$$y = \frac{a_2}{(a_1 + a_2 + a_3)} \tag{7}$$

$$z = \frac{a_3}{(a_1 + a_2 + a_3)}, \tag{8}$$

where a_1, a_2, and a_3 are the total number of M_1–M_1, M_2–M_2, and M_1–M_2 units in the copolymer. For a copolymer, P_{11} is defined as the probability for a monomer of the type M_1 to adjoin the other monomer M_1. The same definition applies also to P_{22}. If a parameter q which is defined as follows:

$$q = \left[(2F_1 - 1)^2 + 4\, r_1 r_2 F_1 F_2\right]^{0.5}. \tag{9}$$

Then the probabilities, P_{11} and P_{22} can be given by the following equations as:

$$P_{11} = \frac{(2F_1 - 1 + q)}{(2F_1 + 2F_2 - 1 + q)} \tag{10}$$

$$P_{22} = \frac{2r_1 r_2 F_2}{(2r_1 r_2 F_2 + 2F_1 - 1 + q)}, \tag{11}$$

where F_1 and F_2 are the mole fractions of M_1 and M_2 units in the copolymer and r_1 and r_2 are the reactivity ratios. x, y, and z are related to P_{11}, P_{22}, F_1 and F_2 through the following relations:

$$x \approx P_{11} F_1 \tag{12}$$

$$y \approx P_{22} F_2 \tag{13}$$

$$z \approx (1 - P_{11}) F_1 + 1\,(1 - P_{22}) F_2. \tag{14}$$

By substituting, Eqs. 10 and 11 in the respective Eqs. 12, 13, and 14, the values of x, y, and z in terms of mole fractions were obtained. The results are shown as triad fraction in Fig. 7. This result further supports the tendency to alternation of the copolymers as determined earlier by the compositional and reactivity ratio studies. It can be observed from the triad fraction that the maximum tendency to alternation occurs at approximately 74 mol%. It is also evident that the triad fraction M_1-M_1 increases with increasing f_1, while triad fraction M_2-M_2 decreases with increasing f_1.

Swelling characteristic of the gels

The equilibrium weight swelling ratio of the gels in water as function of crosslinker content is shown in Fig. 8. The swelling of the gel decreases with increase in the amount of crosslinker. As the amount of crosslinker increases in the gel, the crosslinking density increases leading to the development of higher elastic constraint when the gels are swelled in water. This is an expected trend. What is

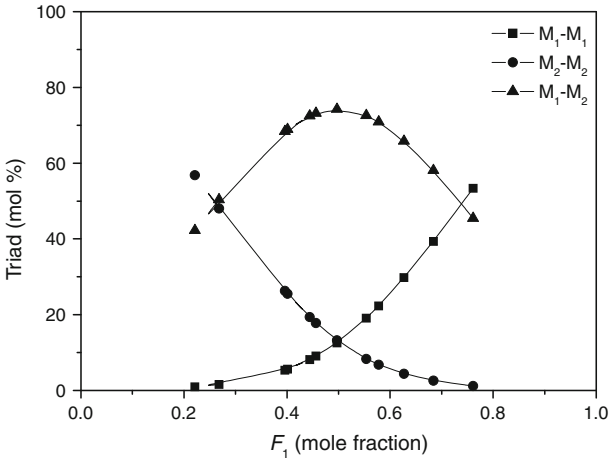

Fig. 7 Dependence of triad fractions on comonomer composition

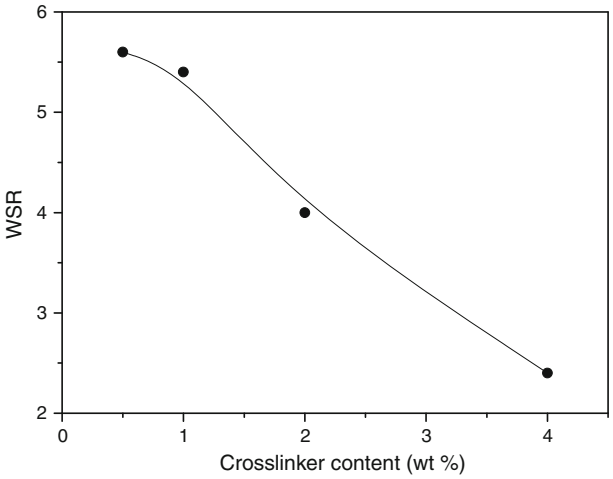

Fig. 8 Effect of crosslinker content on the swelling of the gels measured in water at 25 °C

interesting to note here is the high swelling ratios exhibited by the gels, and this is pronounced even at high crosslinker content of 4 wt%. EGDMA is a fairly hydrophobic crosslinker which should lead to lower swelling degrees compared to hydrophilic crosslinkers [27]. For the gel containing the smallest amount of crosslinker 0.5 wt% (G-0.5), the swelling percentage is about 560% and holds about 85% of water at swelling equilibrium. The gel containing the highest amount of crosslinker 4 wt% (G-4.0), the swelling percentage is about 240% and holds about 70% of water at swelling equilibrium.

This remarkable swelling nature of these gels arises as a direct consequence of the constituent monomers such as AcrNMP and HEMA. Both the monomers are

hydrophilic in nature and thus permit a large intake of water by the crosslinked gel network even though the crosslinker is less flexible and less hydrophilic. As both AcrNMP and HEMA are hydrophilic, the swelling behavior in water at neutral pH will not show any appreciable behavior as function of monomer composition. However, AcrNMP has a tertiary amine moiety which can be protonated at low pH, and these polymers can swell to different swelling degree in solutions of low pH. We have studied a series of copolymers of AcrNMP and MMA where we have demonstrated that changing the composition of ionizable monomer can influence the swelling properties [28–30]. By varying the amount/type of monomers and crosslinker in the gel it is possible to fine tune the gel to obtain the preferred swelling degree. These types of hydrophilic gels thus offer some promise in the development of soft gels (with good swelling) for targeted drug delivery systems, contact lenses, super sorbent gels, chelating resins, etc.

Conclusions

Copolymer of *N*-acryloyl-*N*′-methylpiperazine and 2-hydroxyethyl methacrylate were prepared by free radical polymerization in dioxane. The copolymer compositions were successfully determined by FTIR method and elemental analysis. Both the methods yielded results with good agreement. The reactivity ratios determined indicate random copolymerization with a high tendency of alternating structures. Microstructure analysis by the method of Igarashi further supports the alternating tendency of the copolymer. Crosslinked hydrophilic gels of this system exhibit a remarkably high swelling even above 500%. The copolymer of AcrNMP and HEMA reported in this study thus represents an interesting new hydrophilic polymer system with potential application in targeted drug delivery systems. Some of the application study of this system is currently being pursued in our laboratory.

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