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ORIGINAL CONTRIBUTION

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Amphiphilic urethane acrylate hydrogels having heterophasic gel structure: swelling behaviors and mechanical properties

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Abstract Amphiphilic urethane acrylate hydrogels containing ionic group (dimethylopropionic acid, DMPA) were prepared by varying the molecular weight of the soft segment (polyether type, PTMG) and type of diisocyanate, and their swelling behaviors and mechanical properties were examined. They showed amphiphilic property due to the hydrophilic ionic groups and hydrophobic polyethers comprising the urethane acrylate network. Heterophasic gel structure could be found for the hydrogels prepared in water, but not for the hydrogels in organic solvent (1,4-dioxane), through scanning electron microscopy. Because of this heterophasic gel structure, they were able to take in a large amount of water as well. The hydrophobic interaction generated by the polyether soft segments between urethane acrylate network chains decreased the degree of swelling, however, increased reversibly the tensile strengths at equilibrium swelling state. MDI-based hydrogel showed low swelling ratio and high tensile strength because of its ordered hard domain structure. These amphiphilic urethane acrylate hydrogels showed salt- and pH-dependent swelling behaviors.

Key words Amphiphilic urethane acrylate hydrogels – ionic groups – polyethers – heterophasic gel structure – hydrophobic interaction – salt- and pH-dependent

Introduction

Hydrophobically modified hydrogels or amphiphilic networks which exhibit a hydrophilic/hydrophobic heterophase structure in aqueous media have attracted much interest in recent years on account of their potential importance and fundamental characteristics [1–6]. Heterophasic gel structure of amphiphilic hydrogels has provided versatile controlled delivery features for hydrophilic, hydrophobic, and amphiphilic agents, enhanced biocompatibility due to hydrophilic/hydrophobic balance, and improved mechanical strength.

In our previous works [7–10], we have studied the preparation of amphiphilic urethane acrylate hydrogel (PEG-modified urethane acrylate (PMUA) hydrogel) by using a peculiar emulsion polymerization technique in which both emulsion polymerization and droplet coalescence occur simultaneously in the course of gelation. As was observed, the PMUA hydrogels could swell in both water and organic solvents. The heterophasic gel structure formed by phase separation of hydrophilic PEG domain from hydrophobic urethane acrylate network played an important role in swelling behaviors and mechanical properties. However, if this kind of urethane acrylate hydrogels, are to be used for applications, it is desirable to find hydrogels having easy production procedure, high swelling ability and mechanical properties. In order to satisfy these requirements while retaining amphiphilic property, we synthesized water-soluble urethane acrylate ionomer by incorporating the ionic group into the urethane acrylate molecular backbone and confirmed its ready dissolution in water [11, 12]. Especially, when hydrogel was prepared with this ionomer, high swelling ability and mechanical property could be expected due to the incorporated ionic group and strong network structure of urethane acrylate [13–15].

The present study focuses on the preparation of amphiphilic urethane acrylate hydrogels containing ionic groups and hydrophobic polyether soft segment in the same network. Swelling behaviors and mechanical properties were studied by varying the molecular weight of the soft segment and the type of diisocyanate.

Experimental

Materials

Isophorone diisocyanate (IPDI, Junsei Chemical Co.), toluene diisocyanate (TDI, 80% 2,4-isomer, Tokyo Chemical Industry Co., Ltd.), and 4,4′-diphenylmethane diisocyanate (MDI, Tokyo Chemical Industry Co., Ltd.) were vacuum distilled before use. Polytetramethylene glycol (PTMG, 1.0×10^3, 1.4×10^3, and 2.0×10^3 g mol^{-1}, Hyosung BASF), dimethylopropionic acid (DMPA, Aldrich Chemical Co.), and 2-hydroxyethylmethacrylate (HEMA, Junsei Chemical Co.) were used as received. Potassium persulfate (KPS, Wako Pure Chemicals Co.) and 2,2-azobisisobutyronitrile (AIBN, Junsei Chemical Co.) were recrystallized from DDI water and absolute ethanol.

Synthesis of urethane acrylate ionomer

The composition for the synthesis of urethane acrylate ionomer is listed in Table 1. The reaction procedure and molecular structure designed are presented in Scheme 1. Here, ID, TD, and MD are IPDI- TDI-, and MDI-based urethane acrylate ionomers, respectively. In the ID series, serial numbers, 1, 2, and 3 correspond to the molecular weight of PTMG, 1.0×10^3, 1.4×10^3, and 2.0×10^3 g mol^{-1}. All reactions were carried out in the 4-necked glass reactor equipped with a stirrer, a reflux condenser, thermocouples, and nitrogen gas inlet system. In the first step, diisocyanate was poured into the glass reactor and nitrogen gas was introduced for 10 min to eliminate the residual moisture. After dissolving 1 wt% of dibutyltindilaurate, DMPA dissolved in DMAc was dropped into the reactor slowly at room temperature. The reaction temperature was raised to 80 °C so that 2 mole of IPDI reacted with the 1 mole of DMPA, resulting in the molecular structure having carboxylic acid group in the middle and isocyanates on end sides. At this stage, care must be taken to control the molar ratio of the reaction, so as not to increase the molecular weight. This temperature was maintained for 4 h to retain an acceptable rate of the reaction. The change of NCO value during the reaction was determined using dibutylamine back titration method to find out the end point of the reaction [16].

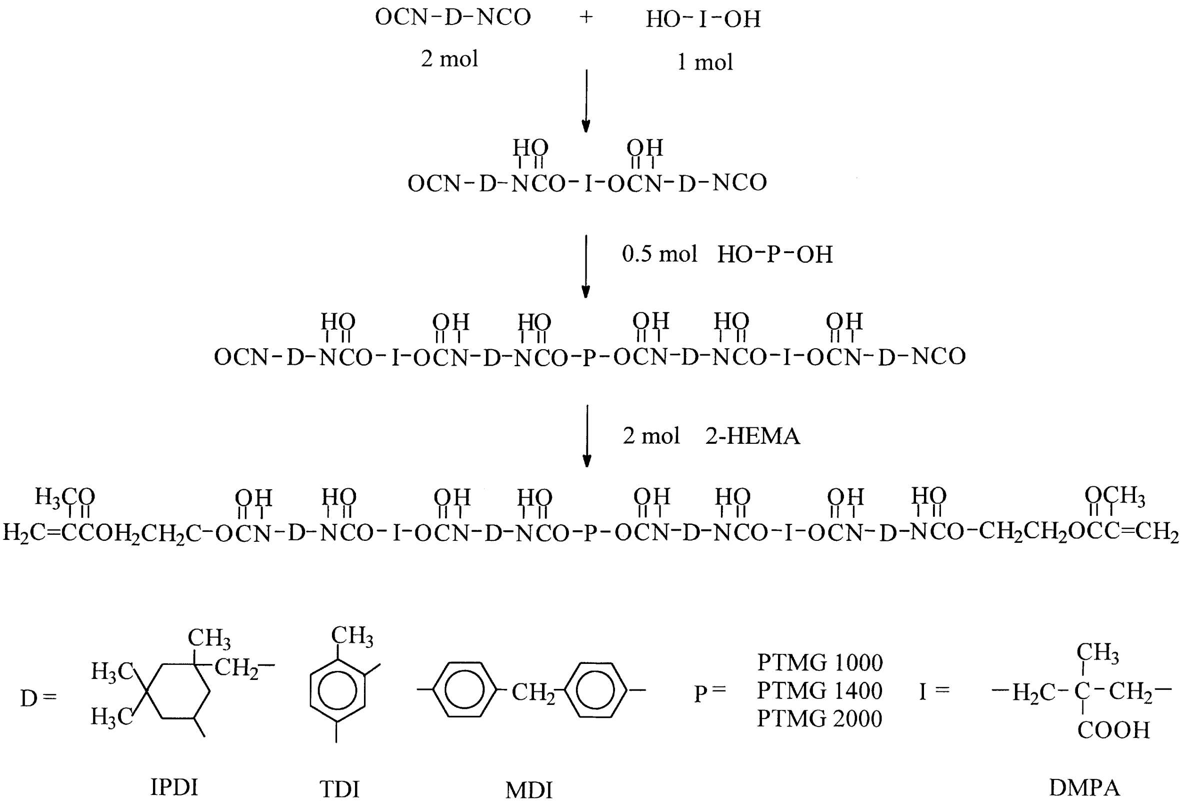
In the second step, 0.5 mole of PTMG was added slowly into the reactor to incorporate the soft segment into the molecular backbone with the same method of the first step. Continuously the reaction was carried out for 4 h at 80 °C. In the last step, after dissolving 1 wt% dibutyltindilaurate into the reactor, 2 mole of HEMA was reacted with the residual NCO group at 45 °C for 12 h, which introduces the reactive vinyl group in the molecular ends. The reaction end point was determined by the disappearance of NCO stretching peak (2270 cm^{-1}) through IR spectroscopy.

To purify DMAc, unreacted 2-HEMA, and DMPA, the reaction mixture was precipitated from the water and filtered several times to give the crude product. The crude product was dried in vacuo. Carboxylic acid group of DUAA was ionized with appropriate amount of triethylamine at room temperature for 1 h. Thus we obtained

Table 1 The composition for the synthesis of urethane acrylate ionomers[a)]

Symbol	IPDI	TDI	MDI	DMPA	PTMG[b)]			HEMA	TEA[c)]
					1.0×10^3	1.4×10^3	2.0×10^3		
ID1	20	—	—	6.03	22.49	—	—	5.85	4.54
ID2	20	—	—	6.03	—	31.49	—	5.85	4.54
ID3	20	—	—	6.03	—	—	44.98	5.85	4.54
TD2	—	20	—	7.70	—	40.19	—	7.47	5.80
MD2	—	—	20	5.36	—	27.97	—	5.20	4.04

[a)] All units are in gram.
[b)] Molecular weight of polytetramethylene glycol (PTMG).
[c)] Triethylamine (TEA) was used as a neutralization agent.



Scheme 1 The reaction procedure and molecular structure of urethane acrylate ionomer

carboxylated urethane acrylate ionomer. The reaction procedure is detailed in our previous works [7–8, 11, 12].

Preparation of urethane acrylate hydrogel

The composition for the preparation of urethane acrylate hydrogels is illustrated in Table 2. Here, HID, HTD, and HMD are hydrogels prepared with ID, TD, MD in water, respectively. SID is the hydrogel prepared with ID in 1,4-dioxane. The mixtures of ionomer and solvent (dioxane or water) including KPS or AIBN were transferred into a mold (10 cm × 15 cm × 0.2 cm) to carry out gelation. Then gelation was performed at 60 °C for 24 h. After the gelation was completed, all samples were fully washed with a large amount of DDI water and methanol. Hydrogels prepared were frozen at −70 °C for 24 h and dried in vacuo. Hydrogels prepared were cut into suitable length for swelling ratio and tensile strength measurements.

Measurements

Molecular weight distributions were measured by a model 410 GPC equipped with Styragel HR 1–4 columns from Waters Associates at 25 °C. The flow rate of the carrier solvent, THF, was 0.5 ml/min. The average molecular weights calculated on the basis of the molecular weight versus retention volume curve of monodisperse polystyrene standards were $M_w = 5.4 \times 10^3$–7.1×10^3 g mol^{-1} and $M_n = 8.3 \times 10^3$–1.4×10^4 g mol^{-1}, respectively.

Equilibrium swelling ratio was determined using conventional gravimetric method as follows:

$$\text{Swelling ratio} = \frac{W_s - W_d}{W_d} ,$$

where W_s is the weight of the sample swollen by solvent and W_d the weight of the dried sample. All swelling ratio measurements were performed in DDI water or benzene at 25 °C.

The fracture surface of hydrogels was examined with scanning electron microscopy (SEM, Philips C. KL-30).

After swelling the dumbbell type specimen, tensile strength was measured in the equilibrium swelling state at 25 °C using Hounsfield Model Instron, Serial No. R100 1231. Crosshead speed was 1 mm/min. Obtained tensile strength was calibrated according to the thickness and width of the swollen specimen. All samples were measured five times and the averages were obtained.

Table 2 Gelation recipe of urethane acrylate hydrogels[a)]

Symbol	Resin	DDI water	Dioxane	KPS	AIBN
HID1	7	21	—	0.21	—
HID2	7	21	—	0.21	—
HID3[b)]	7	21	—	0.21	—
HTD2	7	21	—	0.21	—
HMD2	7	21	—	0.21	—
SID1[c)]	7	—	21	—	0.21

[a)] 60 °C; 24 h All units are in gram.
[b)] HID3 was the dispersed state in water (droplet size: about 30 nm) before gelation.
[c)] SID1 gel was prepared to observe the SEM photograph.

Results and discussion

Urethane acrylate ionomer has a peculiar molecular structure, as shown in Scheme 1. It has two vinyl groups crosslinked to each other at both ends and two ionic groups (carboxylate ions) to hydrate in the molecular backbone. In addition, it also has a long polyether soft segment showing hydrophobicity in the middle of the molecule. Therefore, hydrogels prepared with this urethane acrylate ionomer can be expected to show amphiphilic property due to hydrophilic groups and hydrophobic polyether soft segments and heterophasic gel structure formed by ionic aggregates.

Amphiphilic property of urethane acrylate hydrogel

Figures 1 and 2 show the swelling ratios of HID gels as a function of time in water and benzene, respectively. Equilibrium swelling ratios were reached in about 6 h for all samples. Degree of the swelling ratio changed with the network composition. Comparing the equilibrium swelling ratios of these HID gels to those of PEG-modified urethane acrylate (PMUA) hydrogels [8, 9], we can easily find that the equilibrium swelling ratios were enhanced considerably by introducing ionic groups into the urethane acrylate network (the maximum equilibrium swelling ratio of PMUA hydrogel was in the order of 0.7).

Equilibrium swelling ratios of HID gels in water and benzene are summarized in Fig. 3. As the data indicate, HID gels swelled in both solvents, shows that they have amphiphilic property. However, for HID gels of low molecular weight of soft segment, the degree of swelling was dominated by hydrophilic property. This result was assumed to be attributed to the higher charge density of the gel network. HID gel of lower molecular weight of soft segment has relatively smaller phase volume of hydrophobic soft segment (ID1, ID2, and ID3 resins contain 10.24, 8.88, and 7.41 wt% of DMPA, respectively). For HID gels of higher molecular weight of soft segment, the degree of swelling was dominated by hydrophobic property. Under similar assumptions as above this result also can be explained; lower charge density of gel network and higher phase volume of hydrophobic soft segment.

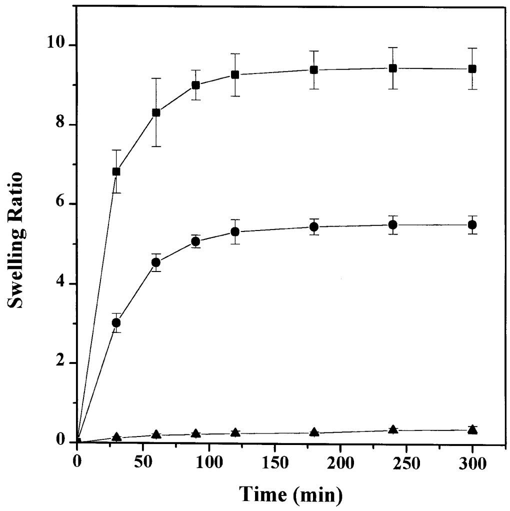


Fig. 1 The swelling ratios of HID1 gel (-■-), HID2 gel (-●-), and HID3 gel (-▲-) as a function of time in DDI water at 25 °C

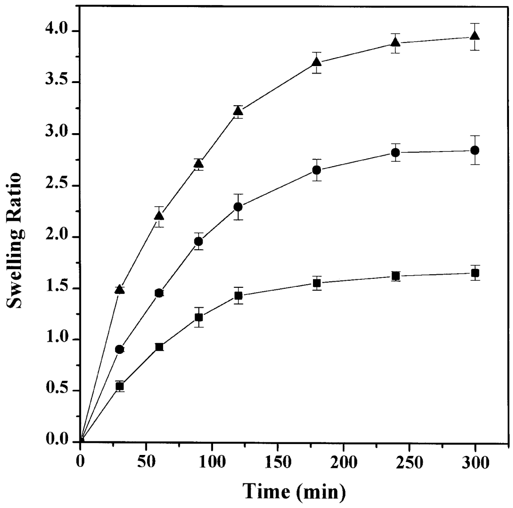


Fig. 2 The swelling ratios of HID1 gel (-■-), HID2 gel (-●-), and HID3 gel (-▲-) as a function of time in benzene at 25 °C

Heterophasic gel structure of urethane acrylate hydrogel

Figure 4 shows SEM photographs of the fracture surface of HID1 gel (a) and SID1 gel (b). For HID1 gel, we could

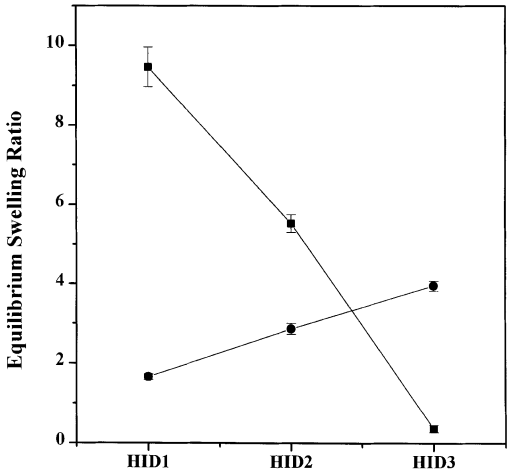


Fig. 3 Equilibrium swelling ratios of HID gels in DDI water (-■-), and benzene (-●-) at 25 °C

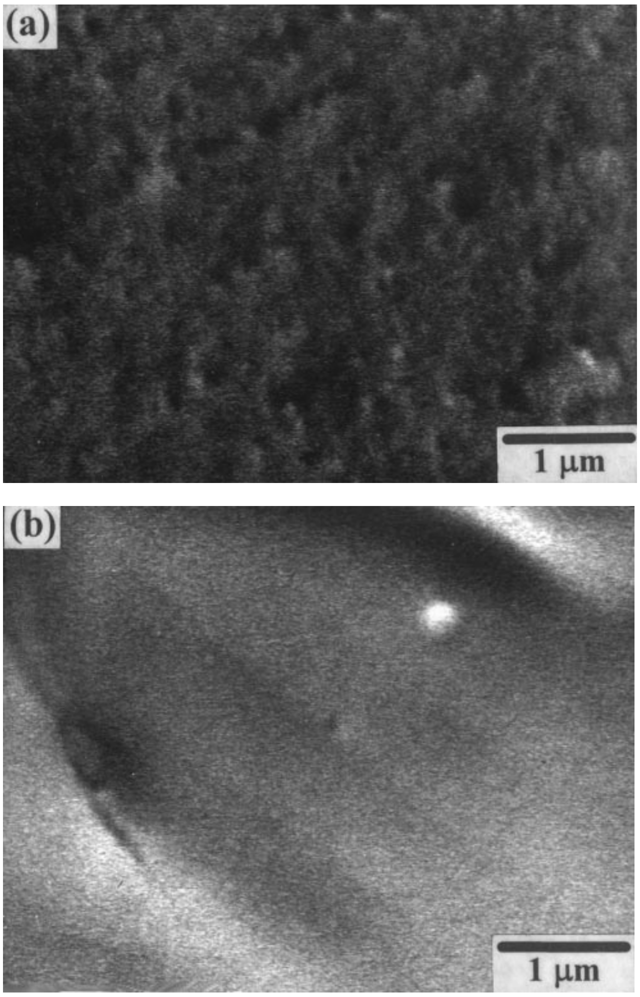


Fig. 4 Scanning electron microscopy (SEM) photographs of HID1 gel (a) and SID1 gel (b)

observe ionic pores separated from the urethane acrylate network. However, SID1 gel did not show any phase separation. This observation of SEM photographs clarifies that hydrogel prepared in water has heterophasic gel structure. Because of the presence of these ionic pores, HID gels seemed to show high swelling ratios.

Based on our previous work [8], we postulated the following procedure related to ionic pore formation; when the gelation is performed in dioxane, the ionic groups distribute randomly in the urethane acrylate network. On the contrary, when the gelation is carried out in water, the ionic groups are hydrated with water while hydrophobic segments aggregate together, which makes it possible to form the ionic domain.

Effect of kind of diisocyanate on the swelling behavior

In order to observe the effect of the kind of diisocyanate on the swelling behavior, equilibrium swelling ratios of HID2, HTD2, and HMD2 gels having the same molecular weight as the soft segment were measured and shown in Fig. 5. The equilibrium swelling ratio showed the following order: HID2 > HTD2 > HMD2. Especially, HTD2 and HMD2 gels showed significantly lower swelling ratio than the HID2 gel. This result can be explained as a consequence of the presence of aromatic ring which gives rise to π-electron interaction in the urethane acrylate network [17]. So we believed that HTD2 and HMD2 gels having aromatic rings could not swell with ease because of this π-electron interaction. Moreover, HMD2 gel showed a lower swelling ratio than HTD2 gel. As Chen et al. said in their works [18, 19], MDI-based urethane ionomers have an ordered

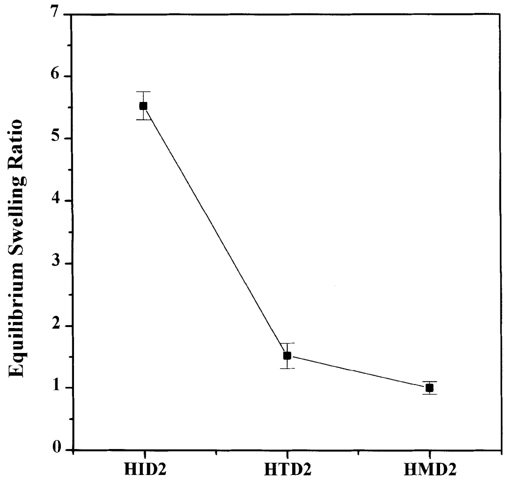


Fig. 5 Equilibrium swelling ratios of HID, HTD, and HMD gels in DDI water at 25 °C

hard domain, because of their symmetric molecular structure, while TDI-based urethane ionomers have a disordered hard domain, because TDI has asymmetric 2,4-isomers. With the above explanation, it can be said that HMD gel cannot take in a large amount of water because of its ordered hard domain. On the other hand, HTD gel having a disordered hard domain can take in water with ease, compared with the HMD gel.

Swelling behavior of urethane acrylate hydrogels with ionic strength and pH

Figure 6 shows the equilibrium swelling ratios of HID gels in a salt solution of NaCl. The swelling ratio increased with the decrease of molecular weight of the soft segment and salt concentration. The swelling curves converged together. These results were attributed to the dependence of the electrostatic repulsion between charged groups on the network chains and to the concentration difference of mobile ions and the external solution [20, 21]. However, differing from other ionic gel networks, equilibrium swelling ratios of HID gels of carboxylate salt were significantly influenced by ionic strength, which is an inherent feature of carboxylate salt in inorganic salt solution [4, 9].

Figure 7 shows the swelling ratios of HID gels as a function of pH. Equilibrium swelling ratios of HID gels increased with the increase of pH, because HID gels contained anionic groups in the network. However, the sensitivity to pH depended on the molecular weight of the soft segment; the swelling ratios of HID1 and HID2 gels increased dramatically between pH5 and pH9, while HID3 gel displayed a slight sensitivity. This can also be explained in terms of the hydrophobic interaction of the polyether soft segment. Hydrophobic interaction of HID gels increases with the increase of molecular weight of the polyether soft segment. So the pH sensitivity of HID gels depended on the molecular weight of the soft segment.

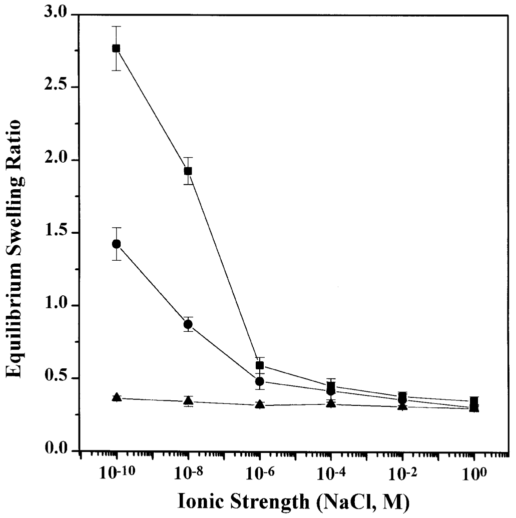


Fig. 6 Equilibrium swelling ratios of HID1 gel (-■-), HID2 gel (-●-), and HID3 gel (-▲-) with the ionic strength (NaCl, M) at 25 °C

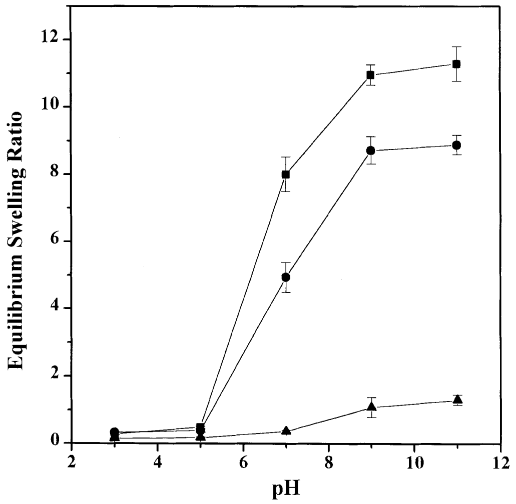


Fig. 7 Equilibrium swelling ratios of HID1 gel (-■-), HID2 gel (-●-), and HID3 gel (-▲-) with the pH at 25 °C

Mechanical property of urethane acrylate hydrogels

The tensile strengths of HID, HTD and HMD gels at the equilibrium swelling state in water were measured and listed in Table 3. For HID gels, tensile strength increased as the molecular weight of the soft segment increased (the reversed trend of the swelling ratio with the molecular weight of soft segment). The tensile strengths of hydrogels having different kinds of diisocyanate at the equilibrium swelling state increased in the following order: HID2 < HTD2 < HMD2. This also can be explained on the basis

Table 3 Tensile strengths of urethane acrylate hydrogels in equilibrium swelling state[a]

Symbol	Tensile strength [Kgf cm^{-2}]	SD[b]	Symbol	Tensile strength [Kgf cm^{-2}]	SD
HID1	0.34	0.21	HID2	1.58	0.30
HID2	1.58	0.30	HTD2	2.77	0.51
HID3	4.18	0.16	HMD2	9.07	1.23

[a] Tensile strength was tested after swelling in water for 6 h at 25 °C.
[b] SD: Standard deviation obtained after five times measurements.

of molecular structure, just as shown in the effect of diisocyanate on the swelling ratio.

In the observation of tensile strengths, it is notable that tensile strengths of these hydrogels in equilibrium swelling state were considerably high. This seemed to be resulting from the strong network structure of urethane acrylate. Hydrogen bond of urethane linkage and hydrophobic interaction of hydrophobic polyether soft segment can contribute to the strong network structure formation between chains [13–15].

Conclusion

Amphiphilic urethane acrylate hydrogels containing an ionic group showed amphiphilic property due to hydrophilic ionic groups and hydrophobic polyethers comprising the urethane acrylate network. Heterophasic gel structure of hydrogels prepared in water improved the swelling ratio. Especially, the molecular weight of the hydrophobic soft segment had an effect on the swelling ratio and mechanical property because of its hydrophobic interaction. Type of diisocyanate determined the hard domain structure of urethane acrylate network. In particular, because of the pH-dependent swelling behavior of these hydrogels, the application to pH-sensitive hydrogel could be considered in further study. Considering swelling behaviors and mechanical properties for hydrogels prepared in this study, we could recommend HID2 gel as the best.

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