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친수성 Poly(HEMA) 수화겔내 물 양성자의 NMR 이완

成 鏞 吉
동국대학교 이과대학 화학과
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NMR Relaxation of Water Protons in Hydrophilic Poly(HEMA) Hydrogels

Yong Kiel Sung
Department of Chemistry, Dongguk University, Seoul 100-715, Korea
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요 약. 2-Hydroxyethyl methacrylate(HEMA)와 ethylene glycol dimethacrylate(EGDMA)로부터 수용액 중에서 친수성 3차원 메타아크릴레이트 고분자 망상의 수화겔을 제조하여 NMR 분석법에 의해 그 친수성 메타아크릴레이트와 물 사이의 상호작용에 대하여 연구하였다. 적은 양의 물을 함유하고 있는 수화겔의 스핀-격자 이완시간(T_1)을 측정한 결과 물 양성자 주위의 다른 두 환경에 따른 T_{1a}와 T_{2b}가 나타났다. Poly(2-hydroxyethyl methacrylate)[p(HEMA)]-(10% H_2O) 수화겔에 대한 T_{1a}와 T_{1b}가 각각 16.4×10^{-3} sec와 58.2×10^{-3} sec이고, 가교된 EGDMA-p(HEMA)-(10% H_2O) 수화겔에 대한 T_{1a}와 T_{2b}가 각각 13.2×10^{-3} sec와 23.1×10^{-3} sec이었다. 또한 수화겔들에 대해 스핀-스핀 이완시간(T_2)를 측정한 결과 p(HEMA)-$(H_2O)_n$ 및 가교된 EDGMA-p(HEMA)-$(H_2O)_n$의 계에 T_2값은 물 함량이 증가함에 따라 증가하였다. T_2값들은 T_1의 값들보다 약 10배 작게 나타나고 스핀이완원리와 일치하였다.

ABSTRACT. The hydrogels of hydrophilic three-dimensional methacrylate polymer networks were prepared from 2-hydroxyethyl methacrylate (HEMA) and ethylene glycol dimethacrylate (EDGMA) in aqueous solution. The interaction of water with the hydrophilic methacrylate polymers in the hydrogels was studied by pulse NMR spectroscopy. The spin-lattice relaxation times (T_1) of low water content hydrogels showed the different double environments, resulting in two spin-lattice relaxation times (T_{1a} and T_1b). The values of T_{1a} and T_{1b} were 16.4×10^{-3} sec and 58.2×10^{-3} sec for a p(HEMA)-(10% H_2O) system, and 13.2×10^{-3} sec and 23.1×10^{-3} sec for a crosslinked EGDMA-p(HEMA)-(10% H_2O) system, respectively. The spin-spin relaxation times (T_2) of the hydrogels were also measured as a function of water content in the p(HEMA)-$(H_2O)_n$ and crosslinked EGDMA-p(HEMA)-$(H_2O)_n$ system. The values of T_2 were approximately 10 times less than those of T_1 in agreement with the principles of spin relaxations.

INTRODUCTION

Synthetic hydrogels obtained from hydrophilic methacrylate polymers are water-swollen networks of macromolecules. Three-dimensional networks of hydrophilic methacrylate polymers can be prepared by several methods.[1,2] Poly(2-hydroxyethyl methacrylate) [p(HEMA)] is one of the hydrophilic methacrylate polymers which are prepared for biomedical applications.[3,4] Biomedical studies and applications utilizing p(HEMA) hydrogels are numerous.[5-11] These include surgical suture materials,[9] burn dressings,[6] antibiotic catheter coatings,[10] hemodialysis,[7] artificial membranes,[11] and soft contact lenses.[8] Some investigators have produced hydro-

gel surfaces on conventional polymer substrates by surface coating.[12,13] The interaction between water and the hydrophilic methacrylate polymer is an important factor for the biomedical purposes. The possible role of water in biocompatibility has been discussed in terms of the minimum interfacial free energy concept.[14] There has been some speculation on the possible correlation between the water content of a hydrogel and its biotolerability.[15]

Using the three-state model,[16] we have determined the amounts of bound water, intermediate water, and bulklike (free) water in the hydrophilic methacrylate hydrogels by differential scanning calorimetry.[17,18]

In this work, nuclear magnetic resonance spectroscopy is used to measure the spin-lattice relaxation times (T_1) and spin-spin relaxation times (T_2) of the water protons in the hydrophilic *p*(HEMA)-(H_2O) hydrogel and crosslinked ethyleneglycoldimethacrylate(EGDMA)-*p*(HEMA)-(H_2O) hydrogel systems. The water structure ordering in the hydrogels are also discussed in terms of T_1 and T_2 values on the basis of the differential scanning calorimetric results.[17,18]

EXPERIMENTAL SECTION

Preparation of NMR Samples. The poly(2-hydroxyethyl methacrylate) hydrogel samples were prepared by thermal initiation of 2-hydroxyethyl methacrylate (HEMA) monomer with 7.84×10^{-3} mole azobis(methyl isobutyrate) as an initiator and 1 mole% crosslinking agent such as EGDMA. The HEMA solution, containing the initiator and the crosslinker, was dissolved in the desired amount of triple distilled water (conductivity$=1.14\times10^{-6}$ /$\Omega\cdot$cm). The HEMA used was supplied by Hydro Med Sciences Inc.; impurities were 0.2% methacrylic acid, 0.16% diethyleneglycolmethacrylate, and 0.01% ethyleneglycoldimethacrylate.

The samples were placed in NMR tubes and sealed after N_2 bubbling and freeze-pump-thaw techniques,[19,20] The samples were polymerized at 60 ℃ for 24 hours and allowed to stand about two months at room temperature.

Measurements of T_1 and T_2. The spin-lattice and spin-spin relaxation times were measured by utilizing Varian XLFT-100 pulsed NMR spectrometer operating at a magnetic field of 23,490 gauss and an rf frequency of 100 MHz for proton resonance. The XL-100 NMR was designated to operate in a frequency-sweep mode. Long-term stability was attained by locking to a resonance line in the spectrum, or to the deuterium resonance of a deuteriated solvent added to the sample. In this system, the magnetic field strength was held constant and the transmitter frequency was swept. Using a π-τ-$\pi/2$ pulse sequence,[21,22] the spin-lattice (longitudinal) relaxation time (T_1) was measured by following the return of magnetization to its equilibrium value after it had been purturbed by an radio frequency field at the resonance frequency. The relaxation delay time is a measure of the time of fluctuations of the local environment. The data of T_1 were determined from the slopes of the semilog plots. The spin-spin (transverse) relaxation times (T_2) were also measured from the width of half maximum absorption following the pulse sequence.[22,23] The temperatures of the samples were controlled at 34± 1 ℃ during the measurements.

RESULTS AND DISCUSSION

The proton NMR spectra obtained from pure water and from the hydrophilic methacrylate of 40% H_2O-*p*(HEMA)-1 mole% EGDMA crosslinked hydrogel are shown in *Fig.* 1. The proton NMR spectrum of pure water shows a narrow and high peak, while the proton NMR spectrum of the water in the hydrogel system shows a broadened peak of decreased height. These results indicate that the water proton environment in the hydrogel is much different from that in the pure water. Similar observations were obtained for hydrated proteins[24,25] and for the water in sintered glass.[26] It had been observed that the spin-lattice relaxation time (T_1) of ice is 0.829 sec at −16.40 ℃.[27]

The spin-lattice relaxation times of low water content hydrogels clearly demonstrate the existence of two distinct phases, as shown in *Fig.* 2 for 10% H_2O-*p*(HEMA) hydrogel and *Fig.* 3 for 10%

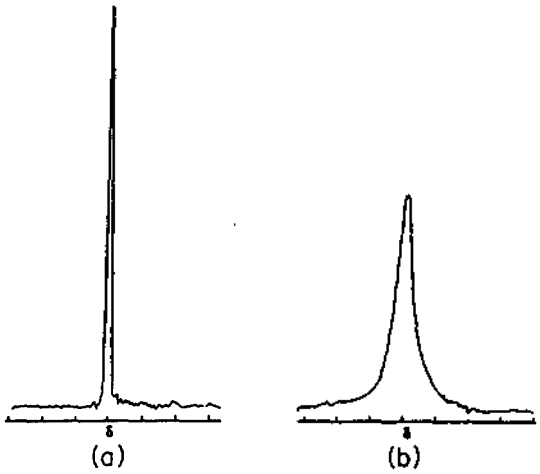

Fig. 1. The NMR spectra of water in pure state (a) and in 40% H_2O-*p*(HEMA)-1 mole% EGDMA crosslinked hydrogel (b) at 34 ℃ and 100 MHz.

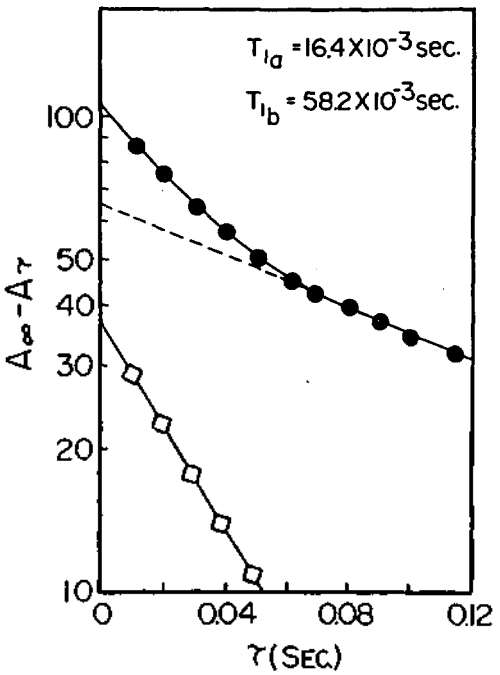

Fig. 2. Spin-lattice relaxation times for water protons in low water content (10% H_2O)-*p*(HEMA) hydrogel at 34 ℃ and 100 MHz illustrating two-phase behavior.

H_2O-*p*(HEMA)-1 mole% EGDMA crosslinked hydrogel. These results show that there are two independent relaxation times such as T_{1a} and T_{1b}.

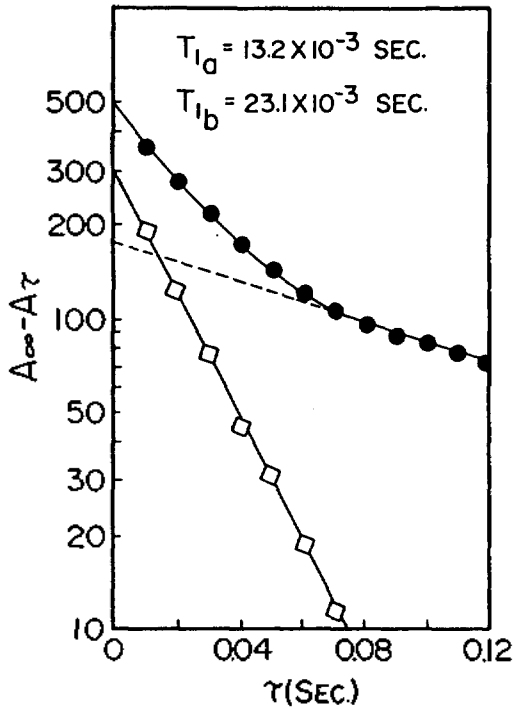

Fig. 3. Spin-lattice relaxation times for water protons in low water content (10% H_2O)-*p*(HEMA)-1 mole% EGDMA crosslinked hydrogel at 34 ℃ and 100 MHz illustrating two-phase behavior.

It has been defined that T_{1a} is the spin-lattice relaxation time for strongly bound water in the hydrophilic methacrylate hydrogel and T_1b is the spin-lattice relaxation time for weakly bound water in the same hydrogel.

The longitudinal moment decay expression in this case can be obtained directly from equation (1).[28]

$$M(\tau)=M_o(\tau)[P_a \exp(-\tau/T_{1a})+P_b \exp(-\tau/T_{1b})] \quad (1)$$

where $M_o(\tau)$ is the equilibrium nuclear magnetization, P_a and P_b are the apparent fractional state populations, and τ is the correlation time. The corresponding signal amplitudes observed are given by equation (2).[29]

$$A(\tau)=\sum_{i=1}^{n} A_o(\tau) \exp(-\tau/T_{ij}) \quad (2)$$

where j is a or b in the state, $A_o(\tau)$ is an exponential amplitude which is directly proportional to the

quantity $M_o(\tau)P_i$.

The plots of $\ln(A_\infty - A_\tau)$ versus τ obtained in this study are shown in *Fig.* 2 for a *p*(HEMA)-(10 % H_2O) hydrogel system at 34 ℃ and 100 MHz. T_{1a} was obtained from the slope of the second plot of the difference between the extrapolated values and the measured values. T_{1b} was also obtained from the slope of the plot of the experimental signal intensities. In the case of *p*(HEMA)-(10% H_2O) system, T_{1a} and T_{1b} were evaluated to be 16.4×10^{-3} sec and 58.2×10^{-3} sec, respectively.

The plots of $\ln(A_\infty - A_\tau)$ versus τ are also shown in *Fig.* 3 for a crosslinked EGDMA-*p*(HEMA)-(10 % H_2O) system at 34 ℃ and 100 MHz. From the slope of the plots, T_{1a} and T_{1b} were evaluated to be 13.2×10^{-3} sec and 23.1×10^{-3} sec, respectively. These data indicate that there are different kinds of spin-lattice relaxations in the hydrophilic methacrylate hydrogels. The data suggest that there are two kinds of bound water, *i.e.* strongly bound water and weakly bound water. T_{1a} of strongly bound water may be due to the primary hydrogen bonding water on the polar sites. T_{1b} of weakly bound water may be due to the secondary or tertiary water in the hydrophilic methacrylate hydrogels.

Comparing the *p*(HEMA)-(10% H_2O) hydrogel systems with the crosslinked EGDMA-*p*(HEMA)-(10% H_2O) hydrogel systems in the spin-lattice relaxation times, the different crosslinking effect was observed. T_{1a} and T_{1b} for the hydrophilic crosslinked EGDMA-*p*(HEMA)-(10% H_2O) system are shorter than those for the hydrophilic *p*(HEMA)-(10% H_2O) system. This trend is in line with the trend of effective surface area, *i.e.*, accessible hydrophilic surface area.[18] The spin-lattice relaxation times of bound water protons in *p*(HEMA) hydrogel systems are much shorter than the spin-lattice relaxation time (0.829 sec) of bound water protons in ice at −16.40 ℃.[27] This suggests that the interaction between the bound water molecules and the gel networks are stronger than that between the bound water molecules in ice structures. Similar results had been found for cell-water systems.[30,31] The single state spin-lattice relaxation times (T_1) of high water content hydrogels were determined. *Table* 1 represents the T_1 data as a function of water content in *p*(HEMA)-(H_2O) hydrogel and crosslinked EGDMA-*p*(HEMA)-(H_2O) hydrogel systems at 34 ℃ and 100 MHz. Comparing the data with the measured spin-lattice relaxation time of pure water protons (4.5 sec at 34 ℃), the average T_1 values of water protons in the hydrogels are greatly reduced. These results indicate that there are considerable interactions between the water molecules and the polymer networks in the hydrogel systems. The short T_1 of water protons in the hydrogel suggests that the water in the hydrogel is less mobile than in pure water. This can be interpreted in terms of the structure ordering of water molecules in the hydrogel networks. The most probable binding positions of water molecules are the polar sites, such as the hydroxyl and carbonyl groups in the methacrylate polymers.

Table 1. Proton NMR spin-lattice relaxation times for hydrogels based on *p*(HEMA) of different total water content at 100 MHz and 34 ℃ (unit: sec)

Wt% of total water content in the hydrogel	*p*(HEMA)-(H_2O)		*p*(HEMA)-1 mole% EGDMA-(H_2O)	
	T_1	T_U	T_1	T_U
25	0.189	0.272	0.186	0.215
30	0.214	0.298	0.198	0.274
35	0.260	0.311	0.220	0.297
40	0.300	0.337	0.259	0.303
45	0.340	0.336	0.296	0.303

T_{1F}/4.5 sec at 34 ℃; T_{1B}=0.169 sec for 18% bound H_2O-*p*(HEMA); T_{1B}=0.176 sec for 20.6% bound H_2O-*p*(HEMA)-crosslinked EGDMA.

The effect of a crosslinking agent, such as EDGMA, produces rather slight changes in T_1 values, though the hydrophilic tendency can be seen. The results are in good agreement with the bound water quantities obtained from the DSC experiments.[17,18] The measured values of the proton spin-lattice relaxation times, T_1, can be considered as an average of three states of water in the hydrogels, as shown in the following equation (3).[16-18]

Table 2. Determination of maximum bound water, intermediate water, and free water in *p*(HEMA) hydrogels containing different water content

Wt% of total water in hydrogels	18.0	20.0	25.0	30.0	35.0	40.0	45.0
Total water/Polymer (gm/gm)	0.22	0.25	0.33	0.43	0.54	0.67	0.82
Bound water/Polymer (f_B)	0.22	0.22	0.22	0.22	0.22	0.22	0.22
Intermediate water/Polymer (f_I)	0	0.03	0.11	0.16	0.16	0.16	0.16
Free water/Polymer (f_F)	0	0	0	0.05	0.16	0.29	0.44

Table 3. Determination of maximum bound water, intermediate water, and free water in 1 mole% crosslinked EGDMA-*p*(HEMA) hydrogels containing different water content

Wt% of total water in hydrogels	20.6	25.0	30.0	35.0	40.0	45.0
Total water/Polymer (gm/gm)	0.26	0.33	0.43	0.54	0.67	0.82
Bound water/Polymer (f_B)	0.26	0.26	0.26	0.26	0.26	0.26
Intermediate water/Polymer (f_I)	0	0.07	0.17	0.21	0.21	0.21
Free water/Polymer (f_F)	0	0	0	0.07	0.20	0.35

$$\frac{1}{T_1} = \frac{f_B}{T_{1B}} + \frac{f_I}{T_{1I}} + \frac{f_F}{T_{1F}} \quad (3)$$

where f_B, f_I, and f_F are the fractions of maximum bound, intermediate, and bulklike (free) water in the hydrogels, and T_{1B}, T_{1I}, and T_{1F} are the spin-lattice relaxation times for maximum bound, intermediate, and bulklike water in the hydrogels, respectively.

The measured T_{1F} was taken to be that of pure water; f_B, f_I, and f_F are evaluated from the DSC data,[17,18] as shown in *Table* 2 for *p*(HEMA) hydrogels and in *Table* 3 for 1 mole% crosslinked EGDMA-*p*(HEMA) hydrogels. T_{1B} corresponds to the measured T_1 for the known content of DSC data.[17,18] Hence, one can estimate T_{1I} for intermediate water in the hydrogels. *Table* 1 also gives T_{1I} values determined for *p*(HEMA)-(H_2O) hydrogel and 1 mole% crosslinked EGDMA-*p*(HEMA)-(H_2O) hydrogel systems. The T_1 values are inversely proportional to the magnitude of the interactions between water protons and lattice environments. The lower value of T_{1I} means a stronger interaction between polymer network and water molecules. The T_{1I} values are approximately 15 times less than that of bulk water.

This indicates that the intermediate water is less mobile and more preferentially ordered than bulk water. According to the data in *Table* 1, the spin-lattice relaxation times (T_{1B}) of bound water in the hydrogels are about 30 times less than that of water protons in pure liquid water. Some water molecules around the polar sites in the polymer networks may be structured and preferentially ordered, probably due to the hydrogen bondings or strong polar-polar interactions in the hydrogels. The temperature effects on the relaxation times may be interpretted in terms of the interactions and different types of water structuring in the pol-

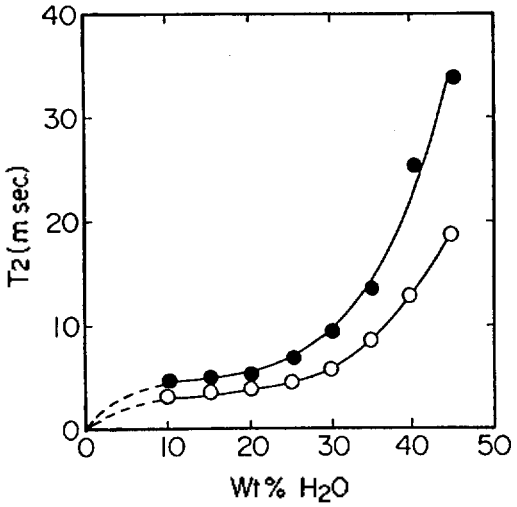

Fig. 4. The spin-spin relaxation times of water protons as a function of water content in hydrophilic methacrylate polymers at 34℃ and 100 MHz: ●, *p*(HEMA)-(H_2O) hydrogels; ⊖, A *p*(HEMA)-EGDMA-(H_2O) hydrogels.

ymeric hydrogels. *Fig.* 4 shows the spin-spin relaxation times (T_2) of water protons as a function of water content in the *p*(HEMA)-(H_2O) hydrogel and crosslinked EGDMA-*p*(HEMA)-(H_2O) hydrogel systems. The values of T_2 are approximately 10 times less than those of T_1, in general agreement with the principles of spin relaxations.[22,23] In the region of less than 20% water content, the values of spin-spin relaxation times are almost constant. Beyond this region, however, spin-spin relaxation (T_2) values rapidly increases as the water content increases. This evidence indicates that more intermediate and bulklike or free water exists, resulting in mobility increase in high water content hydrogels.

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