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ORIGINAL CONTRIBUTION

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Photocurable biodegradable poly(ε-caprolactone)/poly(ethylene glycol) multiblock copolymers showing shape-memory properties

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Abstract Biodegradable multiblock copolymers were synthesized by a polycondensation of poly(ε-caprolactone) (PCL) diols of molecular weight (MW) = 3,000 and poly(ethylene glycol)s (PEG) of MW = 3,000 with 4,4′-(adipoyldioxy)dicinnamic acid (CAC) dichloride as a chain extender in diphenyl ether at 180 °C for 2 h, and were characterized by GPC, ^{1}H-NMR, FTIR, UV, DSC, and WAXS. These photosensitive copolymers were irradiated by a 400-W high-pressure mercury lamp ($\lambda > 280$ nm) from 5–60 min to form a network structure. The gel contents increased with irradiation time, and attained ca. 90% after 60 min for all copolymers. The degree of swelling in a distilled water at ambient temperature, and the rate of degradation in a phosphate buffer solution (pH 7.2) at 37 °C increased with increasing PEG components. The shape-memory tests were performed by a cyclic thermomechanical experiments for the photocured CAC/PCL/PEG (75/25) films. The film with a gel content of 57% showed the best shape-memory property with strain fixity rate of 100% and strain recovery rate of 88%.

Keywords Multiblock biodegradable copolymers · Poly(ε-caprolactone) · Poly(ethylene glycol) · Photocrosslinking · Shape-memory property

Introduction

The shape-memory polymers have drawn much attention because they possess a lot of advantages over shape-memory alloys such as high-shape recovery, easy processing, and low manufacturing cost. Many kinds of shape-memory polymers have been investigated including *trans*-polyisoprene [1], styrene-butadiene copolymers [2], and segmented polyurethanes [3–6]. But most of them are non-biodegradable. The biocompatible, biodegradable shape-memory polymers with the appropriate thermal and mechanical properties are expected as novel types of medical devices such as surgical sutures and catheters. Recently, such biodegradable shape-memory polyurethanes based on poly(ε-caprolactone) (PCL) diols have been reported by Lendlein et al. [7] and Ping et al. [8]. The shape-memory network polymers have also been prepared through the γ-irradiation of PCL (weight-average molecular weight = 40,000–70,000) [9] and through the photocuring of PCL diol dimethacrylates (number-average molecular weight (M_n) of PCL diols = 1,250–10,000) for a potential biomedical application [10, 11], but the biodegradability of these resulting materials was not reported. In the previous paper [12], we have prepared the biodegradable shape-memory network polymers through the photocuring of PCL diol ($M_n = 3{,}000$) chain-extended by 4,4′-(adipoyldioxy)dicinnamic acid (CAC).

In this paper, the photocurable biodegradable multiblock copolymers were prepared from PCL diol ($M_n = 3{,}000$), poly(ethylene glycol) (PEG) ($M_n = 3{,}000$), and CAC as a chain extender. These copolymers were subjected to the photocuring by a ultraviolet irradiation to show shape-memory properties. The effects of copolymer compositions and gel contents on the thermal, tensile, and shape-memory properties as well as the hydrolytic degradation were examined. The shape-memory properties such as strain fixity rate and strain recovery rate were qualified by a cyclic thermomechanical tensile test. In view of their applications as biodegradable medical devices, PCL/PEG block copolymers can exhibit the outstanding properties such as hydrophlicity, permeability, and degradability [13, 14].

Experimental

Materials

CAC (mp, 282–283 °C) was prepared from adipoyl chloride and 4-hydroxycinamic acid, while the diacyl chloride of CAC (mp, 135–136 °C) was prepared by refluxing the latter with thionyl chloride. The synthetic procedures used to prepare these compounds have been described in detail in our previous paper [15]. PCL diol ($M_n = 3{,}000$) [α,ω–dihydroxy poly(ε-caprolactone)] was supplied by Aldrich Co. Ltd. with the following formula: $H[–O(CH_2)_5CO–]_nO(CH_2CH_2O)_2$ $[–CO(CH_2)_5O–]_mH$. PEG ($M_n = 3{,}000$) was a gift from the Sanyo-Chemical Company. These macrodiols were dried over P_2O_5 at ambient temperature in vacuo.

Polymerization

Multiblock copolymers were prepared by a high-temperature solution polycondensation in diphenyl ether. A typical procedure is illustrated as follows. A mixture of 1 mmol (0.476 g) of CAC dichloride, 0.5 mmol (1.50 g) of PCL-diol, 0.5 mmol (1.50 g) of PEG, and 15 ml of diphenyl ether was introduced into a 3-necked round-bottomed flask equipped thermometer, magnetic stirrer, and drying tube, continuing a dry nitrogen flow. The temperature was raised to 180 °C for 30 min and heated at 180 °C for 2 h, and then hot viscous solution was poured into 100 ml of cold hexane. The precipitated block copolymer was filtered off, precipitated from chloroform into cold hexane, and vacuum dried at room temperature. The copolymer sample is designed as CAC/PCL/PEG (50/50).

Characterization

Gel permeation chromatography (GPC) was carried out on a Waters system. Three styragel columns (300 mm×7.8 mm) were placed in series and operated at a flow rate of 1 ml/min in chloroform at 35 °C. Poly(ethylene glycol) and poly(ethylene oxide) standards with low polydispersities were used for calibration. Fourier transform infrared spectra (FTIR) were recorded on a JEOL spectrophotometer using a thin film on a KRS substrate. ^1H-NMR spectra were obtained in $CDCl_3$ using a JEOL JNM-EX90A FT-NMR spectrometer. The thermal analysis was performed at a heating rate of 10 °C/min in a nitrogen atmosphere with a Shimadzu DSC-50 differential scanning analyzer controlled by TA-50 workstation. Wide angle X-ray scattering (WAXS) was performed for film samples with a Rigaku Denki model RAD-IAX-ray diffractometer with nickel filtered CuK_α radiation. UV/VIS spectra were recorded on a Shimadzu UV-2100 spectrophotometer.

Film preparation

The block copolymer films of about 200 μm were prepared by melt-pressed method at 60–70 °C, followed by quenching into an ice-cooled bath, and then dried for 24 h in vacuo.

Photocuring, gel contents, and degree of swelling

Photocuring was conducted using a 400-W high-pressure mercury lamp (Sen Light Company Ltd., Osaka, Japan), through a cooling jacket and Pyrex filter to cut off wavelength below 280 nm. The UV light intensity was measured on a spectrophotometer (Spectroncs DRC100X, New York). The polymers were coated, from chloroform solutions, onto quartz plates for UV studies, and then irradiated for various times. The gel contents were measured for melt-pressed films (ca. 200 μm thickness).

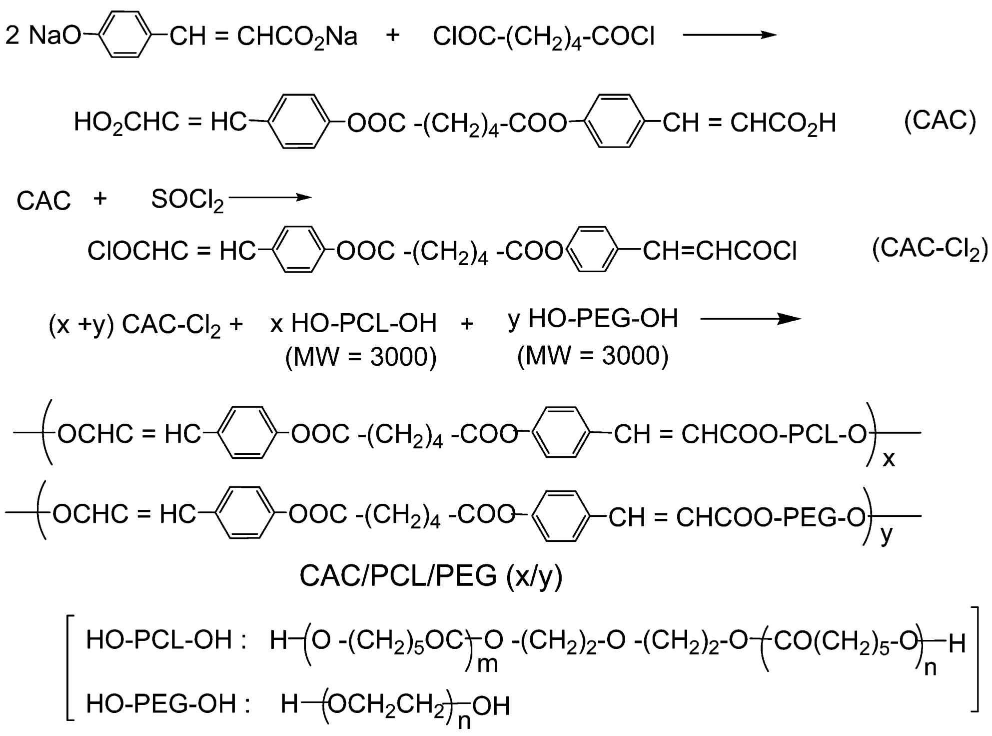
After irradiation for various times, the film was weighed (W) and immersed in chloroform for 24 h, then washed extensively with fresh chloroform to remove the unreacted soluble part of the polymer, and the gels were dried in vacuo and weighed (W_g). The gel content (%) was calculated as 100 W_g/W.

The equilibrium swelling properties in water was measured according to the procedures described elsewhere [15]. Degree of swelling (DS) is defined by: $DS = (W_{wet} - W_{dry})/W_{dry}$, where W_{wet} is the weight of the gel after 24 h in distilled water, W_{dry} is the weight of the gel at the beginning of the experiment.

Hydrolytic degradation

The film specimen (10×10 mm^2, ca. 200 μm thickness) was placed in a small bottle containing 10 ml of 1/15 mol phosphate buffer solution (pH 7.2), which was replaced by freshly prepared solution every 2 days. The bottle was incubated at 37 °C for various periods of

Scheme 1 Synthetic procedure of multiblock copolymers derived from 4,4′-(adipoyldioxy)dicinnamic acid (CAC), poly(ε-caprolactone)diol (PCL-diol), and poly(ethylene glycol) (PEG)



time. After incubation the film was washed with distilled water and dried at room temperature for 24 h in vacuo. The degree of degradation was estimated from the weight loss according to the following equation. Weight loss (%) = 100 ($W_0 - W_t$)/W_0, where W_0 and W_t are the dry sample weight before and after the degradation. The weight loss averaged for two specimens was employed.

Tensile and shape-memory properties

Tensile tests of film specimens (length, 10 mm; width, 5 mm; thickness, ca. 200 μm) were performed at 20 ± 2 °C and 50 ± 2 °C to determine the tensile strength at break (σ_b), elongation at break (ε_b), and Young's modulus (E) using a Shimadzu AG-1 autograph equipped with a temperature-controlled thermo chamber. The strain rate was 20 mm/min. The averaged values for 5–10 specimens were employed with no more than 15% deviation from the mean. Shape-memory tests were carried out by thermocyclic mechanical experiments described in the previous paper [12].

Results and discussion

Synthesis of multiblock copolymers

A novel series of photosensitive CAC/PCL/PEG multiblock copolymers were prepared by a high-temperature solution polycondensation in diphenyl ether at 180 °C for 2 h as outlined in Scheme 1. The results of polycondensation are summarized in Table 1. The higher molecular weight copolymers were obtained in good yields. Their GPC curves showed a narrow and monomodal MW distribution, and this indicated that the copolymers did not contain unreacted PCL-diols and PEGs.

The chemical structures of the copolymers were confirmed by FTIR and ^{1}H-NMR. The FTIR spectra of the copolymers showed characteristic absorption bands at C–H stretching at 2,946 and 2,893 cm^{-1}, C = O ester at 1,726 and 1,760 cm^{-1}, aromatic C–C at 1,602 and 1,508 cm^{-1}, and C–O–C ether at 1,110 cm^{-1}, respectively. In addition, the sharp absorption due to *trans* ethylene group appeared at 1,637 cm^{-1}, suggesting that *trans* cinnamoyl group was successfully introduced into polymer backbone. This was also confirmed by the ^{1}H-NMR spectrum, which exhibited two doublet signals at 6.39 and 7.66 ppm with a coupling constant of 16 Hz, characteristic for *trans* cinnamoyl moiety. The copolymer compositions were determined by the integral peak ratio of 4.05 ppm (–CH_2OCO– of PCL) and 3.60 ppm (–C H_2O CH_2– of PEG) in ^{1} H-NMR spectrum. The observed compositions are listed in Table 1. The copolymer compositions are in good agreement with the feeding monomer compositions.

Photocuring of multiblock copolymers

The photocuring was performed in a dry film, which was cast from chloroform solution onto a quartz plate at

Table 1 Yields, compositions, and molecular weights of copolymers

Copolymer code	Yield (%)	PCL/PEG[a] (mol%)	M_n^b	M_w^b	M_w/M_n^b
CAC/PCL	85	100/0	39,000	56,700	1.42
CAC/PCL/PEG(75/25)	97	75/25	28,700	45,400	1.58
CAC/PCL/PEG(50/50)	93	48/52	26,400	40,500	1.53
CAC/PCL/PEG(25/75)	94	24/76	30,900	50,100	1.62
CAC/PEG	88	0/100	26,300	43,300	1.65

[a] Molar ratios of two components in the copolymers estimated from ^{1}H-NMR
[b] Determined via GPC with poly(ethylene glycol) and poly(ethylene oxide) standards

Table 2 Thermal properties and crystallinity of multiblock copolymers

Copolymer code	T_g^a (°C)	T_{cc}^a (°C)	T_m^a (°C)	ΔH_m^a (J/g)	X_c^b (%)
CAC/PCL	−64	−48	48	56	38
CAC/PCL/PEG(75/25)	−65	−44	34, 45[c]	54	36
CAC/PCL/PEG(50/50)	−64	−47	37, 44[c]	49	36
CAC/PCL/PEG(25/75)	−63	−48	40	56	35
CAC/PEG	−62	−50	40	57	34

[a] Determined for melt-quenched samples by DSC
[b] Degree of crystallinity determined for melt-pressed films by WAXS
[c] Double melting peaks appeared

ambient temperature, by irradiation of a 400-W high-pressure mercury lamp at $\lambda > 280$ nm. The reaction was monitored by UV absorption changes of the cast film of CAC/PCL/PEG(50/50). As shown in Fig. 1, cinnamate absorption at a maximum of 282 nm decreases with irradiation time, indicating that cinnamate group could undergo a photochemical reaction in the film state. Cinnamoyl group is well known to (2+2) photocycloaddition, resulting in the formation of cyclobutane ring [16].

Figure 2 shows gel yields and DS for CAC/PCL/PEG(75/25) melt-pressed film against irradiation time at ambient temperature. An increase in the irradiation time resulted in increased yields of the gel and reduced swellability. The gel contents and DS of the block copolymers after 60–90 min are summarized in Table 3. All films showed gel content of ca. 90%. As anticipated, DS increase with increasing PEG contents due to the increase in content of hydrophilic PEG component.

WAXS and DSC of multiblock copolymers

Wide angle X-ray scattering of the copolymers showed the sharp diffraction peaks (2θ) at around 21.8 ° and 23.8 ° due to PCL phase, and 19.6 ° and 23.8 ° due to

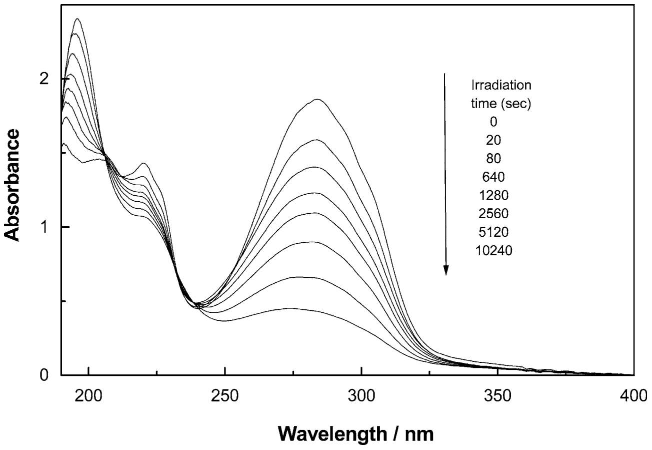


Fig. 1 Changes of the UV spectra absorbance of CAC/PCL/PEG (50/50) thin film upon irradiation with a 400-mW high-pressure mercury lamp at ambient temperature. UV intensity: 0.35 mW/cm^2

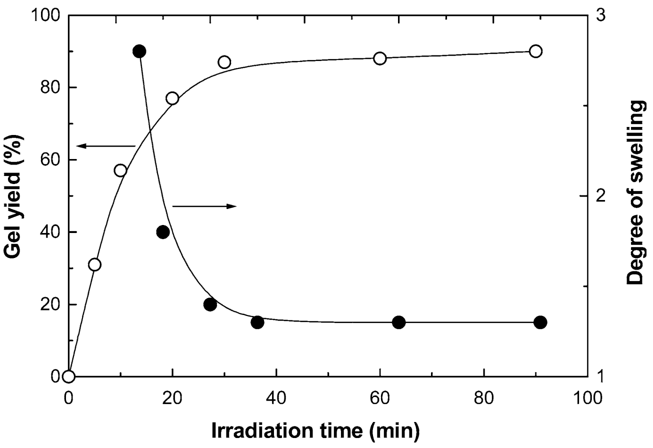


Fig. 2 Gel yields and degree of swelling (DS) of CAC/PCL/PEG (75/25) films against irradiation time. UV intensity: 1.0 mW/cm^2

Table 3 Gel yields and degree of swelling (DS) of multiblock copolymers

Copolymer code	Photocured time (min)	Gel content (%)	Degree of swelling
CAC/PCL	90	94	1.0
CAC/PCL/PEG(75/25)	60	90	1.3
CAC/PCL/PEG(50/50)	60	90	1.9
CAC/PCL/PEG(25/75)	60	94	2.8
CAC/PEG	60	87	5.6

Film thickness: ca. 200 μm. UV intensity: 1.0 mW/cm^2

PEG phase, respectively, showing the existence of PCL and PEG crystalline phases in the copolymers. The overall crystallinities of copolymer films calculated from WAXS patterns are reported in Table 2. They decrease slightly with increasing PEG contents. In addition, half-maximum width of the principal diffraction peak of PCL segments (21.8 °) was smaller for CAC/PCL film than the copolymer films, implying that PEG segments disturb the crystal growth of PCL segments.

The thermal properties of copolymers were determined by DSC for the melt-quenched samples. The phase transition temperatures such as glass transition (T_g), cold crystallization (T_{cc}), and melting (T_m) are summarized in Table 2. T_g was easily detected only in the melt-quenched sample. Single transitions were observed for all copolymers, which was ascribed to the fairy close values of T_g, −64 and −62 °C, respectively, for two components because PCL and PEG have been reported to be thermodynamically immiscible. CAC/PCL/PEG(75/25) and (50/50) showed double melting peaks due to PCL segments and PEG segments, suggesting the existence of two crystalline phases as shown in WAXS.

The effects of photocuring on T_m and ΔH_m of copolymers were examined by DSC for CAC/PCL/PEG(75/25) film. Their T_m and ΔH_m values were little changed during the photocuring for 60 min. This suggests that the crosslinking reactions between polymer main chains do not take place at the crystalline region, but in the amorphous region.

Tensile and shape-memory properties of multiblock copolymers

For the application of materials as novel types of medical devices, we have examined the tensile and shape-memory properties of photocured CAC/PCL/PEG (75/25) melt-pressed films. The results of tensile tests at 20 °C (below T_m) and 50 °C (above T_m) are shown in Table 4. As anticipated, the elongation (ε_b) at 20 °C decreases with increasing photocured time. The photocuring decreases significantly Young's modulus (E) of the copolymers at 20 °C. The tensile strength (σ_b) values of photocured films at 50 °C is one order of magnitude lower than those at 20 °C, which would be ascribed to the melting of crystalline PCL and PEG segments. The stress–strain curves of all photocured films at 20 °C showed a yield point clearly due to semi-crystalline nature of copolymer, whereas those at 50 °C demonstrated the elastic properties of the materials.

Shape-memory properties were determined by a thermocyclic mechanical test following a procedure described in the previous paper [12]. The sample was stretched up to 200% at a strain rate of 20 mm/min at 50 °C. While maintaining this strain for 5 min, the sample was quenched to 20 °C to cause it to crystallize whereby the temporary shape is fixed. After maintaining this strain for 10 min, the stress was removed completely, then the sample was placed in an oven controlled at 50 °C to cause crystallites to melt, and the shrinkage was measured after 10 min residence time. Shape-memory properties were qualified by the strain fixity rate (R_f) and the recovery rate (R_r): R_f (%) = 100 ($L_u - L$)/($L_e - L$), R_r (%) = 100 ($L_e - L_s$)/($L_e - L$), where L is the length of original sample, L_e is the length of extended sample at 50 °C, L_u is the length of the sample after unloading at room temperature, L_s is the length of the sample after shrinkage at 50 °C. Table 5 shows R_f and R_r values of CAC/PCL/PEG(75/25) films of gel contents at 33 and 57%. The thermocyclic mechanical test could not be performed for the films with larger gel contents because they showed much lower elongation than 200% at 50 °C. R_f and R_r do not depend on the cycle number. R_f and R_r of the films of gel contents at 57% are 100 and

Table 4 Gel contents and tensile properties of photocured CAC/PCL/PEG(75/25) films at 20 and 50 °C

Photocured time (min)	Gel content (wt%)	Temperature (°C)	σ_b (MPa)	ε_b (%)	E (MPa)
0	0	20	8.6	800	160
5	33	20	7.9	790	95
		50	0.34	380	0.04
10	57	20	8.0	500	96
		50	0.79	310	0.13
20	77	20	6.3	250	76
		50	0.72	120	0.44
30	87	20	6.0	170	60
		50	0.78	105	0.56

Film thickness: ca. 200 μm, UV intensity: 1.0 mW/cm^2, σ_b: tensile strength at break, ε_b: tensile elongation at break, E: Young's modulus

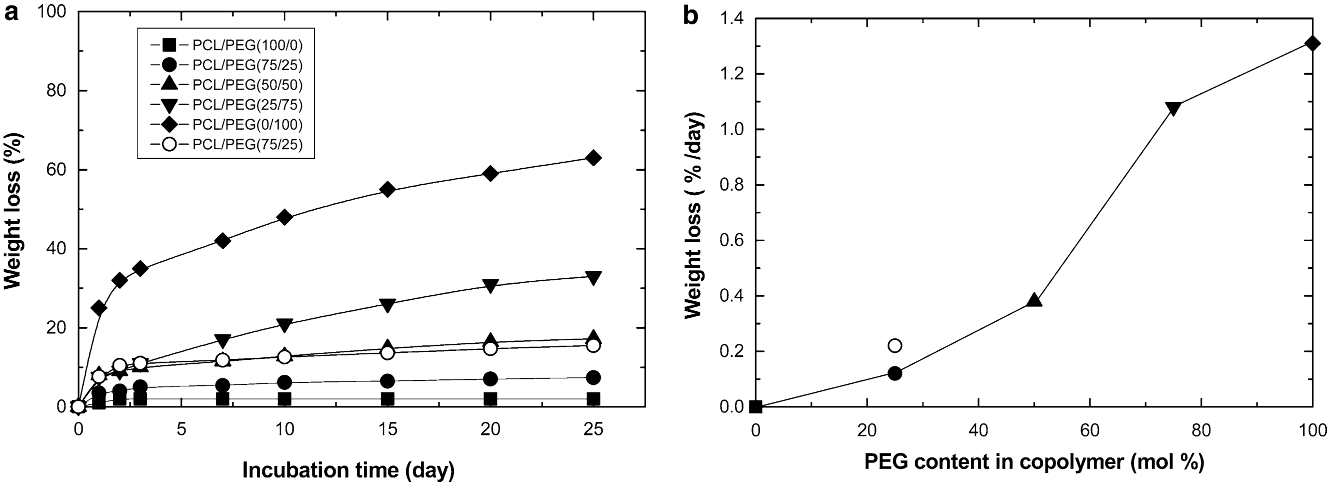


Fig. 3 **a** Weight loss of photocured multiblock copolymer films as a function of time under physiological conditions (1/15 mol phosphate buffer solution, pH 7.2, 37 °C): gel contents of the copolymer films (*closed symbol*) are shown in Table 3 and *open symbol* show the non-photocured film. **b** Degradation rate of photocured multiblock copolymer films as a function of PEG content ; the *symbols* are the same as Fig. 3a

88%, respectively. CAC/PCL film of gel content at 56% showed R_f and R_r of 100% at first cycle of the thermocyclic mechanical test [12]. The lower R_r for CAC/PCL/PEG (75/25) may be ascribed to the decreased crystallinity of the copolymer films mentioned above. R_r of the film of gel content at 33% is smaller than that of gel content at 57%, suggesting that a formation of network structure plays an important role for the shape-recovery at 50 °C. It is interesting to note that the lower response temperature (50 °C) of CAC/PCL/PEG(75/25) films may be favorable in medical applications where the use of high temperature should be avoided. The further studies on shape-memory properties of these multiblock copolymers are now in progress.

Hydrolytic degradation of multiblock copolymers

The hydrolytic degradation was performed under physiological conditions (1/15 mol phosphate buffer solution, pH 7.2, 37 °C). Figure 3a shows weight loss of photocured copolymer films with incubation time. A rapid weight loss is observed at an early period of incubation (within a few days), followed by slower hydrolysis during the latter period of degradation, irrespective of the copolymer composition of the photocured films. The first weight loss would be caused mainly by the degradation of non-crosslinked low molecular weight and/or loosely crosslinked polymer chains in photocured films. Figure 3b shows the rate of degradation, defined as weight loss (%) per day calculated from the approximately constant weight loss per day during the latter period of incubation (a few days to 25 days). The weight loss of CAC/PCL is hardly observed, whereas the rate of degradation increases significantly with increasing PEG content, which would be ascribed to the increased DS described in Table 3. The rate of degradation of CAC/PCL/PEG (75/25) of gel content at 90% (0.12%/day) is slower than that of non-photocured film (0.22%/day), demonstrating that the crosslinked polymer chains are reluctant to be hydrolyzed.

The in vivo degradation products are presumably PEG, monomeric and oligomeric ω-hydroxycaproic acid, and CAC, which was found to be degraded into 4-hydroxycinnamic acid and adipic acid [17]. They are relatively non-toxic and could be metabolized in a body.

Table 5 Strain fixity ratio (R_f) and strain recovery ratio (R_r) of photocured CAC/PCL/PEG(75/25) films

Gel content (%)	R_f(%)[a]			R_r(%)[b]		
	1 cycle	2 cycle	3 cycle	1 cycle	2 cycle	3 cycle
33	95	89	97	70	69	70
57	95	100	100	86	89	88

[a] Strain fixity rate at 20 ± 2 °C. The margin of error was ± 5%

[b] Strain recovery rate at 50 ± 2 °C. The margin of error was ± 5%

Conclusions

High-molecular weight photosensitive biodegradable multiblock copolymers were synthesized from PCL diol (MW = 3,000) and PEG (MW = 3,000) with CAC dichloride as a chain extender. The gel contents increased with UV irradiation time, and attained ca. 90% after 60 min for all copolymers. The DS in a distilled water and the rate of degradation in a phosphate buffer solution increased with increasing PEG components. The photocured CAC/PCL/PEG (75/25) film (gel content = 57%) showed the best shape-memory properties ($R_f = 100\%$ and $R_r = 88\%$). The biodegradable/biocompatible CAC/PCL/PEG (75/25) with shape-memory properties could have new potential biomedical applications such as surgical sutures and catheters.

References

1. Ishii M (1989) Developments of shape-memory polymers. CMC, Tokyo, p 10
2. Karouji M (1989) Developments of shape-memory polymers. CMC, Tokyo, p 30
3. Kim BK, Lee SY, Xu M (1996) Polymer 37:5781
4. Takahashi T, Hayashi N, Hayashi S (1996) J Appl Polym Sci 60:1061
5. Lin JR, Chen LW (1998) J Appl Polym Sci 69:1563–1575
6. Yang JH, Chun BC, Chung YC, Cho JH (2003) Polymer 44:3251
7. Lendlein A, Langer R, (2002) Science 296:1673
8. Ping P, Wang W,Chen X, Jing X (2005) Biomacromolecules 6:587
9. Zhu G, Liang G, Xu Q, Yu Q (2003) J Appl Polym Sci 90:1589
10. Lendlein A, Schmidt AM, Langer R (2001) Proc Natl Acad Sci USA 98:842
11. Lendlein A, Schmidt AM, Schroeter M, Langer R (2005) J Polym Sci Part A Polym Chem 43:1369
12. Nagata M, Sato Y (2005) J Polym Sci Part A Polym Chem 43:2426
13. Petrova PS, Manolova N, Rashkov I, Li S, Vert M (1998) Polym Int 45:419
14. Cohn D, Stern T, Gonzalez F, Epstein J (2002) J Biomed Mater Res 59:273
15. Nagata M, Hizakae S (2003) Macromol Biosci 3:412
16. For example, Egerton PL, Trigg J, Hyde EM, Reiser A (1981) Macromolecules 14:100
17. Nagata M, Hizakae S (2003) J Polym Sci Part A Polym Chem 41:2930