Temperature-Responsive Interpenetrating Polymer Networks Constructed with Poly(acrylic acid) and Poly(*N*,*N*-dimethylacrylamide)

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ABSTRACT: Complex formation between PDMAAm as a hydrogen-bonding acceptor and PAAc as a hydrogen-bonding donor, the temperature dependence of the equilibrium swelling for interpenetrating polymer network (IPN) hydrogels composed of PDMAAm and PAAc, and changes in ketoprofen release of these IPN hydrogels were investigated. Interpolymer complexes between PDMAAm and PAAc were very stable at 70 °C in aqueous solution. Dissociation temperatures of the complex between poly(DMAAm-*co*-AAm) and PAAc shifted to higher values with increasing DMAAm content. These IPNs composed of poly(DMAAm-*co*-AAm) and PAAc showed limited swelling ratios between their swelling transition temperatures and lower swelling ratios above these transition temperatures. Transition temperatures shift to higher values with increasing DMAAm content. Reversible and pulsatile solute release, reflecting the "on" state at higher temperatures and the "off" state at lower temperatures, was achieved by fabricating these IPN hydrogels.

Introduction

Materials which exhibit changes in response to external stimuli such as pH,[1] electric current,[2] and temperature[3–6] have been defined as "intelligent materials"[7] having sensor, processor, and effector functions as single molecules or aggregates of molecules. Such intelligent materials are required for advanced applications, including drug delivery systems capable of supplying varying amounts of drug at required times to the body. These materials are capable of not only suppressing drug side effects but also achieving new therapies.

Hydrogels are water-swollen polymer networks of both fundamental and technological interest. Investigations of water–polymer interactions have been reported by numerous workers. Hoffman *et al.*,[8] Kim *et al.*,[9,10] and Okano *et al.*[11,12] have studied aqueous swelling and drug release from poly(*N*-isopropylacrylamide) (PIPAAm) gels. PIPAAm demonstrates a lower critical solution temperature (LCST) at 32 °C in aqueous solution, signifying hydration of polymer chains under 32 °C and polymer dehydration at higher temperatures. Analogously, cross-linked PIPAAm networks in water exhibit swollen and shrunken states below and above 32 °C, respectively. By utilizing PIPAAm hydrogels, temperature-controlled on–off drug release systems have been developed. Furthermore, complete on–off solute release has been achieved by incorporating butyl methacrylate (BMA) in PIPAAm chains.[13] These network functions are critically reliant upon a balance between hydrophobic and hydrophilic properties of the networks and their interactions with water.

On the other hand, we investigated a new type of material with functions resulting from both polymer–water and polymer–polymer interactions. We had already succeeded in developing a polymeric hydrogel which shrinks at lower temperatures and swells at higher temperatures. In this regard, we have reported positive temperature-dependent swelling changes and sigmoidal transitions within certain characteristic temperature ranges for interpenetrating polymer networks (IPNs).[14,15] This IPN hydrogel is composed of polyacrylamide (PAAm) and poly(acrylic acid) (PAAc), forming interpolymer complexes via hydrogen bonding at lower temperatures which dissociate at higher temperatures.[16–19] Randomly copolymerized hydrogels exhibit less drastic swelling changes in response to temperature changes compared to these IPN systems. Changes between the swollen and shrunken states in this IPN hydrogel are due to both attractive and repulsive polymer–polymer interactions as well as to polymer–water interactions. Drastic swelling changes arise from cooperative polymer–polymer interactions (zipper-like effect). Tanaka *et al.*[20] have reported that PAAm/PAAc IPN hydrogels demonstrate a phase transition at a characteristic temperature in aqueous urea solutions. Release of ketoprofen from PAAm/PAAc IPNs exhibits a pulsatile pattern of release at higher temperatures which is arrested at lower temperatures.[15]

Now, we have two strategies which are conceived for more stable interpolymer complexes, in comparison with those found in the PAAm/PAAc IPN hydrogel. One conception is a method to increase the density of amide groups by incorporating two amide group subtypes per monomer unit. According to this conception, IPN hydrogels composed of poly(*N*-acryloylglycinamide) (PAG) and PAAc have been developed.[21] As expected, the transition temperature for rapid swelling–deswelling changes of this IPN hydrogel shifts to 40 °C. Both PAAm/PAAc and PAG/PAAc IPN hydrogels exhibit collapsed, compact states from formation of interpolymer complexes at lower temperatures and swollen states from dissociation of these complexes at higher temperatures. Formation/dissociation of interpolymer complexes is the primary determinant to alter swollen/shrunken states in these IPN hydrogels.

A second conception is to promote more efficient formation of intermolecular complexes with PAAc by suppressing intramolecular complexes of PAAm. Efficient intermolecular complexes demonstrate more compact

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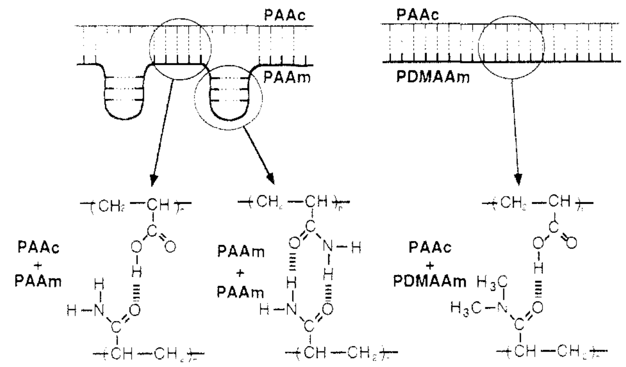

Figure 1. Inter- and intramolecular hydrogen-bonded complexes of the PAAm–PAAc and PDMAAm–PAAc systems.

Table 1. Feed Composition for Poly(DMAAm-*co*-AAm)[a]

code	DMAAm g	DMAAm mol %	AAm/g	APS/g	$M_w/10^5$ [b]
PDA-0 (PAAm)	0.00	0	7.20	0.2	3.0
PDA-10	0.99	10	6.39	0.2	3.8
PDA-20	1.99	20	5.68	0.2	3.5
PDA-23	2.28	23	5.47	0.2	3.0
PDA-27	2.68	27	5.18	0.2	*c*

[a] Polymers were synthesized in 90 mL of H_2O. [b] Measured by laser scattering. [c] No measurement.

shrunken states because of more effective dehydration of IPN polymer chains. On the contrary, the competing intramolecular complex exhibits hydration and swelling states since intermolecular complexes form incompletely. This mixture of molecular complexes favors a low dissociation temperature. On the basis of the idea that the hydrogel phase-transition temperature depends upon the stability of intermolecular complexes, we have investigated a new type of IPN hydrogel composed of poly(*N,N*-dimethylacrylamide) (PDMAAm) and PAAc.

From this perspective, an IPN hydrogel comprising PDMAAm and PAAc has been synthesized, and its swelling and drug release behaviors in response to temperature are presented in this paper.

Experimental Section

Monomers. *N,N*-Dimethylacrylamide (DMAAm) and ketoprofen were supplied by Kohjin Co., Ltd., and Hisamitsu Pharmaceutical Co., Inc., respectively. Acrylamide (AAm), acrylic acid (AAc), butyl methacrylate (BMA), methylenebisacrylamide (MBAAm), dimethyl sulfoxide (DMSO), and ammonium persulfate (APS) were purchased from Wako Pure Chemical Industries, Ltd. AAc, BMA, and DMSO were distilled before use. Other reagents were used as received.

Polymers. PAAm, PAAc, and PDMAAm were polymerized in aqueous solutions at 60 °C for 30 min using APS as an initiator. Poly(DMAAm-*co*-AAm) was synthesized using the feed compositions shown in Table 1. All polymers were purified by dialysis against water and subsequent lyophilization. The designation *X* in PDA-*X* denotes the DMAAm mole percentage in (DMAAm + AAm) for each synthesis.

IPN Hydrogels. Polymer IPNs were prepared by a sequential IPN synthesis.[14] Poly(DMAAm-*co*-AAm) and poly(DMAAm-*co*-AAm-*co*-BMA) as initial gels for the IPN, and then PAAc gels as a secondary gel were synthesized directly within these initial gels. MBAAm (0.5 mol %) was used as a cross-linker for each gel. As shown in Table 2, the designations *X* in both PDA-*X* and PDAB-*X* denote the DMAAm mole percentage of initial gels for each synthesis. In the case of PDAB-*X*, each initial gel was prepared with nearly the same feed composition of BMA. Furthermore, the designations *X* and *Y* in PDAB-(*X*,*Y*) denote the DMAAm and BMA mole percentages, respectively. In these cases, poly(DMAAm-*co*-AAm-*co*-BMA) gels were synthesized as initial gels for IPNs using AIBN, and then a PAAc gel as a secondary gel was polymerized within the initial gel using APS. BMA, a hydrophobic component, was incorporated into poly(DMAAm-*co*-AAm) gels to reinforce their mechanical properties. The initial gels were immersed in pure DMSO for a week to remove unreacted chemicals. Then the gels were further soaked in 75/25, 50/50, and 25/75 vol/vol % DMSO/distilled water solutions for 1 week each, followed by a final soaking in distilled water for 1 week. The obtained IPNs were evaluated after washing for more than 1 week in distilled water.

Table 2. Feed Composition for the Initial Gels of the IPN Gels[a]

code	DMAAm/ (mol %)	AAm/ (mol %)	BMA/ (mol %)
PDA-0/PAAc (PAAm/ PAAc) IPN	0	100.0	0
PDA-20/PAAc IPN	20.0	80.0	0
PDAB-0/PAAc IPN	0	89.0	11.0
PDAB-9/PAAc IPN	8.9	79.6	11.5
PDAB-18/PAAc IPN	17.6	70.6	11.8
PDAB-26/PAAc IPN	26.3	61.4	12.3
PDAB-44/PAAc IPN	43.5	43.5	13.0
PDAB-(17,0)/PAAc IPN	16.7	83.3	0
PDAB-(16,3)/PAAc IPN	16.3	81.2	2.5
PDAB-(16,5)/PAAc IPN	15.8	79.2	5.0
PDAB-(15,8)/PAAc IPN	15.4	77.1	7.5

[a] The initial gels were prepared in 15 mL of DMSO.

Transmittance (% *T*) Measurements. Optical transmittance for aqueous solutions of poly(DMAAm-*co*-AAm)–PAAc mixtures and the solution mixtures containing various concentrations of urea were measured with a Shimadzu UV-240 UV-visible spectrophotometer at 500 nm.[21] The concentration of each polymer in aqueous solution was 2.5 wt %.

FT-IR Measurement. Thin films of pure PDMAAm and pure PAAc were cast from 0.5 wt % distilled water onto separate CaF_2 plates at room temperature. The majority of water contained within the films on the plates was removed by evaporation at 50 °C for 24 h, and the films were then dried at 50 °C *in vacuo* for 24 h. The thin films of PDMAAm/PAAc blends were prepared as follows: 0.5 wt % PDMAAm aqueous solutions were dropped onto the CaF_2 plates followed by dropping 0.5 wt % PAAc aqueous solution onto the same plate, occasionally mixing to achieve homogeneity. Solvent (water) was removed as described above for the homopolymer cases. Fourier transform infrared (FT-IR) spectra of the polymers and the blended films in the dried state were measured on a JEOL JIR-RFX 3001 spectrophotometer using 150 average scans at a resolution of 2 cm^{-1}.

Swelling Measurements. After immersion in water at a desired temperature, the IPNs were removed from the water and tapped with a filter paper to remove excess water on the IPN surface. The IPNs were repeatedly weighed and reimmersed in water at a fixed temperature until the hydrated weight reached a constant value. After equilibration at one temperature, the IPNs were then reequilibrated at a higher temperature. The weight ratio, W_s/W_p, was used to evaluate the swelling ratio, where W_s is weight of absorbed water and W_p is that of the same dried IPN disk.

Drug Loading and Drug Release. Dried IPN disks were immersed for 1 day in ketoprofen ethanol–water (50:50 v/v) solutions at 30 °C. After removal of the drug from the surface by washing with ethanol, the IPNs were dried at −20 °C for 24 h, at −20 °C for 24 h *in vacuo*, and finally at room temperture *in vacuo* for 72 h.

Drug release rate changes in response to temperature changes were investigated by using a flow cell. The medium was distilled water and the flow rate was 1.0 mL/min. The cell volume was 3 cm^3. The drug concentration in elution from the flow cell was continuously monitored with the UV spectrophotometer (254 nm). The flow cell was put into two water baths fixed at 20 and 40 °C and mutually transported between the baths to change the temperature of flow cell.

Results and Discussion

PAAm and PAAc are known to form complexes which dissociate at 25 °C in aqueous PAAm–PAAc solution

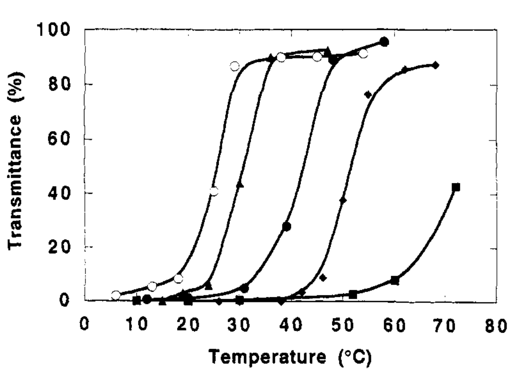

Figure 2. Temperature dependence for transmittance changes in mixed poly(DMAAm-*co*-AAm) and PAAc aqueous solutions: (○) PDA-0(PAAm)/PAAc; (▲) PDA-10/PAAc; (●) PDA-20/PAAc; (♦) PDA-23/PAAc; (■) PDA-27/PAAc.

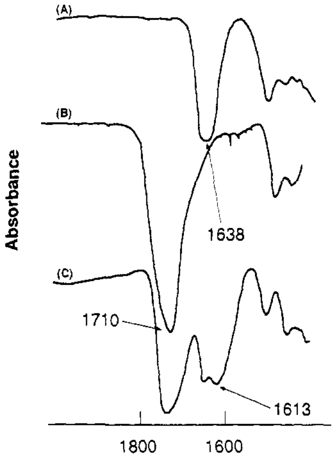

Figure 3. Carbonyl stretching bonds for (A) PDMAAm, (B) PAAc, and (C) PDMAAm/PAAc blends.

mixtures.[14,16–19] By contrast, complexes obtained by mixing PDMAAm and PAAc aqueous solutions were observed in water at 70 °C. This reflects the enhanced stability of intermolecular complexes formed by PDMAAm and PAAc in aqueous solution. To evaluate the complexation capabilities of PDMAAm, PDA-*X* copolymers were synthesized with various compositions of DMAAm. The temperature dependencies for transmittances for aqueous solutions of PDA-*X* and PAAc were then investigated. Each polymer aqueous solution of PDA-*X* and PAAc was transparent over the temperature range from 5 to 70 °C. As shown in Figure 2, transmittance of the mixed polymer solution of PDA-*X* and PAAc were consistently 0% at lower temperatures and 100% at higher temperatures. PDA-*X* and PAAc formed interpolymer complexes at lower temperatures and dissolved in water to dissociate at higher temperatures. Although the transition temperature of complexation and dissociation of PAAm and PAAc was 25 °C, those for copolymers of poly(DMAAm-*co*-AAm) and PAAc were shifted to higher temperatures with increasing DMAAm content in PDA-*X*. This indicates that complexation is stabilized by increasing DMAAm content in the copolymer.

FT-IR studies have been reported which identify interpolymer associations in thin films which may be attributed to hydrogen bond formation.[22–25] We have used FT-IR methods to probe dissociated polymer films cast from aqueous media to help substantiate interpolymer association between PDMAAm and PAAc, despite the fact that polymer complex formation is also believed to occur readily in aqueous solution. Figure 3 shows FT-IR spectra for the carbonyl stretching regions for pure PDMAAm, pure PAAc, and mixed PDMAAm/PAAc blends. Carbonyl stretching bonds for pure systems of PDMAAm and PAAc are observed at 1638 and 1713 cm^{-1}, respectively. A distinctly different absorption band at 1613 cm^{-1} is observed for the PDMAAm/PAAc blends, attributed to PDMAAm carbonyl groups involved in hydrogen-bonded complexes.

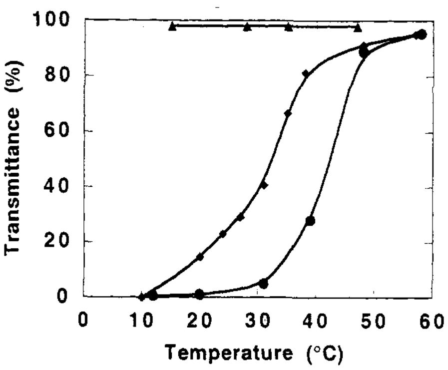

Figure 4. Influence of urea on the temperature dependence of the transmittance for aqueous solutions of PDA-20 and PAAc. Urea concentration: (●) 0 M; (♦) 0.1 M; (▲) 3 M.

Temperature dependencies for transmittance of PDA-20 and PAAc aqueous solutions containing urea are shown in Figure 4. Transmittance for the mixed solution of PDA-20 and PAAc was 0% below 40 °C and 100% at higher temperatures. Therefore, like the previous composition, PDA-20 and PAAc formed interpolymer complexes below 40 °C and dissociated at higher temperatures. Addition of urea, which is known to break hydrogen bonding and hydrophobic interactions, decreases the dissociation temperature of this interpolymer complex. The transmittance for the copolymer and PAAc aqueous solutions containing 3 M urea was 100% independent of temperature. This reveals that this complex completely dissociates in the presence of 3 M urea. The results suggest two possible effects of urea on interpolymer complexes. Urea is well-known to strongly disturb hydrogen bonding and hydrophobic interactions. The two effects were therefore attributed to polymer dissociation processes. The results reported here show that PDMAAm–PAAc complexes form readily at lower temperatures and dissociate rapidly at higher temperatures in aqueous media—a phenomenon consistent with hydrogen bond formation between interpolymer complexes. In fact, Tanaka *et al.*[20] have also reported that gel-volume phase transitions in the IPN hydrogels composed of PAAm and PAAc are distinctly different from transitions in gels governed strictly by ionic or hydrophobic interactions. These gels were experimentally proven, confirming theory, to form intermolecular complexes mediated by hydrogen bonding. Our results with the PDMAAm–PAAc system are structurally analogous and phenomenologically similar. Hydrogen-bonding associations are likely, particularly in the absence of other predominant intermolecular forces. Our FT-IR results, combined with solution-phase transmittance results for mixed polymer systems, are entirely consistent with interpolymer associations and thermal dissociation between PDA-*X* and PAAc mediated by hydrogen bonding.

Our evidence suggests that PDMAAm and PAAc form more stable interpolymer complexes via hydrogen bonding than PAAm and PAAc. DMAAm residues have a different water solvation mechanism than AAm. As shown in Figure 1, PAAm can display an intermolecular complex in water.[26,27] Therefore, PAAm does not form a 100% efficient intermolecular complex with PAAc, resulting in the observed low temperature of dissociation. Silberberg

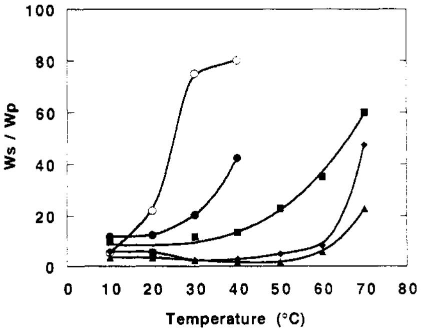

Figure 5. Temperature dependence of equilibrium swelling degrees for IPN gels: (○): PDA-0(PAAm)/PAAc IPN; (●) PDA-25/PAAc IPN; (■) PDA-50/PAAc IPN; (◆) PDA-75/PAAc IPN; (▲) PDA-100(DMAAm)/PAAc IPN.

et al.[28] have reported the role of intramolecular hydrogen bonding on the intrinsic viscosity of PAAm. Also, Bae *et al.* have pointed out that the Flory–Huggins parameter of PAAm under 20 °C is higher than that of PDMAAm due to intramolecular hydrogen bonding.[26] On the other hand, PDMAAm can only form intermolecular complexes with PAAc, and the resulting dissociation temperatures of this complex with PAAc shift to higher temperatures. This phenomenon is consistently observed in each swelling ratio for the polymer IPN hydrogels. In the case of identical hydrogel cross-link density, PAAm hydrogels exhibit lower swelling ratios than poly(*N*-alkyl-substituted acrylamide) hydrogels such as PDMAAm hyrogels at lower temperatures.[26] This reveals that PAAm hydrogels have collapsed states from strong intramolecular complexes via AAm residues and that poly(*N*-alkyl-substituted acrylamide) hydrogels have swollen states from both hydration of monomer residues and lack of molecular complexes. The heat of dilution of PAAm in water is endothermic whereas those of N-substituted polymers are exothermic;[27] PAAm residues require separation of the amide dipoles for hydration. The *N,N*-dimethyl-substituted structure in PDMAAm does not promote dipole interaction or intramolecular complexation, and the two terminal methyl groups maintain only minimal mobility. Furthermore, the dimethylamide group is reported to be a hydrogen bond acceptor.[29,30] Therefore, DMAAm remains a powerful hydrogen-bonding acceptor, and interpolymer complexes between PDMAAm and PAAc are very stable in aqueous solution. Morawetz *et al.*[31] have reported interpolymer complexes are formed using PDMAAm as a strong hydrogen-bonding acceptor and PAAc as a hydrogen-bonding donor in water solutions.

The temperature dependence for the equilibrium swelling ratios for IPN hydrogels composed of PDMAAm and PAAc is shown in Figure 5. PAAm/PAAc and PDMAAm/PAAc IPN hydrogels start to swell at 25 and 60 °C, respectively. Transition temperatures between the shrunken and swollen states for PDA-*X*/PAAc IPN hydrogels shift to higher values with increasing content of DMAAm in the copoly(DMAAm-*co*-AAm) chain. Additionally, swelling ratios both below and above the transition temperature are decreased. Both the transition temperature shifts to higher temperatures and the decreased swelling ratios below the transition temperature are due to stable interpolymer complexes between poly(DMAAm-*co*-AAm) and PAAc.

The influence of DMAAm content in poly(DMAAm-*co*-AAm) on the equilibrium swelling ratios for PAAc-containing IPN hydrogels at 10 °C are shown in Figure 6. The equilibrium swelling ratios for the hydrogel exhibit maximum and minimum values when poly(DMAAm-*co*-AAm) contained 25 and 100 mol % of DMAAm content, respectively. Since PDMAAm clearly does not form complexes with PAAm according to transmittance changes detected for mixed solutions, changes in swelling ratio were rationalized as follows. PAAm gel exhibits high swelling mediated by strong hydration of amide groups. However, multiple chain–chain intramolecular complexes suppress full expansion of the hydrated polymer network. At low DMAAm content in poly(DMAAm-*co*-AAm), the copolymer gels swell to much higher magnitudes than that oberved in homopolymer gels of pure PAAm due to the disrupting effect of DMAAm on the intramolecular interaction between AAm chains. Therefore, IPN hydrogels show relatively high swelling ratios. At higher DMAAm contents, poly(DMAAm-*co*-AAm) chains dissociate the intramolecular complexes between AAm residues. Simultaneously, poly(DMAAm-*co*-AAm) segments and PAAc segments form intermolecular complexes and the IPN hydrogel composed of poly(DMAAm-*co*-AAm) and PAAc exhibits a lower swelling ratio. However, it is conceived that PAAc also forms intramolecular complexes, resulting in the PDMAAm and PAAc IPN hydrogel exhibiting an incomplete collapsed state.

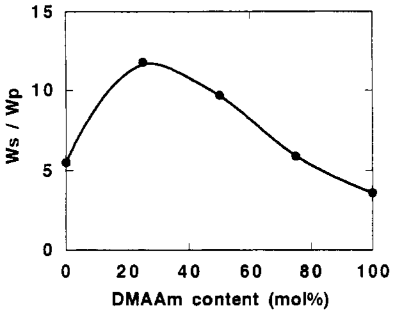

Figure 6. Equilibrium swelling degrees for IPN gels as a function of DMAAm content in initial gels at 10 °C.

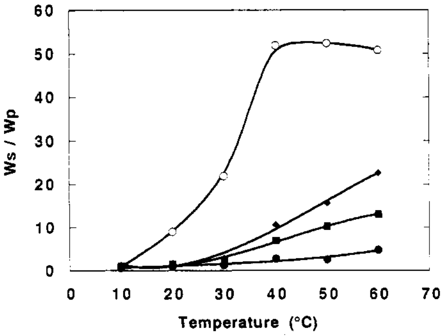

Figure 7. Temperature dependence of equilibrium swelling degrees for IPN gels: (○) PDAB-(17,0)/PAAc IPN; (◆) PDAB-(16,3)/PAAc IPN; (■) PDAB-(16,5)/PAAc IPN; (●) PDAB-(15,8)/PAAc IPN.

The equilibrium swelling ratios of IPN hydrogel composed of poly(DMAAm-*co*-AAm-*co*-BMA) and PAAc were measured. This composition was used to study the effect of incorporating a hydrophobic component. As shown in Figure 7, by incorporating BMA into poly(DMAAm-*co*-AAm), the equilibrium swelling ratios of the IPN hydrogels show low values and PDAB-(15,8)/PAAc IPN hydrogel has a very limited swelling. In these cases, both hydrogen bonding and additional hydrophobic interactions contributed to gel shrunken states for these IPN networks. Because hydrogen bonding and hydrophobic interactions stabilize the interpolymer complex, the high degree of swelling of the IPN hydrogels above the transition temperature is significantly influenced. In particular, it is noted that the transition temperatures shift to higher

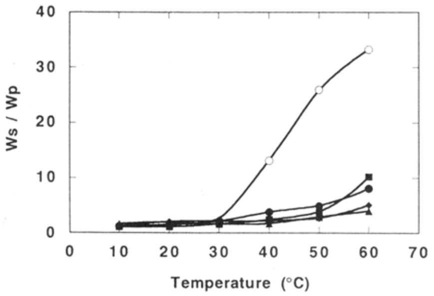

Figure 8. Temperature dependence of equilibrium swelling degrees for IPN gels: (○) PDAB-0/PAAc IPN; (■) PDAB-9/PAAc IPN; (●) PDAB-18/PAAc IPN; (◆) PDAB-26/PAAc IPN; (▲) PDAB-44/PAAc IPN.

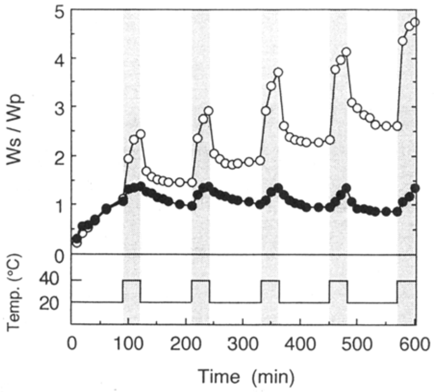

Figure 9. Reversible changes in swelling of the IPN gels between 20 and 40 °C in distilled water: (○) PDAB-0/PAAc IPN; (●) PDAB-18/PAAc IPN.

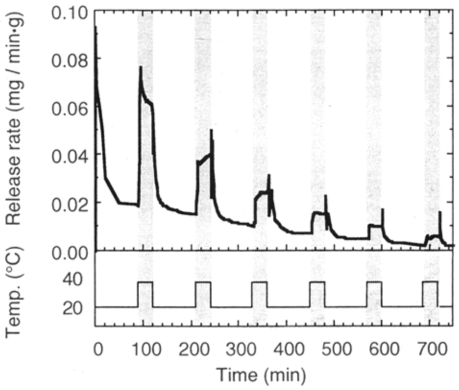

Figure 10. Release rate changes of ketoprofen from PDAB-0/PAAc IPN gel in response to stepwise temperature changes between 20 and 40 °C in distilled water.

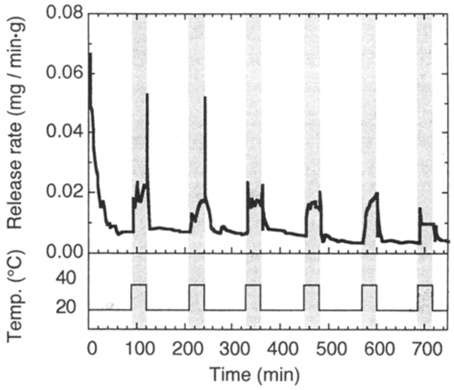

Figure 11. Release rate changes of ketoprofen from PDAB-18/PAAc IPN gel in response to stepwise temperature changes between 20 and 40 °C in distilled water.

values and swelling changes are greatly reduced above the transition temperature compared to non-BMA IPNs.

The influence of DMAAm content on the equilibrium swelling ratios of PDAB-*X*/PAAc IPN hydrogel is shown in Figure 8. The temperature dependence for the equilibrium swelling ratio of PDAB-0/PAAc IPN hydrogel exhibits a drastic swelling decrease under 30 °C. Further, swellings of PDAB-*X*/PAAc IPN hydrogels at lower temperatures were observed to decrease with increasing DMAAm content in the poly(DMAAm-*co*-AAm-*co*-BMA) chain.

Swelling changes for both PDAB-0/PAAc and PDAB-18/PAAc IPN hyrogels in response to stepwise temperature changes between 20 °C for 1.5 h and 40 °C for 0.5 h are shown in Figure 9. The measurement of the swelling degrees of the IPN hydrogels were started from the dried states of the IPNs. Both IPN hydrogels showed shrunken states at lower temperatures and swollen states at higher temperatures. Although the swelling change for the PDAB-18/PAAc IPN hydrogel is reversible within a constant range, the swelling ratio for the PDAB-0/PAAc IPN hydrogel gradually increases in response to repeated temperature fluctuations. In the case of PDAB-0/PAAc IPN hydrogel, the equilibrium swelling ratio showed high values at both 20 and 40 °C and the differences between the swelling ratios at 20 and 40 °C were large. Therefore, large swelling changes in response to temperature fluctuations are observed and the swelling ratio as a whole increases. PDAB-18/PAAc IPN hydrogels showed low swelling ratios and small swelling changes between 20 and 40 °C. Swelling change reversibility was also observed. Differences in swelling changes in response to temperature changes are attributed to the relative stabilities of interpolymer complexes. Intramolecular complexes of AAm residues lower the stability of the interpolymer complex with PAAc in PDAB-0/PAAc IPN hydrogels. The interpolymer complex is dissociated at 20 °C and each segment in this IPN hydrates to show high swelling values. In PDAB-18/PAAc IPN hydrogels, poly(DMAAm-*co*-AAm-*co*-BMA) and PAAc form stable interpolymer complexes. The complex mediated by hydrogen bonding is maintained at both 20 and 40 °C.

Release rate changes from PDAB-0/PAAc and PDAB-18/PAAc IPN hydrogels in response to temperature changes between 20 and 40 °C are shown in Figures 10 and 11, respectively. Both profiles shown in Figures 10 and 11 exhibit high release rates at higher temperatures which are reduced with the number of temperature fluctuations. Release rate changes from PDAB-0/PAAc IPN hydrogel gradually damp with temperature fluctuation. This is in accordance with the increasing swelling ratios observed at 20 °C for this IPN with repeated temperature jumps, as shown in Figure 9. Ketoprofen diffusion is rapid in PDAB-0/PAAc IPN hydrogels, which show high swelling ratios at 40 °C. The decreased amount of drug remaining in this IPN hydrogel after each temperature step affects the decreasing release rate. As shown in Figure 11, the PDAB-18/PAAc IPN hydrogel demonstrates a constant change of release rate in response to stepwise temperature changes between 20 and 40 °C. This result is based on the fact that this IPN hydrogel shows small and reversible swelling changes between 20 and 40 °C (Figure 9).

Conclusion

Complex formation between PDMAAm as a hydrogen-bonding acceptor and PAAc as a hydrogen-bonding donor, the temperature dependence of the equilibrium swelling for IPN hydrogels composed of PDMAAm and PAAc, and changes in ketoprofen release of these IPN hydrogels have been investigated.

1. Interpolymer complexes between PDMAAm and PAAc are very stable at 70 °C in aqueous solution. Dissociation temperatures of the complex between poly(DMAAm-*co*-AAm) and PAAc shift to higher temperatures with increasing DMAAm content.

2. Dissociation of these polymer complexes with treatment of urea indicates that these interpolymer complexes occur via hydrogen bonding. PDMAAm and PAAc form very stable interpolymer complexes because PDMAAm, as a powerful hydrogen-bonding acceptor, efficiently forms complexes with PAAc.

3. IPN hydrogels composed of PDMAAm and PAAc have also been synthesized. These IPNs show limited swelling ratios below their swelling transition temperatures and lower swelling ratios above these transition temperatures. Transition temperatures shift to higher values with increasing DMAAm content.

4. IPN hydrogels incorporating BMA have very reduced swelling. Both hydrogen bonding and hydrophobic interaction provided reversible swollen/shrunken states in response to temperature changes between 20 and 40 °C.

5. Reversible and pulsatile solute release, reflecting the "on" state at higher temperatures and the "off" state at lower temperatures, was achieved by fabricating these IPN hydrogels.

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Author-Supplied Registry No. PDMAAm, 26793-34-0; PAAm, 9003-05-8; poly(DMAAm-*co*-AAm), 30973-80-9; PAAc, 9003-01-4.

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