

열 감수성 수화겔인 Methacryloyl-(L)-Alanine Methylester 공중합체

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Methacryloyl-(L)-Alanine Methylester Containing Copolymers as Thermoresponsive Hydrogels

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요 약 : 새로운 형태의 온도 감수성 수화겔을 방사선 중합법으로 합성하였다. 그중 MA(L)AlaOMe/HPMA (95/5 vol-%) 공중합겔에 열응답성이 가장 높아 수분흡수가 0°C에서 3,000%서부터 40°C에서 65%로 되었다. 95/5나 90/10(vol-%) 비율의 MA(L)AlaOMe/HPMA 수화겔이 온도에 따라 다른 비율의 수화겔에 비하여 수분흡수가 크게 일어났으며 물리적인 강도도 적당하였다. 반복된 흡탈착 실험에서 이 수화겔들은 60°C까지 가역반응을 보였다. 이들 겔의 표피는 40°C에서 5시간후 부터 생기기 시작하였다. 용매로서 메타놀은 가장 큰 원통형 구멍을 형성하는 수화겔을 만드는데 가장 효과적인 물질이었다.

Abstract : A series of new thermo-sensitive hydrogels was synthesized by gamma-ray irradiation. Among them MA(L)AlaOMe/HPMA copolymer gels showed the highest thermo-response : the water absorption changed from 3,000% at 0°C to 65% at 40°C. The copolymer having 95/5 or 90/10 MA(L)AlaOMe/HPMA composition demonstrated appropriate sensitivity to the temperature as well as physical strength in water absorption. In repeated use, the hydrogel showed good reversible response up to 60°C. The surface appearance of the gel was created after 5 hours at 40°C. Methanol was the most effective solvent to form the biggest cylindrical pores of the hydrogel.

INTRODUCTION

A living organism has various sensory systems with responsive functions for external stimuli. In these systems, α -amino acid, nucleic acid, lipid and carbohydrate play important roles. These bio-func-

tional materials containing hydrogels change their structure and physical properties in response to external signals and have promising potential in the design of control processes in bio-industry and pharmacy.¹⁻⁶ In particular self-regulating or auto feedback delivery systems may be achieved by uti-

lizing these stimuli-response polymers.⁷⁻⁹

For this purpose, we have synthesized the methacryloyl derivatives containing α -amino group in its side chains, e.g. methacryloyl-(L)-alanine methylester (MA(L)AlaOMe).¹⁰ The MA(L)AlaOMe was copolymerized with a variety of monomers by gamma-rays because of the low mechanical strength of α -amino acid containing homopolymers. These co-polymeric gels shrink (de-swell) in aqueous solutions when the temperature is raised and also exhibit reversible swelling behaviour when cycled in solutions at different temperatures.¹¹⁻¹³

This new system is of usefulness in basic and applied fields as a new method to achieve improved sensing devices in developing biosensors.¹⁴⁻¹⁶

In this report, we describe the thermo-response of the hydrogel with α -amino acid in various conditions.

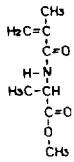
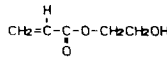
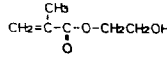
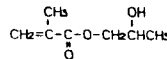
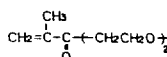
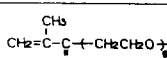
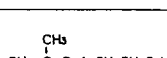
EXPERIMENTAL

Materials

All the materials used were purchased from Kokusan Chemical Works (Tokyo, Japan) and Shin-Nakamura Chemical Co. (Osaka, Japan). The chemical formulae of these monomers are shown in Fig. 1. MA(L)AlaOMe was provided by Gunma University of Japan.

Preparation of Hydrogels

The monomer mixtures such as MA(L)AlaOMe/HEA, MA(L)AlaOMe/HEMA and MA(L)AlaOMe/HPMA, with composition of 80/20 wt%, were charged into a 5 mm interval diameter glass ampoule. The ampoule was sealed after the sample was well de-gassed and charged with nitrogen gas. The irradiation for polymerization of the monomer mixture was carried out for two hours at a dose rate of 10 kGy/hr at 25°C, using gamma-rays from a Co⁶⁰ source. The irradiated samples were washed with excess methanol to remove unreacted monomer. The cylindrical copolymer gels including alcohol were cut into tablet shaped with 5 mm thickness and then allowed to swell in deionized

MA(L)AlaOMe	Other vinyl monomer	Abbreviation
		HEA
		HEMA
		HPMA
		2G
		9G
		14G

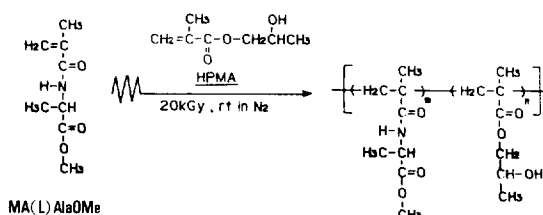


Fig. 1. Structural formulas of MA(L)AlaOMe and various vinyl monomer and their polymerization scheme.

water. Each material was swollen in water at 0°C (ice-water system) until equilibrium was reached.

Water Absorption

The weight changes of the gels, incubated in water at 0, 10, 20, 30, 40, and 50°C, were recorded at 24 hours intervals after wiping the excess surface water from the gel. The degree of swelling (water absorption) can be estimated from the following equation:

Water absorption(%) = $100 (W - W_0) / W_0$
 where W is the weight of swollen gel and W_0 is the weight of dried gel. The surface structures of the hydrogels were observed with a JXA-733 scanning electron microscope (SEM).

RESULTS AND DISCUSSION

The temperature dependence of water absorption for various copolymer gels containing α -amino acids, such as MA(L)AlaOMe/HPMA, MA(L)AlaOMe/HEMA, and MA(L)AlaOMe/HEA(80/20 Wt%) is shown in Fig. 2. These gels swell when immersed in ice-water, but with the rise of temperature, the swollen samples underwent shrinkage because of dehydration. In this case, the degree of swelling of the gel is strongly influenced by the kind of the copolymerized substances. Of these hydrogels, the MA(L)AlaOMe/HPMA copolymer gels displayed the fastest thermo-response. They showed different swelling behaviors by the change of the composition of copolymer. The water absorption ranged from 1000% at 0°C to 65% at 40°C.

The effect of monomer composition on the water absorption to copoly(MA(L)AlaOMe/HPMA) gels is shown in Fig. 3. The degree of swelling of the gels strongly depended by the monomer composition: MA(L)AlaOMe 100% gel gave the fastest thermo-response and HPMA 100% gel gave the

lowest thermo-response. But, considering the physical strength such as crumbling, the copolymer composition of 95/5 or 90/10 MA(L)AlaOMe/HPMA, was appropriated for the sufficiently high thermo-response hydrogels because HPMA was copolymerized to improve the physical strength.

As a function of repeated use, the swelling-deswelling profiles of MA(L)AlaOMe/HPMA copolymer gels among 0 and 40°C, 0 and 60°C, and 0 and 80°C at 24 hour intervals are shown in Fig. 4 on copoly(MA(L)AlaOMe/HPMA) gels of 90/10% and in Fig. 5 on copoly(MA(L)AlaOMe/HPMA) gels of 70/30%.

Although showing good reversible response between 0 and 40°C, and 0 and 60°C, the hydrogels collapsed at higher temperature (0 and 80°C), when the regular thermo-response disappears. These phenomena, that physical quantities of a matter changes linearly according to the external thermal stimulus were the same in two different copolymer

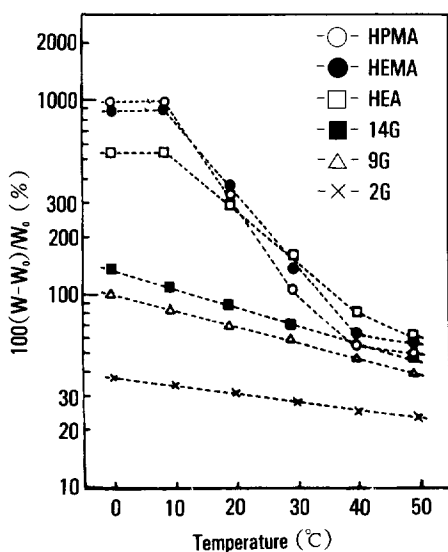


Fig. 2. Effect of kinds of 80 vol-% MA(L)AlaOMe containing hydrogels on the water absorption: the hydrogels were treated for 24 hours at each temperature after saturating previously with water at 0°C

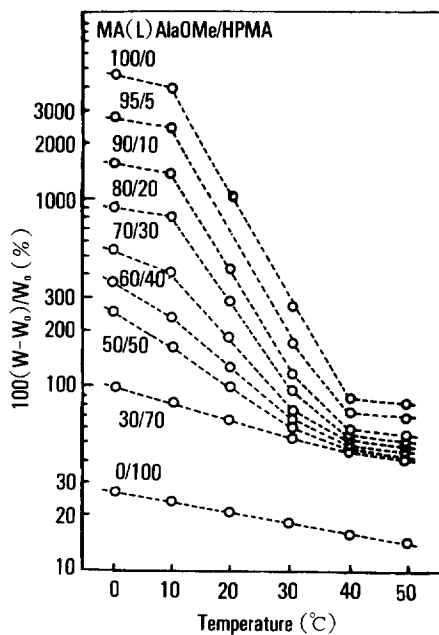


Fig. 3. Effect of monomer composition on the water absorption of copoly(MA(L)AlaOMe/HPMA) gels: the hydrogels were treated for 24 hours at each temperature after saturating previously with water at 0°C.

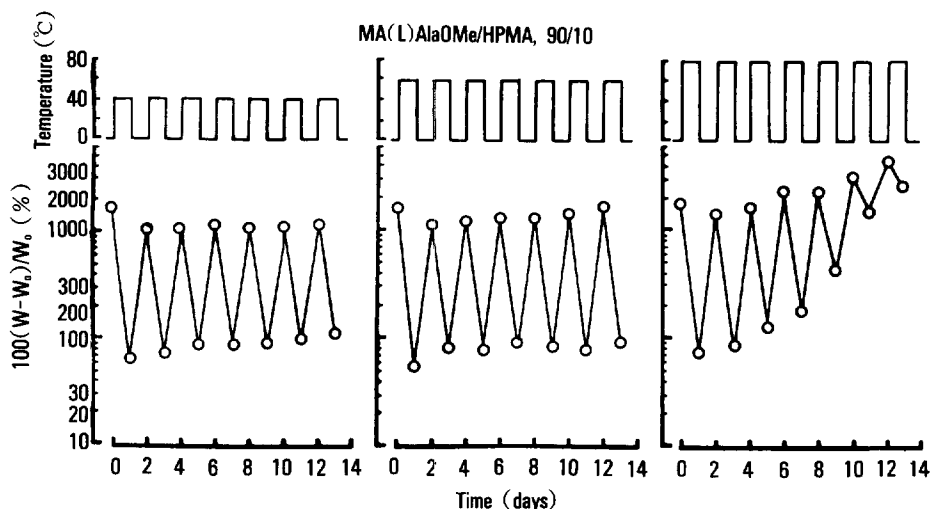


Fig. 4. Swelling-deswelling behaviors of copoly(MA(L)AlaOMe/HPMA, 90/10 vol-%) gels treated at 24 hour-intervals among 0°C and 40°C, 0°C and 60°C, and 0°C and 80°C : in case of high temperature difference (0°C and 80°C), the absorption range was smaller and smaller like a slacken elastic cord.

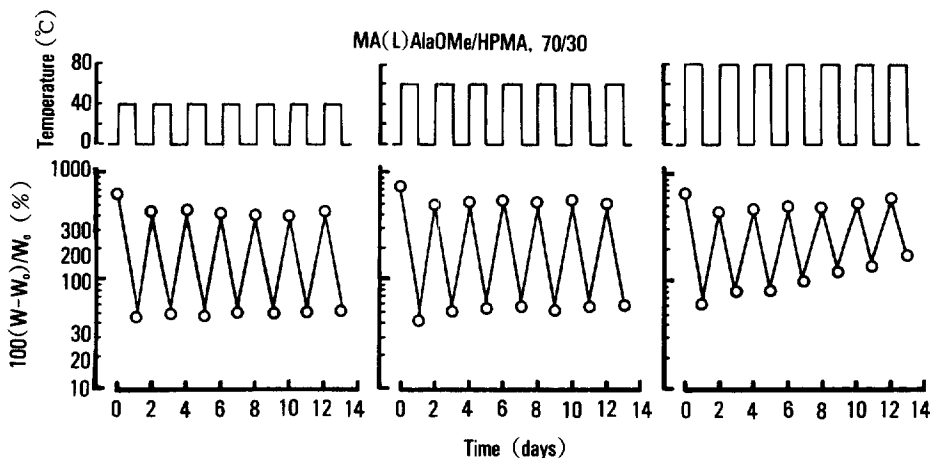
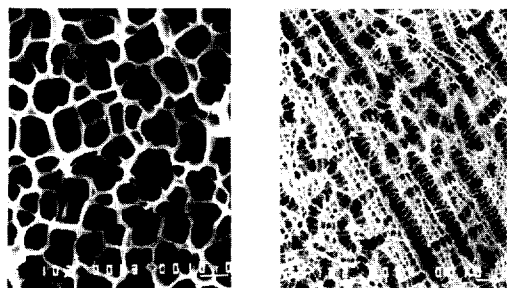


Fig. 5. Swelling-deswelling behaviors of copoly(MA(L)AlaOMe/HPMA, 70/30 vol-%) gels treated at 24 hour-intervals among 0°C and 40°C, 0°C and 60°C, and 0°C and 80°C : in case of high temperature difference (0°C and 80°C), the absorption range was smaller and smaller like a slacken elastic cord.

gels even though the degree was different. In order to clarify these phenomena, the interior structure of copoly(MA(L)AlaOMe/HPMA) gels was observed by scanning electron microscopy (SEM), which was shown in Fig. 6. At 40°C the pore shrank to the same degree in every turn. This effect is closely related to the increase of molecular mobility among the interwinded chains of linear poly-

mers, owing to repetition of the swelling-deswelling procedure.

The freeze dried surface structure of copoly(MA(L)AlaOMe/HPMA) gel by SEM was shown in Fig. 7. The surface was solidified even though the interior preserved their pores. From this fact we can postulate that the hydrogel is solidified from the surface and made a barrier to prevent permea-



0°C 40°C

Fig. 6. SEM-photographs of interior structure of copoly(MA(L)AlaOMe/HPMA, 80/20 vol-%) gels treated for 24 hours at 0°C and 40°C.

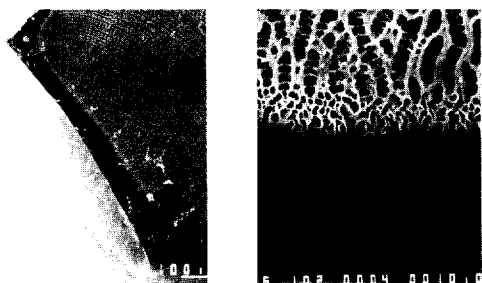


Fig. 7. SEM-photographs of interior and surface structure of copoly(MA(L)AlaOMe/HPMA, 80/20 vol-%) gels treated for 24 hours at 40°C.

tion from the exterior in high temperature, while at low temperature the pore is expanded from the surface in order to facilitate substance delivery and absorption, which was diagrammed in Fig. 8.

With the passage of time, the deswelling kinetics of copoly(MA(L)AlaOMe/HPMA) gels at different temperatures were shown in Fig. 9. The water temperature was first kept at 0°C until the gel was saturated with water, then adjusted to each temperature. The deswelling kinetics were varied at different temperatures. But, after 8 hours, all the samples had undergone shrinkage of more than 90 %. SEM-photographs of copoly(MA(L)AlaOMe/HPMA) gels treated for the period of 0, 1, 5, and 48 hours at 40°C clearly depicted the phenomena of the surface appearance of the gel : first after 1

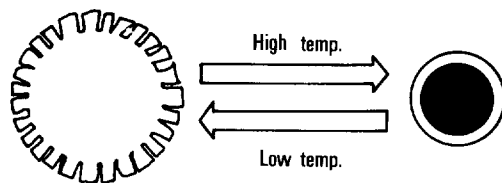


Fig. 8. Schematic diagram for the swelling-deswelling mechanism of copoly(MA(L)AlaOMe/HPMA) gels.

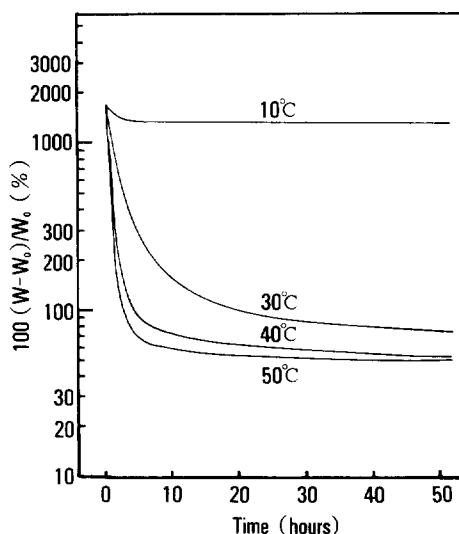


Fig. 9. Time-dependence in deswelling of copoly(MA(L)AlaOMe/HPMA, 95/5 vol-%) gels treated at different temperatures after saturating previously with water at 0°C.

hours, the pore shrank and followed creation of surface barrier after 5 hours, and thickened after 48 hours, which was shown in Fig. 10.

The effect of an organic solvent in the deswelling of the gel was shown in Fig. 11. Among solvents, methanol was the most effective in the swelling and deswelling being from 6000% to 80% of water absorption. SEM-photographs of copoly(MA(L)AlaOMe/HPMA) gels of 95/5% swollen at 0°C showed the greatest size of cylindrical pores in methanol solvent (Fig. 12).

In conclusion, these experimental results demonstrate that MA(L)AlaOMe containing copolymeric hydrogels were prepared successfully by radia-

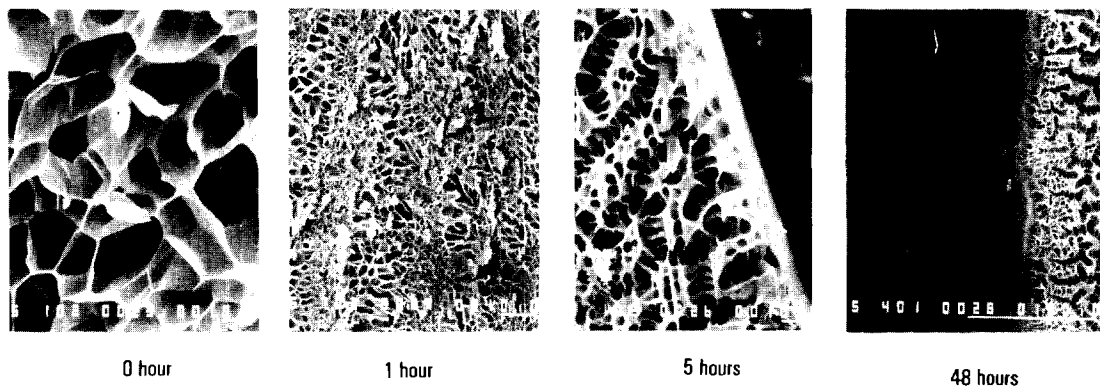


Fig. 10. SEM-photographs of copoly(MA(L)AlaOMe/HPMA, 90/10 vol-%) gels treated for period of 0, 1, 5, and 48 hours at 40°C after saturating previously with water at 0°C.

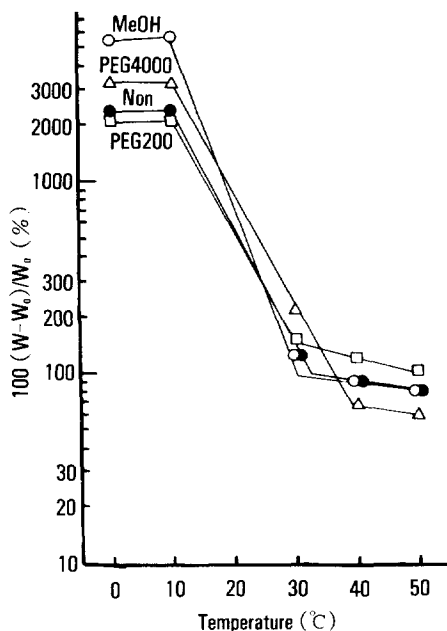


Fig. 11. Temperature dependence in deswelling of copoly(MA(L)AlaOMe/HPMA, 95/5 vol-%) gels, which were copolymerized in the presence of various organic solvent : the hydrogels were treated for 24 hours at each temperature after saturating previously with water at 0°C. Composition of monomer/organic solvent : 90/10 vol-%.

tion induced polymerization. And the most reasonable temperature-response was observed for co-

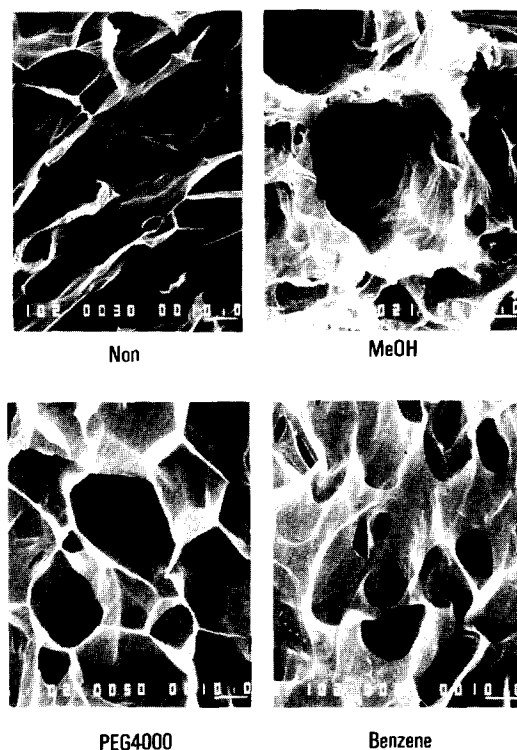


Fig. 12. SEM-photographs of copoly(MA(L)AlaOMe/HPMA, 95/5 vol-%) gels swollen at 0°C.

poly(MA(L)AlaOMe/HPMA) gel showed a reversible swelling-deswelling response (e. g. surface regulating system) that is applicable to a wide ra-

nge of sensory systems, for example, drug delivery systems and sensors as on-off switch functions.

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