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Synthesis and Physical Properties of pH-sensitive Semi-IPN Hydrogels Based on Poly(dimethylaminoethyl methacrylate-*co*-PEG dimethacrylate) and Poly(acrylic acid)

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Abstract: Hydrogels of semi-interpenetrating polymer networks (semi-IPNs) were prepared by two step reactions. Dimethylaminoethyl methacrylate (DMAM) and poly(ethylene glycol)-dimethacrylate (PEGDM) were copolymerized to yield hydrogels, and then acrylic acid (AA) monomer were adsorbed in the hydrogels followed by polymerization of AA to produce semi-IPNs. The swelling behavior of semi-IPNs depends largely on pH of medium, showing that the degree of swelling of the semi-IPNs exhibits a minimum at pH 6.0. It is observed that the elastic modulus of semi-IPNs is closely related to its swelling behavior.

Keywords: Acrylic acid, Complex, Dimethylaminoethyl methacrylate, Hydrogel, Semi-IPNs

Introduction

In recent years, considerable research attention has been focused on hydrogels that are able to alter their volume and properties in response to environmental stimuli such as pH, temperature, ionic strength, and electric field [1-5]. Because of their drastic swelling behavior in response to environmental stimuli, polymeric hydrogels have been investigated for many biomedical and pharmaceutical applications [6,7], such as controlled drug delivery [8-10], molecular separation [11,12], tissue culture substrates [13], enzyme activity controlling systems [14,15], and materials for improved biocompatibility [16].

More recently, it has been reported that hydrogels are prepared from interpenetrating polymer networks (IPNs) or semi-IPNs. One of advantages of IPNs and semi-IPNs is to attain combination of properties of two component polymers. Since there is no chemical bonding between two component networks, each network may retain its own property while the proportion of each network can be varied independently. Interpenetration of two networks may also lead to much higher mechanical strength than the corresponding homopolymer network [17-25]. Hence, hydrogels from IPNs or semi-IPNs may overcome the shortcoming of weak mechanical strength of conventional hydrogels.

Poly(acrylic acid) (PAA) is an ionizable hydrophilic polymer, and cross-linked PAA swells in water. The swelling behavior of cross-linked PAA is largely dependent upon pH due to ionization/deionization of carboxylic acid groups in PAA. At low pH, e.g., a pH value less than 4.5, the carboxyl acid groups are not ionized and therefore the PAA network is at its collapsed state. At high pH, however, the carboxyl acid groups are ionized and thus the charged groups repel each other, leading to swelling of PAA networks in water. PAA can form an inter-macromolecular complex with poly(ethylene glycol) (PEG) due to the hydrogen bonding between carboxyl acid groups of PAA and ether oxygen atoms of PEG. The formation of hydrogen-bonded complex is highly sensitive to a change in the concentration and molecular weight of PEG, temperature, and pH. The complex formation of PAA networks with PEG may be quite different from that of linear PAA. It has been reported that the absorption of PEG leads to contraction of the PAA gel and that the degree of swelling of the gel is lowered by a factor of 1.5-3.0 [26].

In general, it has been known that the formation of interpolymer complex in polymer network significantly changes the network structure. Here, the state of complex in polymer network can be affected by many parameters such as the size and concentration of interacting polymer chain as well as the nature of environmental fluid. The primary objective of this work is to synthesize pH-sensitive semi-IPNs from a polymer network with cationic and anionic pendant group, and to investigate the swelling behavior and elastic modulus of semi-IPNs as function of pH, molecular weight of cross-linker and the composition of component polymers. For the purpose, dimethylaminoethyl methacrylate is copolymerized with poly(ethylene glycol) dimethacrylate to yield a cross-linked hydrogel, and then the hydrogel is swollen with acrylic acid (AA) monomer followed by polymerization of AA to produce semi-IPNs (see Scheme 1).

Experimental

Materials

Dimethylaminoethyl methacrylate (DMAM) and acrylic acid (AA), ammonium persulfate (APS), *N,N,N',N'*-tetramethylethylenediamine (TEMED), phosphate buffer solution (PBS), poly(ethylene glycol) (PEG) (M_n = 550, 2000, 4600, 10000),

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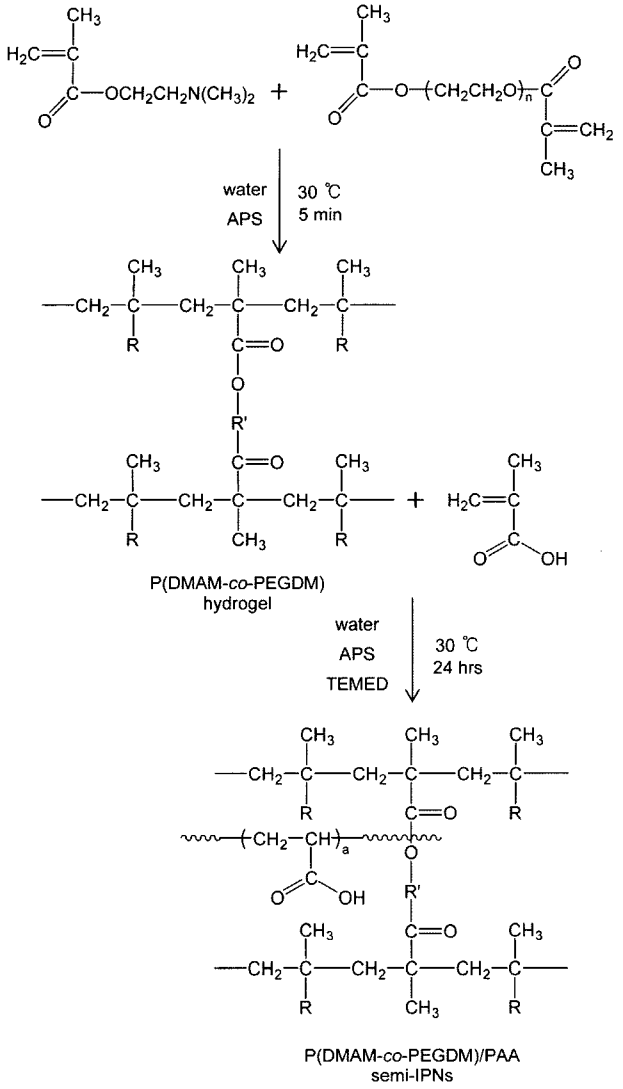

Scheme 1. Synthetic route of P(DMAM-*co*-PEGDM) hydrogels and P(DMAM-*co*-PEGDM)/PAA semi-IPNs.

methacryloyl chloride (MAC), triethylamine (TEA), methylene chloride (MC) were purchased from Sigma. DMAM, AA and MAC were purified by vacuum distillation prior to use, and the others are used without further purification.

Synthesis of Cross-linker

PEG (10 g) was dissolved in MC (50 m*l*), and TEA (5 m*l*) and 3 moles of MAC per 1 mole of hydroxyl group in PEG were added dropwise to the reactor, maintaining the temperature below 5 °C. After 12 hrs reaction, the triethylamine hydrochloride salt precipitated was filtered off and then the solvent was removed in a rotary evaporator to yield the product, PEG-dimethacrylate (PEGDM).

Preparation of Hydrogels

When DMAM and PEGDM were copolymerized in aqueous media with APS (1 mol% of DMAM) as an initiator at room temperature, the gelation took place within 5 min. The hydrogels were washed with water until the weight of hydrogel becomes unchanged. To prepare a semi-IPN, the dried P(DMAM-*co*-PEGDM) hydrogels were swollen in an AA aqueous solution (10 vol%, 50 m*l*) to which APS (1 mol% of AA) and TEMED (1 m*l*) were added. After the hydrogel swollen with AA was placed in a test tube of 1 cm diameter and 3.0 cm height for 48 hrs to allow AA to polymerize, the hydrogel of semi-IPN was carefully removed from the tube. The semi-IPN was washed with water for 48 hrs to remove unreacted monomers. The content of AA in hydrogel (m_{AA}) is defined as $m_{AA} = [AA]/([AA] + [EO])$, where [AA] and [EO] denote the number of moles of AA and ethylene oxide (EO) units in hydrogel. The number of moles of AA and EO units in hydrogel was determined from elemental analysis (EA1110, CE Instrument).

Swelling of Hydrogel

Hydrogels in cylindrical shape with a diameter of 1 cm were cut into pieces of 1 cm height. In equilibrium swelling experiment, dried hydrogels were placed in the pH buffer solution with a specific pH value and were allowed to swell to an equilibrium at 25 °C. Swelling was evaluated in terms of the degree of swelling (DS): $DS\ (\%) = (W_s - W_d)/W_d \times 100$, where W_s is the weight of hydrogel at an equilibrium swelling, and W_d is the weight of hydrogel dried after equilibrium swelling.

Stress-strain Measurement

The hydrogels in cylindrical shape were cut into pieces of 0.5 cm height. Before compressive experiment, the hydrogels were kept at a desired pH for 24 hrs. Uniaxial compression experiment was performed on hydrogels at a specific pH using a thermal mechanical analyzer (TMA 2940), where the crosshead speed was 1.0 cm/min. It should be noted that each compressive experiment is carried out within 1 min to avoid loss of water during the measurement. The elastic modulus (E) was determined from the slope of linear dependence of the equation $\sigma = F/S_0 = E(\alpha - \alpha^{-2})$, where σ is the applied stress ($Pa \cdot m^{-2}$), F is the measured force, S_0 is the cross-section of undeformed swollen specimen, and α is the relative deformation of the specimen.

Results and Discussion

Effect of pH on the Degree of Swelling of P(DMAM-*co*-PEGDM) Hydrogels

Four P(DMAM-*co*-PEGDM) hydrogels and four P(DMAM-*co*-PEGDM)/PAA semi-IPNs with different compositions were synthesized. The copolymer compositions of hydrogels and semi-IPNs are listed in Table 1. Overall synthetic route for preparation of hydrogel is represented in Scheme 1. When the degree of swelling of P(DMAM-*co*-PEGDM)

Table 1. Characterization of P(DMAM-*co*-PEGDM) hydrogels and P(DMAM-*co*-PEGDM)/PAA semi-IPNs

Code	PEGDM (M_n)	Composition[a] (in hydrogel)		m_{AA}
		PEGDM/ DMAM (mole ratio)	AA/DMAM (mole ratio)	
H-0.55K	550	0.152	–	–
H-2.0K	2000	0.087	–	–
H-4.6K	4600	0.103	–	–
H-10.0K	10000	0.093	–	–
SIH-0.55K	550	0.152	3.02	0.69
SIH-2.0K	2000	0.087	2.96	0.43
SIH-4.6K	4600	0.103	2.91	0.21
SIH-10.0K	10000	0.093	2.77	0.12

[a]Determined by elemental analysis.

hydrogels with different lengths of cross-linker is plotted as a function of pH, it reveals that the degree of swelling decrease as the pH increases, as shown in Figure 1. This is easily explained by considering the following fact. At pH above 7.0, the pendent amine groups of DMAM moiety in hydrogel are not ionized and therefore are more hydrophobic than their ionized counterpart. As a result, DMAM units in hydrogel associate with each other at pH above 7.0 and exclude water molecules from hydrogel, resulting in lower degree of swelling. When the pH is lower than the pKa value of the ionizable amine group (the pKa of DMAM = 7.5), the amine groups are protonated, resulting in generation of positive charges pendant to polymer backbone. Protonation of the pendant amine groups contributes to the swelling of hydrogel for two reasons. First, the positively charged amine groups repel each other, causing the polymer chains to move apart spatially. Second, solvated counter-anions are drawn into the polymer gel to keep the gel neutral, resulting in expansion of gel. Another interesting feature from Figure 1 is that the change of the degree of swelling with pH becomes larger as the length of cross-linker decreases. In other words, the degree of swelling becomes more sensitive to pH as the length of cross-linker decreases. This is probably because longer chains have higher probability of chain entanglement which may suppress the change of volume with pH.

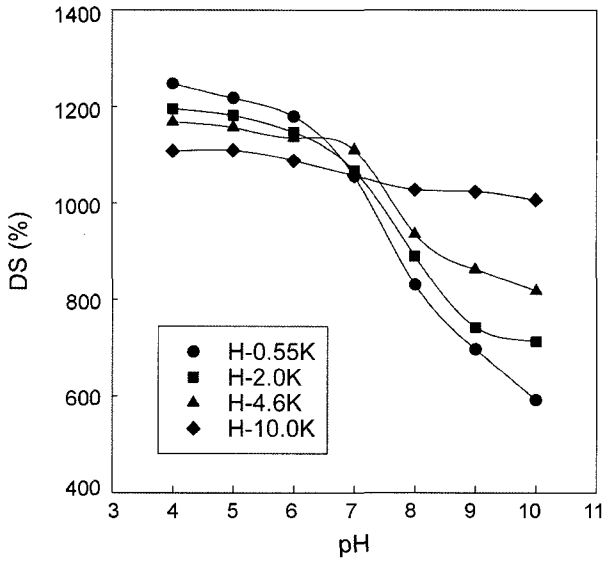

Figure 1. The effect of pH on the degree of swelling of P(DMAM-*co*-PEGDM) hydrogels.

Swelling behavior of P(DMAM-*co*-PEGDM)/PAA Semi-IPNs

When P(DMAM-*co*-PEGDM)/PAA semi-IPNs are prepared from P(DMAM-*co*-PEGDM) hydrogels, the amount of AA monomer adsorbed is proportional to the degree of swelling of P(DMAM-*co*-PEGDM) hydrogel, as shown in Figure 2.

As AA is polymerized in the P(DMAM-*co*-PEGDM) hydrogel to yield P(DMAM-*co*-PEGDM)/PAA semi-IPN, PAA may form a complex with poly(ethylene glycol) in the hydrogel due to hydrogen bonding between PAA and PEG in semi-IPN. Complex formation between PAA and PEG in semi-IPN depends upon pH of external environment. Since the swelling behavior of semi-IPN is dependent upon the capability to form a complex between PAA and PEG in semi-IPN, the degree of swelling becomes dependent upon pH of hydrogel. When a complex is formed between PAA and PEG in the semi-IPNs, the complex may play a role as an additional junction point in the network. Consequently,

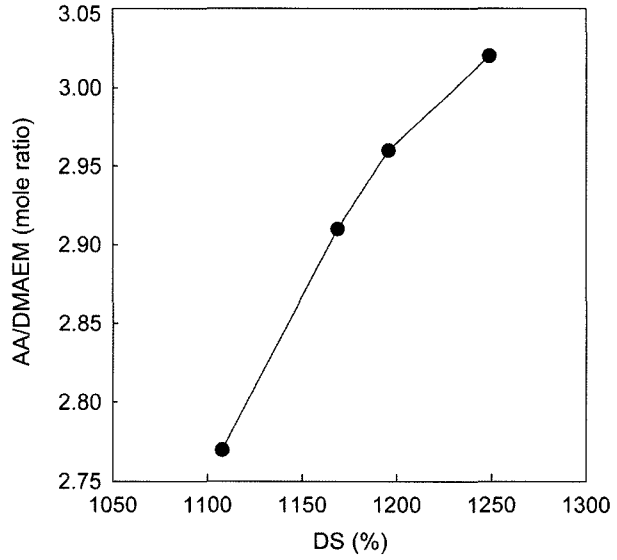

Figure 2. Effect of the degree of swelling of P(DMAM-*co*-PEGDM) hydrogels at pH 4.0 on adsorption of AA in semi-IPN hydrogels.

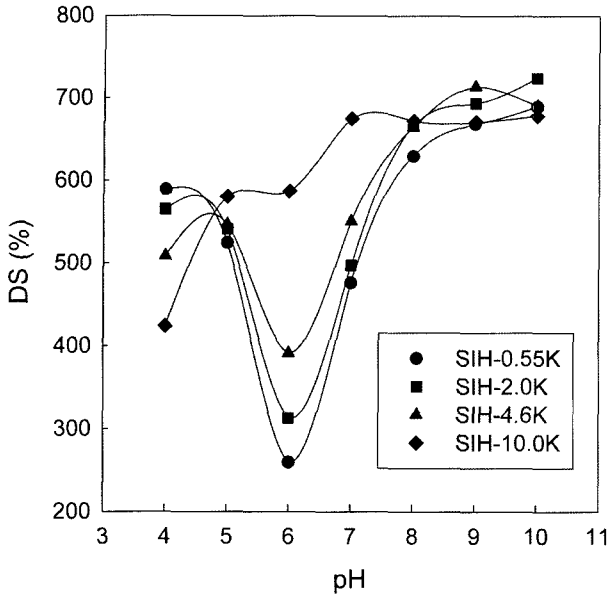

Figure 3. The effect of pH on the degree of swelling of P(DMAM-*co*-PEGDM)/PAA semi-IPNs.

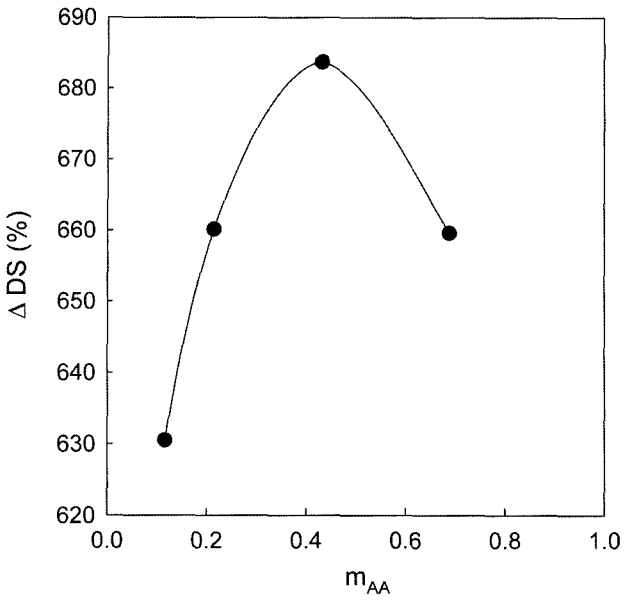

Figure 4. The effect of AA mole fraction on the difference of the degree of swelling ($\Delta DS = DS_{P(DMAM\text{-}co\text{-}PEGDM)} - DS_{P(DMAM\text{-}co\text{-}PEGDM)/PAA}$) at pH 4.0.

the end-to-end distance between junction points becomes shorter, and as a result the degree of swelling will be smaller. Unlike covalently cross-linked structures, the physical cross-links due to complex formation are not permanent. In the present system of P(DMAM-*co*-PEGDM)/PAA semi-IPNs, a complex is formed under acidic condition due to hydrogen bonding between the carboxylic acid of PAA and the ether oxygen atom of PEG moiety, producing additional physical cross-links. The formation of these physical cross-links is thus dependent upon pH and is reversible in nature. Therefore, it is expected that the swelling behavior of semi-IPNs is also dependent upon pH of environment.

When the degree of swelling of semi-IPNs is plotted against pH, the degree of swelling decreases and then increases as the pH increases, showing a minimum at pH 6.0, as shown in Figure 3. At pH 4.0, the degree of swelling of all semi-IPNs (DS = 400-600) is much smaller than that of non-complexing P(DMAM-*co*-PEGDM) hydrogels (DS = 1050-1250) (compare Figure 1 with Figure 3), because the formation of physical cross-links acts to stunt the swelling of hydrogels. In the range of pH 4.5-6.0, the degree of swelling decreases with increasing the pH of media. This is because the number of protonated amine groups in P(DMAM-*co*-PEGDM) decreases with increasing the pH of media and therefore the electrostatic repulsion between chains decreases to induce hydrophobic association of chains, resulting in a decrease of mesh size of the semi-IPN. Under higher pH media (pH > 6.0), the complex formed under acidic condition becomes dissociated as the AA groups in PAA are ionized, and consequently the degree of swelling of semi-IPNs increases with increasing the pH.

To evaluate the degree of complex formation of the semi-IPNs, the difference of the degree of swelling between P(DMAM-*co*-PEGDM) hydrogel and semi-IPNs was measured at pH 4.0 and plotted as a function of the mol fraction of acrylic acid (m_{AA}), as shown in Figure 4. The difference shows a maximum at $m_{AA} \approx 0.5$, indicating that the highest degree of complex formation is obtained when the mole ratio of AA unit in PAA to ethylene oxide unit in PEO is unity.

Effect of pH on Mechanical Property of Hydrogels

It is generally known that the elastic modulus of polymer network is largely dependent upon the chain length of cross-linker. When the elastic modulus of P(DMAM-*co*-PEGDM) is plotted against the molecular weight of cross-linker under various pHs, it is realized that the elastic modulus is nearly unchanged with the molecular weight of cross-linker at pH 9.0 and 10.0 while the elastic modulus increases with increasing the chain length of cross-linker under pHs below 8.0 (Figure 5).

Figure 6 compares the elastic moduli for P(DMAM-*co*-PEGDM) hydrogels and P(DMAM-*co*-PEGDM)/PAA semi-IPNs at 25 °C. It is observed that the elastic moduli of the P(DMAM-*co*-PEGDM) hydrogels increase with increasing the pH of medium, while the elastic moduli of semi-IPNs show a maximum at pH 6.0. An increase of elastic modulus of the P(DMAM-*co*-PEGDM) with pH is easily understood by considering the dependence of the degree of swelling on pH. As the hydrogel becomes more swollen, the network density of hydrogel is lower and subsequently the hydrogel

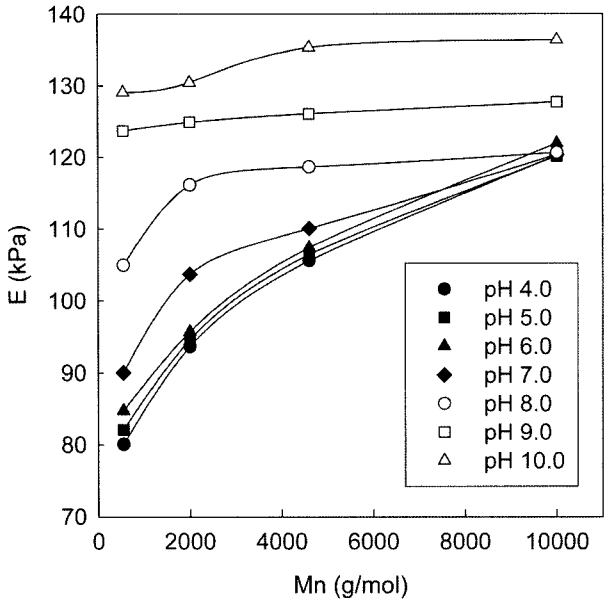

Figure 5. The effect of molecular weight of cross-linker on the elastic modulus of P(DMAM-*co*-PEGDM) hydrogels.

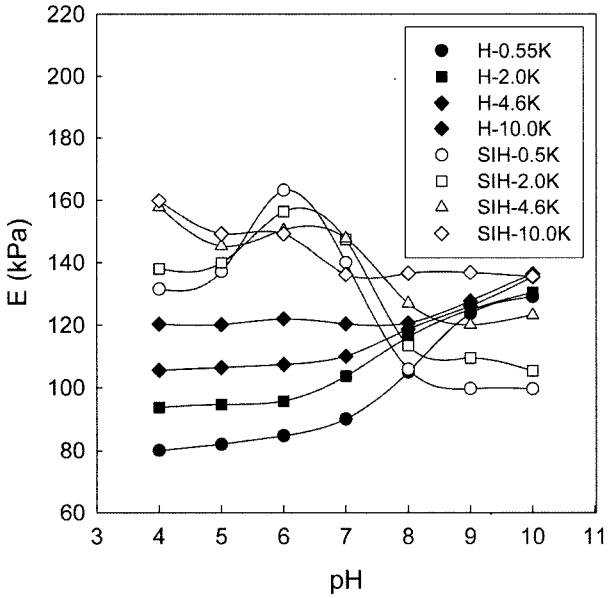

Figure 6. The effect of pH on the elastic modulus of P(DMAM-*co*-PEGDM) hydrogels and P(DMAM-*co*-PEGDM)/PAA semi-IPNs.

becomes softer. In other words, the higher the degree of swelling, the lower the modulus, as realized by comparing Figure 3 with Figure 6. For P(DMAM-*co*-PEGDM)/PAA semi-IPNs, the modulus exhibits a maximum at pH 6.0, i.e., the modulus increases as the pH increases from 5.0 to 6.0, and then decreases as the pH is further increased. The positive dependence of the elastic modulus upon pH is due to deswelling by a decrease in electrostatic repulsion P(DMAM-*co*-PEGDM) chains as the number of protonated amine groups decreases

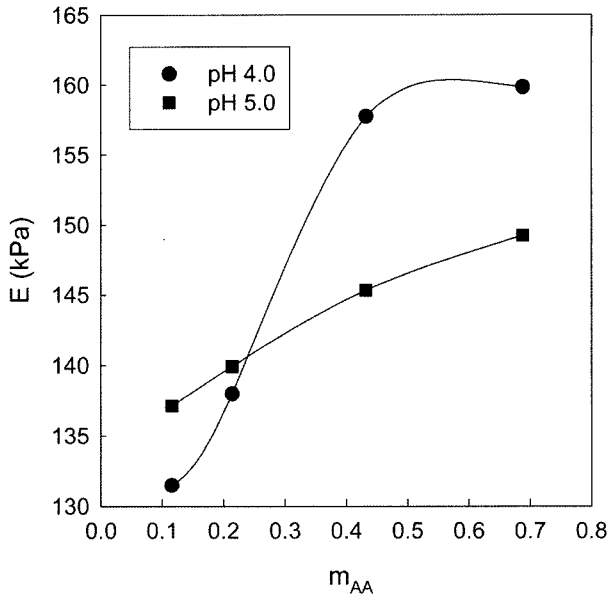

Figure 7. Effect of the AA mole fraction on the elastic modulus of P(DMAM-*co*-PEGDM)/PAA semi-IPNs at pH 4.0 and 5.0.

with increasing the pH of medium. As pH is further increased, the complex between PAA and PEO in semi-IPNs becomes dissociated and thus the semi-IPNs become more swollen, resulting in a decrease of the elastic modulus. When the elastic modulus of semi-IPN is plotted against the mole fraction of AA, as shown in Figure 7, it reveals that the elastic modulus reaches plateau above $m_{AA} = 0.5$ under pH 4.0 because the complex formation between acrylic acid and ethylene oxide is saturated at $m_{AA} \approx 0.5$. At pH 5.0, the complex starts to dissociate and therefore the elastic modulus of semi-IPNs increases with increasing the mole fraction of AA, since all the acrylic acid groups and ethylene oxide groups may not form a complex at pH 5.0.

Conclusions

Semi-IPNs were synthesized by two step reactions. First, DMAM and PEGDM were copolymerized to yield P(DMAM-*co*-PEGDM) hydrogels, and then AA monomers were adsorbed in the hydrogel followed by polymerization of AA to produce P(DMAM-*co*-PEGDM)/PAA semi-IPNs. The swelling behavior of semi-IPNs depends upon the mole fraction of AA in the semi-IPN, the chain length of cross-linker (PEG), and the pH of medium. Particularly, the degree of swelling of semi-IPNs strongly depends on whether the complex is formed or not under a given condition. Below pH 4.5 corresponding to the pKa of AA, the complex is formed and therefore the degree of swelling of semi-IPN is much lower than P(DMAM-*co*-PEGDM) hydrogels. In the pH range of 4.5-6.0, the degree of swelling is further decreased due to electrostatic repulsion between protonated amine groups in P(DMAM)

backbone. Above pH 6.0, the degree of swelling increases as the complex becomes dissociated. When the elastic modulus of semi-IPN hydrogels is measured as functions of pH and chain length of cross-linker, it is found that the elastic modulus is closely related to the degree of swelling of semi-IPNs.

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References

1. D. Dhara, G. V. N. Rathna, and P. R. Chatterji, *Langmuir*, **16**, 2424 (2000).
2. M. Ebara, T. Aoyagi, K. Sakai, and T. Okano, *Macromolecules,* **33**, 8312 (2000).
3. B. Zhao and J. S. Moore, *Langmuir,* **17**, 4758 (2001).
4. S. Brahim, D. Narinesingh, and A. Guiseppi-Elie, *Biomacromolecules,* **4**, 497 (2003).
5. M. Casolaro, S. Bottari, A. Cappelli, R. Mendichi, and Y. Ito, *Biomacromolecules,* **5**, 1325 (2004).
6. S. Brahim, D. Narinesingh, and A. Guiseppi-Elie, *Biomacromolecules,* **4**, 1224 (2003).
7. M. Torres-Lugo and N. A. Peppas, *Macromolecules,* **32**, 6646 (1999).
8. J. H. Han, J. M. Krochta, M. J. Kurth, and Y. L. Hsieh, *J. Agric. Food Chem.*, **48**, 5278 (2000).
9. D. Mandracchia, G. Pitarresi, F. S. Palumbo, B. Carlisi, and G. Giammona, *Biomacromolecules,* **5**, 1973 (2004).
10. K. Kataoka, H. Koyo, and T. Tsuruta, *Macromolecules,* **28**, 3336 (1995).
11. E. C. Muniz and G. Geuskens, *Macromolecules,* **34**, 4480 (2001).
12. J. Zhang and N. A. Peppas, *Macromolecules,* **33**, 102 (2000).
13. D. Wang, C. G. Williams, Q. Li, B. Sharma, and J. H. Elisseeff, *Biomaterials,* **24**, 3969 (2003).
14. H. F. Liang, M. H. Hong, R. M. Ho, C. K. Chung, Y. H. Lin, C. H. Chen, and H. W. Sung, *Biomacromolecules,* **5**, 1917 (2004).
15. D. A. Gough and J. D. Andrade, *Science,* **180**, 380 (1973).
16. A. S. Sawhney, C. P. Pathak, and J. A. Hubbell, *Macromolecules,* **26**, 581 (1993).
17. H. Katono, A. Maruyama, K. Sanui, N. Ogata, T. Okano, and Y. Sakurai, *J. Control. Release*, **16**, 215 (1991).
18. A. M. Lowman and N. A. Peppas, *Macromolecules*, **30**, 4959 (1997).
19. O. E. Philippova, N. S. Karibyants, and S. G. Starodubtzev, *Macromolecules,* **27**, 2398 (1994).
20. N. A. Peppas and S. L. Wright, *Macromolecules*, **29**, 8798 (1996).
21. E. Díez-Peña, I. Quijada-Garrido, P. Frutos, and J. M. Barrales-Rienda, *Macromolecules,* **35**, 2667 (2002).
22. R. A. Stile and K. E. Healy, *Biomacromolecules*, **3**, 591 (2002).
23. T. Miyoshi, K. Takegoshi, and K. Hikichi, *Polymer*, **38**, 2315 (1997).
24. M. Koussathana, P. Lianos, and G. Staikos, *Macromolecules,* **30**, 7798 (1997).
25. P. H. Corkhill and B. J.Tighe, *Polymer,* **31**, 1526 (1990).
26. N. A. Peppas and J. Klier, *J. Control. Release,* **16**, 203 (1991).