N-isoproylacrylamide 와 sulfadimethoxine monomer 로 이루어진 pH 및 온도 동시민감성 수화겔

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pH / Temperature bifunctional sensitive hydrogels composed of N-isopropylacrylamide and sulfadimethoxine monomer

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Intoduction

Hydrogels sensitive to electric field[Osada et al.,1992], light or UV[Suzuki et al.,1990], pH[Allcock et al.,1996;Siegel et al.,1988], ions and temperature[Boyer et al.,1985;Gutowska et al.,1994] are being studied for applications in engineering systems such as mass seperation[Cussler et al.,1984] and chemical valves[Osada,1987] as well as biomedical applications including artificial organs and drug delivery systems. In paticular, most of the study has been centered on the pH and temperature effects due to the importance of variable in chemical, physiological and biological systems[Chen et al.,1995;].

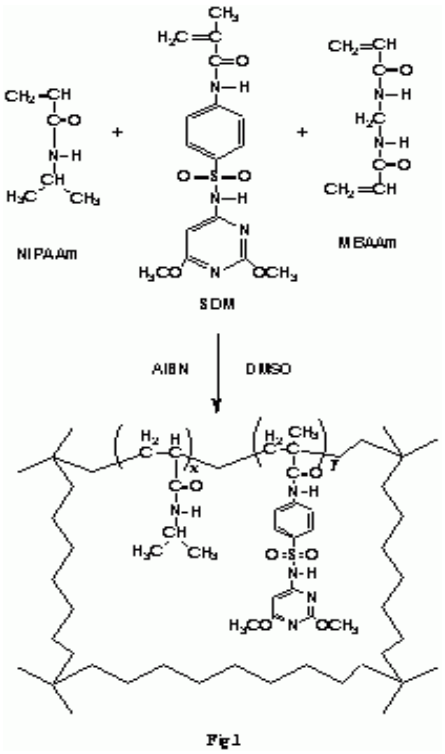

Fig 1

The aim of this study was to develop a new kind of hydrogels able to respond to both pH and temperature simultaneously. The hydrogels incorporate two kinds of monomers (N-isopropylacrylamide (NiPAAm), sulfadimethoxine monomer (SDM)), each having a different role ; Ionizable component of SDM is able to ionize or deionize according to pH changes, and NiPAAm component allows the gel to swell or shrink reversibly in response to temperature changes. The pH or temperature dependent swelling behavior of the hydrogels in buffer solution was investigated in detail.

Theory / Experiment

Sulfadimethoxine (SD) (10mmol) and sodium hydroxide (10mmol) were dissolved in aqueous acetone (40ml, 1:1 v/v). And then, methacryloyl chloride (10mmol) was dropped into the

solution under stirring at 10 °C. The precipitated product was filtrated and dried under vacuum at room temperature for 48 hours. SDM was purified by recrystallization in methanol and washing with distilled water several times.

Using that SDM and NiPAAm, hydrogels were synthesized by radical polymerization as shown in Fig.1. The two monomers (NiPAAm and SDM), AIBN (0.2mol% to tatal monomer moles), and MBAAm(1.5mol% to total monomer moles) were dissolved in DMSO (50%w/v to total solute). The mixture was bubbled with dried nitrogen gas for 30 minutes and then injected into between glass plate having 3 mm thick rubber spacer. The mold was sealed and placed in a dry oven at 70 °C for 20hrs. After polymerization, the hydrogel sheets were separated from the glass plates and punched into 1cm diameter circular disks for swelling measurements. All disks were washed in ethanol for 1hour and then soaked in aqueous sodium hydroxide solution (1M) for 3days to remove all unreacted compounds. Then, the disks were soaked in an aqueous hydrogen chloride solution (1M) for one day to neutralize them and washed several times with distilled water. Continuously, the disks were dried under air for 1days and then dried under vacuum at 40 °C for 2days. Dried disks were immersed and equilibrated in buffer solution of various pHs and temperatures for 3 days. Each sample was taken from its respective buffer solution, wiped with a towel to remove excess water on surface of the disks, and weighed directly. The swelling ratio was calculated by $(W_s-W_d)/W_d$, where W_s and W_d are the weights of the swollen gel and dried gel, respectively.

The hydrogels with different compositons were prepared with varying NiPAAm/SDM ratio, as shown in Table 1.

Table 1. The composition of hydrogels composed of NiPAAm and SDM.

Monomers / Sample name	Feed ratio of monomers	
	NiPAAm	SDM
G-1	100 mol %	0 mol %
G-2	95 mol %	5 mol %
G-3	90 mol %	10 mol %
G-4	85 mol %	15 mol %
G-5	70 mol %	30 mol %

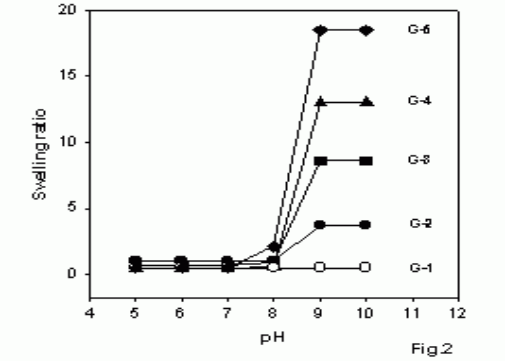

Fig.2

Results and Discussion

The pH-dependent equilibrium swelling of a series of hydrogels (G-1~G-5) at 37 °C was shown in Fig.2. G-1 exhibited no swelling at any pH ranges due to the lower crytical solution temperature (LCST) property of NiPAAm, as reported in previous papers[Park et al.,1994;Schild,1992]. Poly(N-isoproylacrylamide) hydrogel is one of the typical gels with a negative temperature-

sensitivity. So, below the LCST, the hydrogel swells in the aqueous medium. The chains are extended and surrounded by water molecules. Above the LCST, that hydrogel deswells because of phase separation between polymer chains and water molecules.

But the pH-dependent swelling of other hydrogels (G-2 ~ G-5) is mainly attributed to the degree of ionization of SDM. The hydrogels (G-2 ~ G-5) didn't take place swelling behaviors at low pH (from pH 4 to pH 8) due to the LCST property of NiPAAm and interactions between SDM residues in the networks while their swelling levels at higher pH (pH>8) were remarkably elevated. It is reason that the H of ^{1}N(sulfonamide) become deprotonated at high pH because of the strong electronegativity of the oxygen atoms of the sulfonyl group. So the charge density of the network increases and the mobile counterion content in the network increases[Bell et al.,1942]. Thus the internal osmotic pressure increases and the swelling ratio increases. Accordingly, the swelling ratio of the hydrogels increased at high pH (pH > 8), as the contents of SDM increased. (G-2 < G-3 < G-4 < G-5)

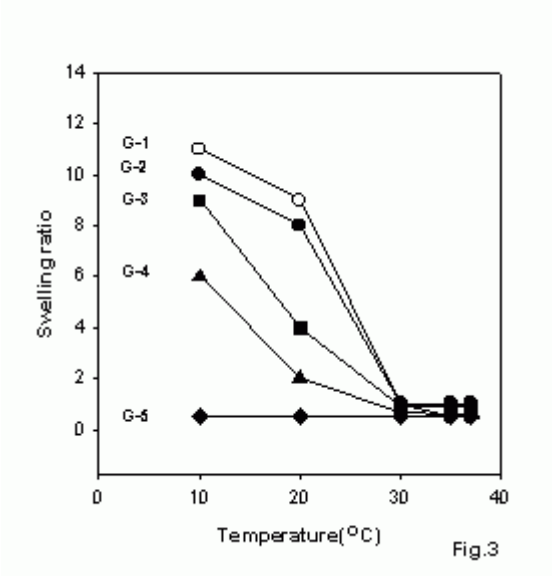

Fig.3

Fig.2 also indicates all hydrogels(G-1~G-5) show little change at 37 °C with the pH change from 4 to 8. However, some hydrogels (G-1 ~ G-4) showed swelling behaviors at pH 8 as temperature decreased, as shown in Fig.3. This is due to the LCST property of NiPAAm which can swell at low temperature. As pointed out in above, hydrogels containing NiPAAm swell in the aqueous medium below the LCST (about 32 °C) because the chains are extended and surrounded by water molecules.

Also, in Fig.3, as the content of SDM increased, equilibrium swelling ratio of hydrogel became lower (G-1 > G-2 > G-3 > G-4 > G-5). It is due to hydrophobic interaction of SDM on hydrogel. The units of deionized sulfadimethoxine on the hydrogel are hydrophobic[Narula et al.,1987;Yang et al.,1972]. The interaction of the hydrophobic part induces deswelling behavior of the hydrogels at lower pH region. As the contents of SDM increase, hydrophobic interaction of SDM on hydrogel become stronger and consequently the hydrogel swells less. G-5 didn't take place a swelling behavior in 10 °C buffer solutions because of the very strong hydrophobic interation of SDM.

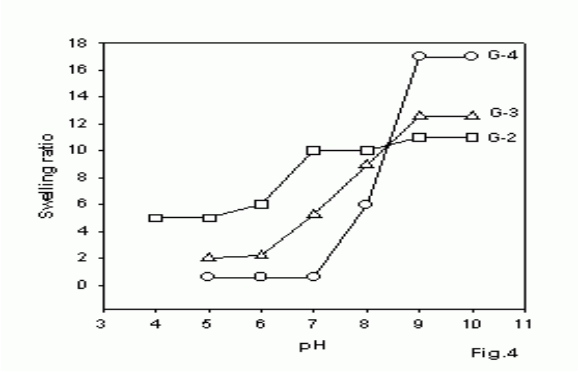

Fig.4

For better understanding of the swelling behavior of the hydrogels and associated interactions in the hydrogels, the effects of temperature on pH-dependent equilibrium swelling were studied in detail. Fig. 4 shows the pH-dependent equilibrium swelling of G-2 ~ G-4 at 10°C. When the temperature decreased, curve of pH-dependent equilibrium swelling was shifted toward the

upper-left. It is due to the LCST property of NiPAAm which can swell at low temperature in addition to ionization property of SDM able to ionize in higher pH as mentioned in previous part. As the contents of SDM decreased, the LCST property of NiPAAm appeared strongly. G-2 and G-3 showed the swelling behaviors of hydrogels occurred even in region of low pH in Fig.4. It is reason that the power of NiPAAm to swell at low temperature is stronger than the interaction of SDM residues in low pH regions. Compared with Fig.2, that showed the property of NiPAAm able to swell below LCST in addition to the ionization property of SDM very well. Finally, appropriate compositon of NiPAAm and SDM is necessary to synthesize hydrogels able to respond to both pH and temperature, simultaneously.

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