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Ultraslow Thermoresponse in Hydrogels Synthesized with Radiation Technique

**Akihiro Hiroki,[†,‡] Yasunari Maekawa,[†] Ryoichi Katakai,[‡] Takashi Yamashita,[§]
Yusa Muroya,[∥] Yosuke Katsumura,[⊥] and Masaru Yoshida[1*,†]**

Quantum Beam Science Directorate, Japan Atomic Energy Agency, 1233 Watanuki, Takasaki, Gunma 370-1292, Japan, Department of Chemistry, Faculty of Engineering, Gunma University, 1-5-1 Tenjin, Kiryu, Gunma 376-8515, Japan, Department of Industrial Engineering Chemistry, Faculty of Science and Technology, The Science University of Tokyo, 2641 Yamazaki, Noda-shi, Chiba 278-8510, Japan, Nuclear Professional School, Faculty of Engineering, The University of Tokyo, 2-22 Shirakata-shirane, Tokai-mura, Naka-gun, Ibaraki 319-1188, Japan, and Department of Nuclear Engineering and Management, Faculty of Engineering, The University of Tokyo, 7−3−1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

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ABSTRACT: Hydrogels, which were synthesized by simultaneously occurring processes of radiation-induced polymerization and cross-linked reactions of acryloyl-L-proline methyl ester (APM) at 0 °C in aqueous alcohol solutions, exhibit an ultraslow volume change in response to variations in external temperature. The shrinking speed of the hydrogels prepared in aqueous alcohol is 1000 times slower than that of the hydrogel prepared in pure water; e.g., the hydrogel prepared in aqueous 1-propanol solution shrunk in 6 months. It is revealed that the ultraslow thermoresponse consists of quick- and slow-shrinking periods; the ratio between the two periods depends on the alcohol molecules in the solution. The generation of a hydroxyl group in the polymer network by the coupling reaction between α-hydroxyalkyl radical of alcohols and α-radical of proline moiety was confirmed by GC/MS analysis of the radiation products. The hydrogen bonding domain containing the hydroxyl groups is proposed to be responsible for the ultraslow response.

Introduction

The kinetics of the volume phase transition of a thermoresponsive hydrogel plays an important role in applications such as drug delivery systems, selective membranes, and biosensors.[1−5] There have been many reports on the hydrogels that exhibit a rapid response to temperature variation, and there have been many attempts to enhance response speed by controlling the chemical and cross-linked network structures and the homogeneity of the hydrogels.[6−10] However, there have been no attempts to prepare a slow responsive hydrogel. This hydrogel can be expected as a useful material to slowly release the fertilizer in the vegetable field over a period of long time.

To prepare hydrogels, we employed a radiation processing in which both the radical polymerization and the self-bridging occur during γ-irradiation for a mixture of vinyl monomers and water, as illustrated in Figure 1. It is confirmed that the self-bridged hydrogels are also obtained by irradiating the linear polymers in the presence of water. These processes allow us to prepare hydrogels without the use of chemical impurities such as initiators, cross-linkers, and accelerators.[11,12]

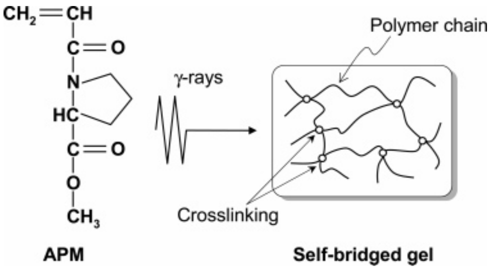

Figure 1. The preparation method of APM hydrogels. Polymerization of APM monomers is initiated with the radicals such as OH and H formed in the γ-radiolysis of water followed by a self-bridging reaction between two radicals produced with the abstraction of hydrogen from APM polymer.

We have focused on a polymer that contains an amino acid residue in the side chain because amino acids as an ingredient of polymers are expected to enhance the biocompatibility in vivo and biodegradability of the polymers. An acryloyl-L-proline methyl ester (APM) monomer as the acrylate derivative is especially interesting in an original monomer with the amino acid in the side chain. We have found that the linear polymer of APM exhibits the phase transition in water at a lower critical solution temperature (LCST) of 14 °C, which is lower than 32 °C of *N*-isopropyl acrylamide (NIPA) polymer.[13,14] The APM hydrogels obtained by the simultaneously occurring processes of the polymerization and the self-bridging exhibit the volume phase transition at around 14 °C.

The APM hydrogels with homogeneously and heterogeneously cross-linked structures were obtained by γ-irradiation of aqueous APM solutions at lower and higher temperatures than the LCST of the APM polymer, respectively.[15] The latter gel had a faster shrinking rate than the former gel. This is due to the structure of the polymers obtained at the initial stage of irradiation: the polymer chains expand below LSCT to finally form a homogeneous cross-linked network on a nanoscopic scale, whereas the polymer chains collapse above LSCT to form a heterogeneous cross-linked network.

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* Corresponding author. E-mail: yoshida.masaru@jaea.go.jp.

[†] Quantum Beam Science Directorate, Japan Atomic Energy Agency.

[‡] Department of Chemistry, Faculty of Engineering, Gunma University.

[§] Department of Industrial Engineering Chemistry, Faculty of Science and Technology, The Science University of Tokyo.

[∥] Nuclear Professional School, Faculty of Engineering, The University of Tokyo.

[⊥] Department of Nuclear Engineering and Management, Faculty of Engineering, The University of Tokyo.

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The APM hydrogels also exhibit the volume phase transition in response to the change in the composition of water and alcohol, and completely shrink at the 20% v/v alcohol composition.[16] The polymer chains collapse in 20% v/v aqueous alcohol solution in the range of 0−40 °C. Accordingly, we expect fast-responsive APM hydrogels to be prepared by the irradiation of APM in 20% v/v aqueous alcohol solution, which results in the formation of heterogeneously networked APM hydrogels. Contrary to our expectation, however, the APM hydrogels prepared in aqueous alcohol solutions exhibited quite a slow shrinking speed, slower than that observed in conventional gels. Such ultraslow shrinking behaviors disappeared for the NIPA hydrogels that respond to changes in the temperature as well as the alcohol composition. In this paper, the NIPA hydrogels are used to clarify an effect of polymer side chain on the ultraslow response. We also present the shrinking kinetics of the APM hydrogels prepared in aqueous alcohol solutions along with the proposed mechanism for the ultraslow response.

Experimental Section

Preparation of Hydrogels. Both acryloyl-L-proline methyl ester (APM) as a monomer and *N*-isobutyryl-L-proline methyl ester (M-APM) as a model compound of APM polymer were synthesized in the same manner as previously reported.[17] APM hydrogels were synthesized by simultaneously occurring processes of radiation-induced polymerization and cross-linking of the generated polymers of APM in an aqueous alcohol solution without any cross-linker and initiator. After bubbling a dry nitrogen, APM solutions (30% v/v) dissolved in pure water or in the mixture of water and alcohol (methanol (MeOH), ethanol (EtOH), 1-propanol (1-PrOH), 2-propanol (2-PrOH), 2-butanol (2-BuOH), and *tert*-butyl alcohol (*t*-BuOH)) with a composition of 80:20% v/v were charged into a glass ampule of 5 mm inner diameter. The ampules containing the above-mentioned seven kinds of APM solutions were irradiated at 0 °C (ice−water temperature) with doses of 7.5, 15, 20, 20, 60, 45, and 10 kGy, using γ-rays from a ^{60}Co source under nitrogen atmosphere, respectively, in that order. In addition, an aqueous 1-PrOH solution with APM was irradiated at 40 °C with a dose of 45 kGy in the same way. The APM hydrogels with both the same gel fraction and the same swelling ratio were prepared by changing irradiation dose. The obtained hydrogels were taken out of the ampules and cut off to the same length as the diameter. The APM hydrogels were washed with a large amount of acetone, which is a good solvent for the APM polymer, and finally with distilled deionized water during one week to remove the unreacted monomer and homopolymer. The composition of acetone and water was gradually varied in order to completely replace the solvent into water for the APM hydrogels.

N-isopropyl acrylamide (NIPA) hydrogels were also prepared by the simultaneously occurring processes of radiation polymerization and self-bridging in water−alcohol mixtures at 0 °C. The NIPA solutions (20% w/w) dissolved in pure water and in a mixture of water and alcohols (MeOH and 1-PrOH) with 80:20% v/v were charged into a glass ampule of 5 mm inner diameter after bubbling with nitrogen gas, and then irradiated at 0 °C with doses of 15, 60, and 90 kGy under nitrogen atmosphere, respectively. The gels obtained were treated in analogy with the APM hydrogels.

Swelling Ratio Measurements. The Swelling ratio (*Sw*) of APM hydrogel was calculated from the following equation, $Sw = (W_s - W_d)/W_d$, where W_s is the weight of a swollen gel at a certain temperature and W_d is the weight of dried one, respectively. The weight of the hydrogel was measured gravimetrically after wiping excess water at its surface. The hydrogels were first swollen at 0 °C (ice−water system) until the equilibrium is reached, and then the swollen hydrogel was transferred in water kept at 40 °C. At the prescribed time interval, the hydrogel was taken out from water and weighed after wiping the excess water at its surface. The temporal change of hydrogel swelling was evaluated by using the normalized *Sw*.

Pulse Radiolysis Measurements. Pulse radiolysis experiments were performed by using an electron pulse of 10 ns and 28 MeV from a linear accelerator at the Nuclear Engineering Research Laboratory, the University of Tokyo. Details have been given elsewhere.[18] The absorbed dosage was determined to be ca. 73 Gy per pulse by using 10^{-2} mol dm^{-3} KSCN solution saturated with N_2O and a $G\epsilon(SCN)_2^{\bullet-}$ of 5.2×10^{-4} m^2 J^{-1} at 475 nm.[19]

Gas Chromatography−Mass Spectrometry Measurements. Shimadzu GC-17A, with a fused silica column (CP−Sil 5CB: 30 m × 0.25 mm) and Shimadzu QP-5000 were used for gas chromatography (GC)/mass spectrometry (MS). The column temperature was programmed as follows; a halt at 80 °C for 2 min, an increase at 10 °C min^{-1} for 17 min, and finally a halt at 250 °C for 11 min. The mass spectra were recorded by using electron ionization (ionization energy 70 eV); the mass spectrometer was a quadrupole analyzer. M-APM solutions (30% v/v) dissolved in the mixture of water/2-PrOH (80:20% v/v) were irradiated at 0 °C for 6 and 16 h at a dose rate of 10 kGy/h, using γ-rays from a ^{60}Co source under nitrogen atmosphere. After irradiation, water and 2-PrOH were removed by evaporation. The concentrated solution was diluted to 3% v/v with MeOH.

Results and Discussion

To compare the response rate, the hydrogels with the same size and the same cross-linking density should be used because its rate is proportional to the square of the characteristic diameter.[20] For this purpose, the APM hydrogels with a gel fraction of ca. 95% and a swelling ratio of ca. 20 in water at 0 °C were obtained by changing the irradiation dose, exhibiting the volume phase transition at around 14 °C.

Temporal changes in gel swelling were evaluated by using the normalized *Sw*, which is expressed as $(Sw_t - Sw_{40})/(Sw_0 - Sw_{40})$, where Sw_t is the swelling ratio of the hydrogel at time t after the temperature jumped from 0 to 40 °C, and Sw_0 and Sw_{40} are the swelling ratios of the equilibrated hydrogels at temperatures of 0 and 40 °C, respectively. Figure 2 shows the change of normalized *Sw* of APM hydrogels along with NIPA hydrogels as a function of time when the swollen hydrogels equilibrated at 0 °C are quickly immersed in water at 40 °C (above LCST). As shown in Figure 2a, the APM hydrogels prepared in pure water (Gel[H_2O]) had totally shrunk in about 3 h. In contrast, the hydrogel prepared in the aqueous 1-PrOH solution (Gel[nPr]) showed the same initial shrinking speed as Gel[H_2O] (normalized *Sw* is 0.4 at 3 h); the shrinking speed then slowed suddenly and took about half a year to reach an equilibrated shrinking state; $dT_{0.01}$, which is defined as the time required until the normalized *Sw* decreased to less than 1% of the initial hydrogel volume, is 174 days. The existence of the alcohols during radiation decreases the shrinking speed of the obtained hydrogels by more than 1000 times. Furthermore, the hydrogel prepared in aqueous 1-PrOH at 40 °C (Gel[nPr40]) shrank at a slow speed even at the initial stage and took about 5 months to reach an equilibrated state ($dT_{0.01} = 143$ days); namely, most of the hydrogel volume consists of the component that exhibits the ultraslow response. On the other hand, the shrinking profiles of NIPA hydrogels prepared in pure water and those prepared in the mixture of water and 1-PrOH were quite similar, and the hydrogels had shrunk in about 3 h.

To investigate the effect of the alcohol molecules in the aqueous monomer solution on the shrinking speed of gels, we examined the shrinking kinetics of the gels prepared at 0 °C in aqueous MeOH, EtOH, 2-PrOH, 2-BuOH), and *t*-BuOH (Gel[Me], Gel[Et], Gel[^{i}Pr], Gel[^{s}Bu], and Gel[tBu]) for comparison with those of Gel[H_2O] and Gel[nPr]. Figure 2b shows the change of the normalized *Sw* as a function of time when the swollen hydrogels equilibrated at 0 °C are quickly immersed

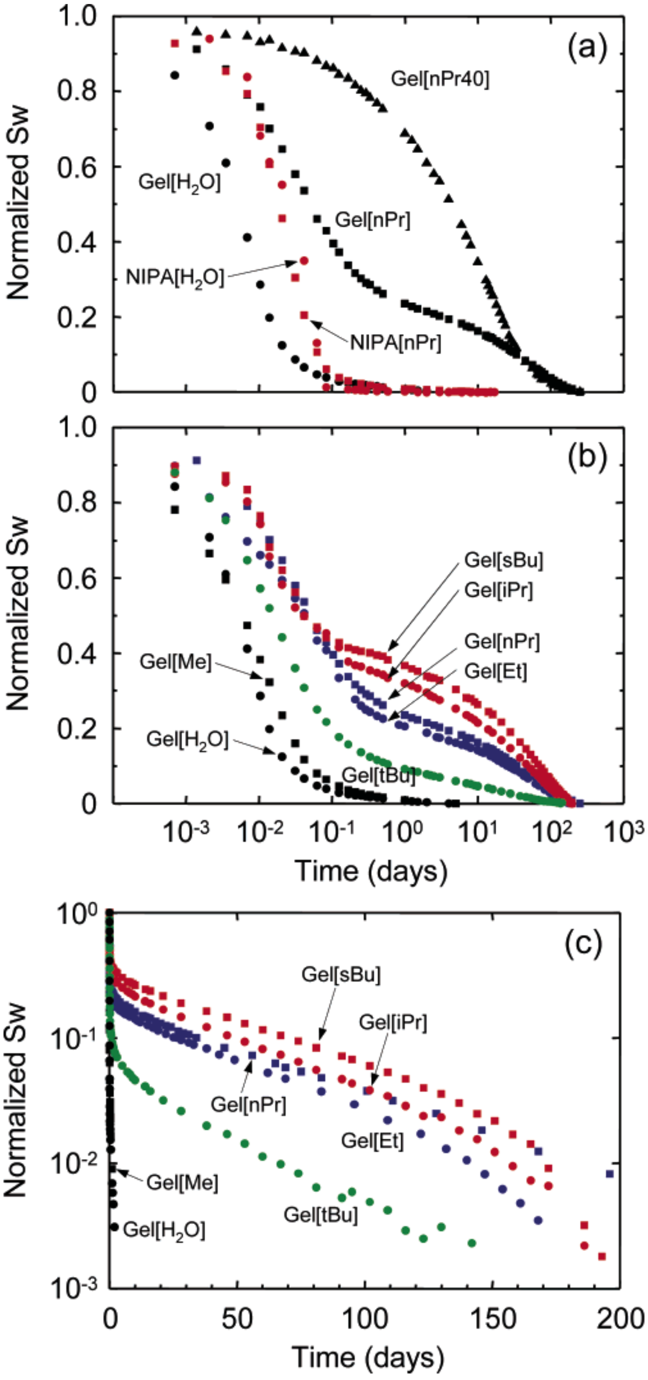

Figure 2. Normalized swelling ratio (*Sw*) of APM hydrogels along with NIPA gels as a function of time when the swollen hydrogels equilibrated at 0 °C are quickly immersed in water at 40 °C. (a) Comparison of the normalized *Sw* of the APM hydrogels prepared in pure water at 0 °C (black circles), aqueous 1-PrOH at 0 °C (black squares) and at 40 °C (black triangles), and NIPA gels prepared in pure water (red circles) and aqueous 1-PrOH (red squares) at 0 °C, respectively. (b) Comparison of normalized *Sw* of the APM hydrogels prepared in aqueous MeOH (black squares), EtOH (blue circles), 1-PrOH (blue squares), 2-PrOH (red circles), 2-BuOH (red squares), and *t*-BuOH (green circles) at 0 °C. (c) A semilogarithmic plot of the normalized *Sw* as a function of time.

Table 1. Time Constants for the Fast and Slow Processes

sample	$\tau_{f1} \times 10^3$ (day)	τ_{f2} (day)	τ_s (day)	R_s	$dT_{0.01}$
Gel[H$_2$O]	4.24	0.0687		0	0.15
Gel[Me]	0.77	0.0156		0	0.83
Gel[Et]	1.84	0.0670	38.5	0.20	140
Gel[nPr]	9.15	0.117	44.5	0.22	174
Gel[^{i}Pr]	9.54	0.213	44.2	0.30	154
Gel[^{s}Bu]	13.0	0.973	58.3	0.32	168
Gel[tBu]	2.73	0.0334	10.8	0.11	65
Gel[^{i}Pr40]	18.7		21.0	0.57	143

in water at 40 °C. Gel[Me] showed a shrinking profile similar to that of Gel[H$_2$O] and reached equilibrium in 20 h. On the other hand, Gel[Et], Gel[^{i}Pr], and Gel[^{s}Bu] shrank at a high speed at an early stage; then the shrinking speed suddenly slowed and required about 5−6 months to reach the equilibrium state, as it was also observed in Gel[nPr]. Gel[tBu] showed a median shrinking profile between those of Gel[H$_2$O] and Gel-[nPr] for both fast and slow processes, and it reached equilibrium in a shorter time ($dT_{0.01} = 65$ days). Therefore, the shrinking profiles of hydrogels in the range from 10^{-1} to 10^2 days were greatly controlled by selecting the alcohol used for hydrogel preparations.

It is considered that one of the causes to induce the slow response of APM hydrogels is due to a slight amount of alcohol that remained in polymer networks. To confirm the effect of remaining alcohol, the APM hydrogels prepared in pure water were first immersed in 1-PrOH for a long time and then washed with water again, as its shrinking profile was not changed by alcohol treatment. The other is due to the formation of a dense layer. It is well-known that the dense layer formed at the surface of hydrogels in the initial stage of shrinking suppresses a diffusion of water from the interior of the hydrogels.[15] In the case of the APM hydrogels prepared in aqueous solutions of MeOH and 1-PrOH, the cross-section of shrunken samples was carefully observed by means of scanning electron microscopy, but it showed only porous structures without the formation of a dense layer.

As the next step, to analyze the slow shrinking profile of the APM hydrogels prepared in the coexistence of alcohols and water, we attempted to quantitatively interpret it by using the shrinking kinetics of the hydrogels. As a general rule, the shrinking kinetics of hydrogels can be analyzed by the first-order manner (single-exponential decay).[7] However, it was found that the shrinking kinetics of the APM hydrogels did not follow the first-order manner. Thereupon, the shrinking profiles of Gel[H$_2$O] and Gel[Me], which shrank only at a high speed as mentioned above, were fitted by double-exponential decay in eq 1,

$$\text{Normalized } Sw = A_{f1} \exp(-k_{f1}t) + A_{f2} \exp(-k_{f2}t) \quad (1)$$

In contrast, as shown in Figure 2c, a semilogarithmic plot of the normalized *Sw* as a function of time clearly shows extra exponential decay in the shrinking profiles of Gel[Et], Gel[nPr], Gel[^{i}Pr], and Gel[^{s}Bu]. These shrinking profiles were fitted by the sum of the three exponential components in eq 2,

$$\text{Normalized } Sw = A_{f1} \exp(-k_{f1}t) + A_{f2} \exp(-k_{f2}t) + A_s \exp(-k_s t) \quad (2)$$

where the subscripts "f1" and "f2" in the former two components represent "stage 1 and stage 2 of the fast process", respectively, and the subscript "s" represents "slow process". The former two components correspond to the initial fast response, as seen in conventional hydrogels, and the latter component corresponds to the ultraslow response. For quantitative evaluation of the shrinking speed of the hydrogels, the time constants for fast and slow processes, τ_{f1}, τ_{f2}, and τ_s, which represent the time required for half-shrinking, are listed in Table 1. The time constants for the slow process (τ_s) of ultraslow responsive hydrogels were similar to each other in the range from 38.5 to 58.3 days, except for the Gel[tBu] hydrogels.

The ratio between the preexponential coefficients, A_f (= $A_{f1} + A_{f2}$) and A_s, in eq 2 corresponds to that between the gel volume shrinking in a fast process and that shrinking in a slow process. Therefore, we defined coefficient ratio R_s (= $A_s/(A_f + A_s)$) as an indicator of the ratio of the hydrogel volume that shrinks in slow processes to the total hydrogel volume. As shown in Table 1, Gel[Et] and Gel[nPr] prepared in primary alcohols had R_s values 0.20 and 0.22 that were similar to each other. The R_s values of Gel[^{i}Pr] and Gel[^{s}Bu] prepared with secondary alcohols were also similar (0.30 and 0.32) to each other but somewhat larger than those of Gel[Et] and Gel[nPr]. On the other hand, Gel[Me] prepared in primary alcohol (e.g. methanol) shrank without any slow process ($R_s = 0$). From these results, the ratio of the slow process in these hydrogels seems to be related to the stability of the carbon radical at the α-position, i.e., the α-hydroxyalkyl radical in the alcohol molecule, where the α-hydroxyalkyl radicals are stable in order of $\cdot CRR'OH > \cdot CHROH > \cdot CH_2OH$, because of the increased electron density of the α-position by alkyl groups. These findings are in agreement with the general knowledge of the hydrogen abstraction reaction, e.g., the rate constants of various α-hydroxyalkyl radicals with aromatic thiols were in order of $\cdot C(CH_3)_2OH > \cdot CH(CH_3)OH > \cdot CH_2OH$ (in the range between 1.5×10^{-9} and 0.3×10^{-9} dm^3 mol^{-1} s^{-1}).[21,22] Gel[tBu] prepared in tertiary alcohol exhibited τ_s and R_s values between those of Gel[Et] and Gel[nPr] and that of Gel[Me], as it does not have a proton at the α-position, but has nine protons at the β-position, which should act as a radical coupling point, resulting in an ultraslow response. Therefore, the relation between the stability of the α-hydroxyalkyl radicals and the coefficient ratio (R_s) strongly indicates that the ultraslow response results from a change in the chemical structure of the hydrogels in the radiolytic reactions with the α-hydroxyalkyl radicals of alcohols.

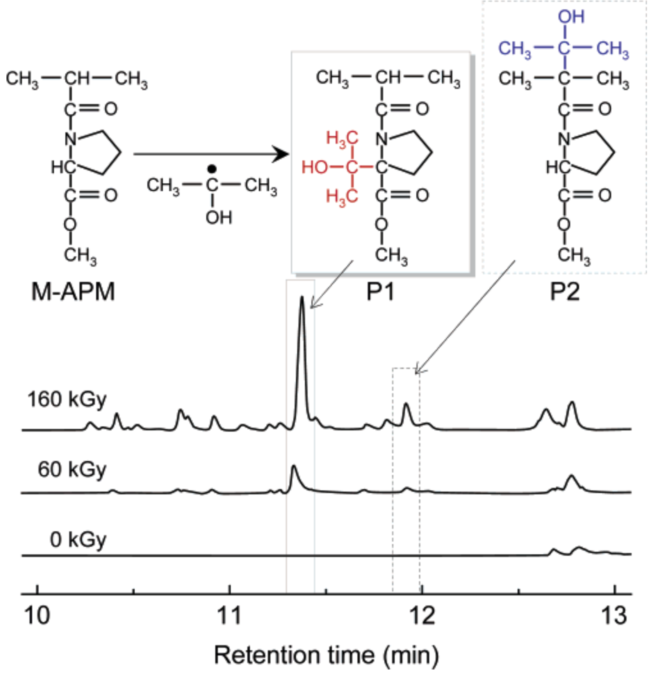

Figure 3. GC/MS analyses of the samples of M-APM in an aqueous 2-PrOH solution irradiated with doses of 0, 60, and 160 kGy. P1 and P2 represent the adducts of 2-PrOH at α-carbon of the proline ring and at the α-carbon of the carbonyl group in M-APM, respectively.

To investigate the structural changes caused by the α-hydroxyalkyl radicals in the APM hydrogels, we analyzed the radiolytic products of alcohols and the model unit of the corresponding polymer, *N*-isobutyryl-L-proline methyl ester (M-APM), by the GC/MS technique. When the model M-APM was irradiated in aqueous 2-PrOH solution, dimers of 2-PrOH or M-APM, adducts of 2-PrOH to M-APM, and unknown products were detected in the GC/MS analysis. The relative concentrations of the product eluted at 11.4 min, obtained by γ-irradiating with doses of 60 and 160 kGy, were found to be 2 and 7%, respectively (Figure 3). This product was assigned to adduct of 2-PrOH to M-APM at the α-carbon of proline (P1) on the basis of the base peak at $m/z = 257$, with other fragment ions at $m/z = 198$, 140, and 70. The other adduct of 2-PrOH to M-APM at the α-carbon of the carbonyl group (P2) was observed with a dose of 160 kGy; the intensity of the peak, however, was much lower than that of P1. On the other hand, no adduct was observed when the M-APM was irradiated in aqueous methanol, even when the doses were increased up to 500 kGy. The α-carbon radical of proline would be expected to display a greater stability owing to the synergistic effect of electron-donating and electron-withdrawing groups on the α-carbon, an effect that is commonly referred to as captodative stabilization.[23] Accordingly, it should be clear that the α-carbon radical of alcohols generated by the abstraction of the hydrogen by OH radical can react with the captodatively stabilizing α-carbon radical of proline in the polymer, resulting in the introduction of hydroxyl groups in the hydrogel network; the hydroxyl groups would be responsible for the ultraslow response of the APM hydrogels. This consideration is further supported by the fact that NIPA hydrogels show only the fast shrinking response because no radicals in the side chain could be stabilized by the captodative effect.

The hydroxyalkyl radicals of the alcohols and the radicals generated on the gel network are mainly produced by the hydrogen abstraction of OH radicals that are one of the main radiolytic products of water. To estimate the rate constant of OH radical with the hydrogel network, M-APM instead of APM polymer was used, because the APM polymer collapses in aqueous solution at room temperature. The rate constants for the reactions of the OH radicals with the M-APM were measured by using pulse radiolysis of aqueous solutions. Because the radicals derived from M-APM cannot be observed spectroscopically, the reaction rate constants of OH radicals with M-APM were determined by the carbonate competition method.[24,25] Figure 4 shows the decay of $CO_3^{\bullet-}$ absorption observed at 600 nm based on the radiolysis of an aqueous M-APM solution. The absorbance of the produced $CO_3^{\bullet-}$ varies with the [M-APM]/[CO_3^{2-}], which is given by the equation

$$1/A = 1/A_0 \{1 + k_1[\text{M-APM}]/k_2[CO_3^{2-}]\} \qquad (3)$$

where k_1 and k_2 are the rate constants for the reactions of OH radical with M-APM and CO_3^{2-}, respectively. A is the absorbance under a certain condition, and A_0 is the absorbance when all OH radicals are converted to the $CO_3^{\bullet-}$. From the changes in the yield of $CO_3^{\bullet-}$, the rate constant of M-APM was obtained to be $k_1 = 3.1 \times 10^9$ dm^3 mol^{-1} s^{-1}, which is almost the same as those of the primary and secondary alcohols, EtOH, 1-PrOH, 2-PrOH, and 2-BuOH (1.9×10^9, 2.8×10^9, 1.9×10^9, and 3.1×10^9 dm^3 mol^{-1} s^{-1}), but differs from those of MeOH and *t*-BuOH (9.7×10^8 and 6.8×10^8 dm^3 mol^{-1} s^{-1}).[26] Furthermore, the rate constants of OH radicals with alcohol molecules such as MeOH and 2-PrOH in the presence of M-APM were also determined by the above-mentioned competition method because absorption maxima of alcohol-derived radicals (ca.

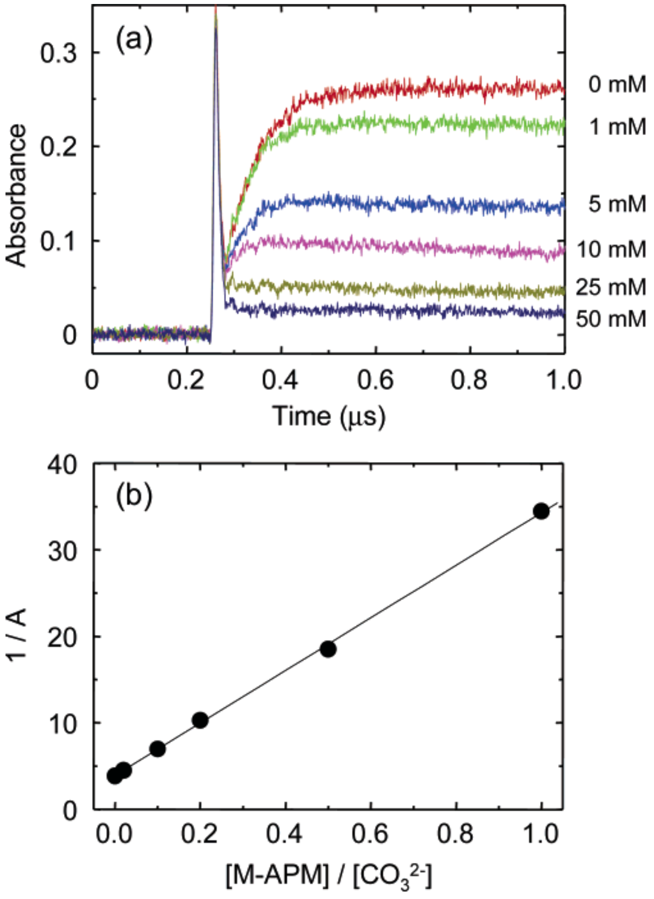

Figure 4. Time profiles of $CO_3^{\bullet -}$ formed in the aqueous M-APM solution. (a) Transient absorbance, observed at 600 nm, from the pulse radiolysis of M-APM with concentrations of 0, 1.0, 5.0, 10, 25, and 50 mM in aqueous 50 mM Na_2CO_3 solutions saturated with N_2O. (b) Variation of [absorbance]$^{-1}$ with the [M-APM]/[CO_3^{2-}] ratio for the $CO_3^{\bullet -}$ at 600 nm.

220−240 nm) were below the measurement range of the apparatus (>300 nm). The rate constants of OH radicals with alcohol molecules in the presence of M-APM are 1.3×10^9 and 2.6×10^9 dm^3 mol^{-1} s^{-1}, respectively, as these values agreed roughly with those reported by Buxton.[26] Similar rate constants of OH radicals with alcohol and M-APM do not necessarily imply anything about the ratios of the recombination products. However, as mentioned above, the cross-coupling of α-hydroxyalkyl radicals with the α-carbon radicals of the proline in the APM polymer network certainly competes with the self-coupling of these radicals. The coupling reactions of α-hydroxyalkyl radical with α-carbon radicals seem to efficiently proceed as each reaction has similar rate constants. From these analyses of the model reactions using M-APM, it can be concluded that the hydroxyl groups in the polymer chains generated by the radical coupling of alcohols and the proline in the hydrogel play a decisive role in determining the ultraslow response.

It is well-known that poly(vinyl alcohol) hydrogels with OH groups in the side chain hold a large amount of water molecules in polymer networks, even when the external temperature is changed. Furthermore,the following two facts should be noted: (1) the incorporation of hydroxyl groups in polymer networks decreases the shrinking speeds but does not affect the volume phase transition temperature of about 14 °C, and (2) the extent of the hydroxyl groups incorporated into hydrogels is related to the volume ratio but does not affect the shrinking speed in the slow process. From these results, it is suggested that the hydroxyl groups in the hydrogels create the ultraslow responsive "hydrogen bonding domain", which hampers the hydrophobic aggregation of polymer networks in addition to the diffusion of water in the shrinking process, as illustrated in Figure 5. The hydrogen bonding domain increases with the increase of the hydroxyl groups, resulting in the increases of the volume ratio of the two processes; however, the number of the hydroxyl group cannot affect the shrinking rate constants in the hydrogen bonding domain.

Conclusion

APM hydrogels were synthesized by simultaneously occurring processes of radiation-induced polymerization and self-bridging at 0 and 40 °C in aqueous alcohol solutions. Although the hydrogels prepared in pure water shrank in about 1 min, the hydrogels prepared in the aqueous 1-propanol solution exhibit the ultraslow response, which took 6 months to reach an equilibrated shrinking state. That is, the existence of the alcohols during γ-irradiation decreases the shrinking speed of the hydrogels by more than 1000 times. On the other hand, the ultraslow responsive behavior disappeared for the NIPA hydrogels prepared in the aqueous alcohol solution as well as in pure water.

The APM hydrogels prepared in aqueous alcohol solutions show two durations of shrinking periods: a fast response period followed by an ultraslow response period. The ratio between the two shrinking periods depends on the alcohol molecules in the solutions. The content of ultraslow response is very consistent with the stability of α-hydroxyalkyl radicals generated by abstraction of hydrogen from alcohol molecules. The radiation products with the hydroxy group generated by the coupling reaction between the α-hydroxyalkyl radicals and the α-radical of proline residue was recognized by the GC/MS analysis of the γ-irradiated aqueous alcohol solution containing

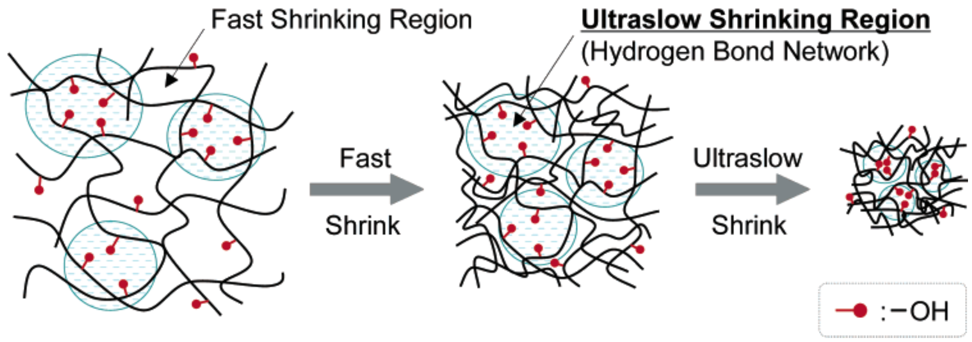

Figure 5. The "hydrogen bonding domain" model for the ultraslow responsive APM hydrogels containing hydroxyl groups. First, the domain of the hydrogel containing a few amount of hydroxyl groups shrinks at the conventional speed (minute to hour); then, the "hydrogen bonding domain" of the hydrogel shrinks with ultraslow response (month to year).

M-APM as a model compound of APM polymer. Similar reactivities of alcohols and M-APM with the OH radical, which was mainly generated upon radiolysis of water, were observed by means of pulse radiolysis using LINAC. The hydroxyl group of the hydrogel matrixes decreases the shrinking kinetics due to the existence of a hydrogen bonding domain in the hydrogels.

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