

# Morphology and Hydrolysis of PCL/PLLA Blends Compatibilized with P(LLA-*co*- $\epsilon$ CL) or P(LLA-*b*- $\epsilon$ CL)

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**ABSTRACT:** The effect of the compatibilizers, P(LLA-*co*- $\epsilon$ CL) and P(LLA-*b*- $\epsilon$ CL), on the morphology and hydrolysis of the blend of poly( $\epsilon$ -caprolactone) (PCL) and poly(L-lactide) (PLLA) was investigated. An addition of P(LLA-*co*- $\epsilon$ CL) or P(LLA-*b*- $\epsilon$ CL) into the blend could enhance the compatibility between the dispersed PCL domains and the PLLA matrix. The size of the PCL domains in the PLLA/PCL (70/30) blend containing P(LLA-*co*- $\epsilon$ CL) reduced more significantly with an increase in the content of the compatibilizer than that in the blend containing P(LLA-*b*- $\epsilon$ CL). The

molecular weight of the PLLA/PCL blend films compatibilized with P(LLA-*co*- $\epsilon$ CL) or P(LLA-*b*- $\epsilon$ CL) decreased during the hydrolysis and the decrease of the molecular weight of the blend films compatibilized with P(LLA-*co*- $\epsilon$ CL) was much more significant than that of the blend films compatibilized with P(LLA-*b*- $\epsilon$ CL). © 2002 Wiley Periodicals, Inc. *J Appl Polym Sci* 86: 1892–1898, 2002

**Key words:** biodegradable; blends; compatibilization; copolymerization; morphology

## INTRODUCTION

There has been growing interest in the biodegradable polymers for biomedical applications such as drug-releasing implants, bioresorbable surgical suture, or short-term fixation devices.<sup>1–5</sup> Among the biodegradable polymers, poly(L-lactide) (PLLA) and poly( $\epsilon$ -caprolactone) (PCL) are well known as biocompatible materials. These biodegradable polymers have been frequently studied as biodegradable matrices for prosthetics and controlled drug delivery. For drug-delivery systems, PLLA shows rapid hydrolysis with low permeability, whereas PCL shows good permeability with slow hydrolysis.<sup>6</sup>

Copolymerization and blending have been widely applied for optimizing properties of these biodegradable aliphatic polyesters. Random and block copolymers of L-lactide and  $\epsilon$ -caprolactone were utilized for regulating the degradation rate, mechanical properties, and drug release profiles.<sup>7–8</sup> The blend systems of PLLA with more flexible PCL have been investigated previously.<sup>9–11</sup> Only two studies on the blend of PLLA and PCL containing a compatibilizer, a triblock copolymer, has been reported.<sup>12–13</sup> In blends, the compatibility of components usually plays an important role

in determination of the properties of the blended polymers which influence the degradation of polymers.

In this work, we have used the blending technique to combine the good permeability of PCL with fast hydrolysis of PLLA for controlling the degradation rate of the matrix for drug deliveries. The blocky random copolymer or diblock copolymer was used as a compatibilizer of the blend to enhance the compatibility between PLLA and PCL in the blend. The effect of the compatibilizer on morphology and hydrolysis properties of the PLLA/PCL blend was studied.

## EXPERIMENTAL

### Materials

L-lactide (Aldrich) was purified by several recrystallizations with ethyl acetate and dried for 48 h at 50°C under vacuum. The  $\epsilon$ -caprolactone ( $\epsilon$ -CL, Aldrich) was dried over calcium hydride for 48 h at room temperature and then distilled under reduced pressure in a nitrogen atmosphere prior to use. Poly(ethylene glycol) methyl ether ( $M_w = 350$ ) purchased from Aldrich was dried by molecular sieve of 4 Å for 3 days. PLLA ( $M_w = 200,000$ ) and PCL ( $M_w = 170,000$ ) were purchased from Shimatzu and Union Carbide, respectively. P(LLA-*co*- $\epsilon$ CL) used as a compatibilizer for the PLLA/PCL blend was synthesized by ring-opening polymerization using stannous octoate as a catalyst as described in our previous article.<sup>14</sup> The composition of P(LLA-*co*- $\epsilon$ CL) used in this work was  $\epsilon$ -CL/L-LA = 50/50. The average number of sequential comono-

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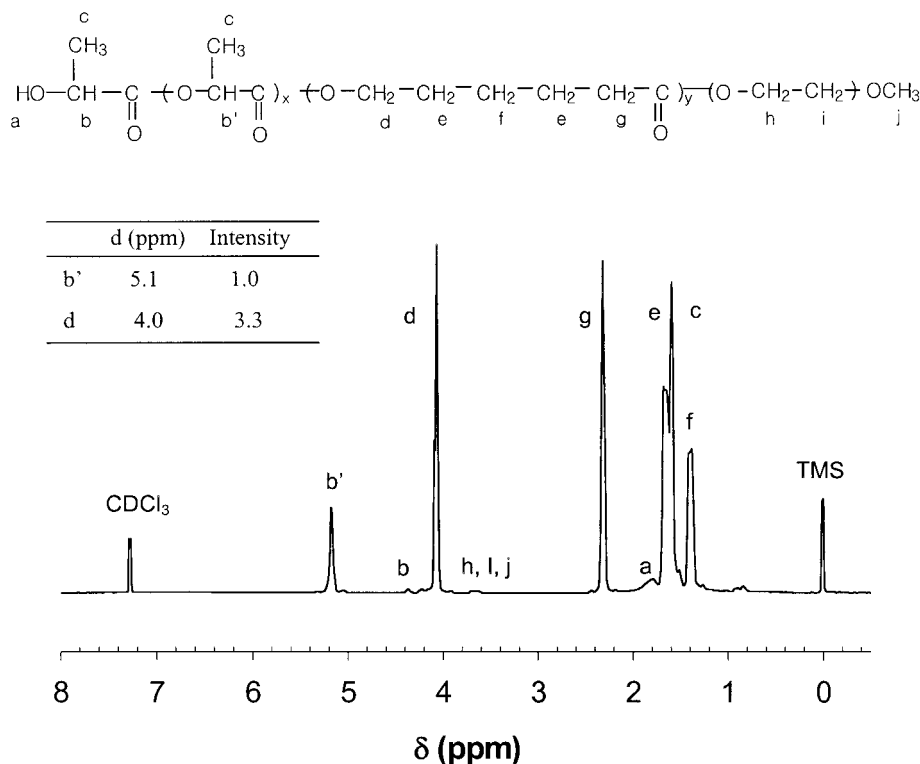


Figure 1  $^1\text{H-NMR}$  spectrum of P(LLA-*b*- $\epsilon\text{CL}$ ) copolymer.

mer units of  $\epsilon\text{-CL}$  and L-LA unit per P(LLA-*co*- $\epsilon\text{CL}$ ) chain were 3.4 and 2.0, respectively, which were determined from the  $^{13}\text{C-NMR}$  spectra of P(LLA-*co*- $\epsilon\text{CL}$ ). The average molecular weight of the random copolymer, P(LLA-*co*- $\epsilon\text{CL}$ ) ( $M_w = 51,000$ ), and the diblock copolymer, P(LLA-*b*- $\epsilon\text{CL}$ ) ( $M_w = 15,200$ ), was determined by gel permeation chromatography (GPC, Waters 150-CV).

#### Synthesis and characterization of P(LLA-*b*- $\epsilon\text{CL}$ )

P(LLA-*b*- $\epsilon\text{CL}$ ) was synthesized by ring-opening polymerization of  $\epsilon$ -caprolactone and L-lactide by using  $\text{CH}_3\text{-(PEG)-O}^-\text{K}^+$  as an initiator in a dry box filled with argon. The initiator,  $\text{CH}_3\text{-(PEG)-O}^-\text{K}^+$ , was prepared by following the procedures described elsewhere.<sup>15</sup> The copolymerization was conducted in a nitrogen-purged glass reactor equipped with magnetic stirring bar. The mixed solution of the  $\epsilon\text{-CL}$  and tetrahydrofuran (THF, dried over sodium) was added into the glass reactor and subsequently the initiator solution was introduced into the reactor under stirring. The polymerization was kept at  $30^\circ\text{C}$  for 3 min and then the THF solution of the L-lactide was added to the reactor. The polymerization continued further at  $80^\circ\text{C}$  for 10 min. The reaction products were precipitated with a sufficient amount of water and filtered, and then washed with hot water. After filtering, the product was washed with cold acetone several times

and dried under reduced pressure at  $40^\circ\text{C}$ . The composition of the resulting copolymers was determined by  $^1\text{H-NMR}$  spectrum obtained on a Bruker-AMX-500 NMR spectrometer. The mole fraction of  $\epsilon\text{-CL}$  unit in P(LLA-*b*- $\epsilon\text{CL}$ ) was calculated from the relative area of the peaks corresponding to the methine (L-LA, appeared at 5.11–5.14 ppm) and methylene ( $\epsilon\text{-CL}$ , appeared at 4.0 ppm) protons as shown in Figure 1 and thus the mole ratio of  $\epsilon\text{-CL/L-LA}$  in diblock copolymer was 62/38.

#### Preparation of blend films

The blend films with  $240\ \mu\text{m}$  thickness were prepared with a conventional solution casting method using chloroform as a solvent. The resulting films were dried *in vacuo* for 2 days to remove the solvent completely. The composition of all the blends was fixed at 70/30 (PLLA/PCL) by weight. The amount of the compatibilizer added into the PLLA/PCL blend varied from 5 to 15 phr.

#### Differential scanning calorimetry (DSC)

The thermal behavior of the noncompatibilized and compatibilized PLLA/PCL (70/30) blends was investigated by using DSC techniques (DuPont TA 2000). Each sample was scanned from  $-100$  to  $200^\circ\text{C}$  by heating at a rate of  $10^\circ\text{C}/\text{min}$  for the first run and

quenched to  $-100^{\circ}\text{C}$  and then heated again to  $200^{\circ}\text{C}$  for the second run under nitrogen atmosphere.

### Scanning electron microscopy (SEM)

The morphology of the polymer films was investigated by SEM by using a Philips SEM 535M. The specimens for the SEM images of the cross section of the films were prepared by fracturing the corresponding films in liquid nitrogen and then extracting the dispersed PCL domains from the PLLA/PCL blends.

### Hydrolysis

Hydrolysis was performed by using films of  $8\text{ mm} \times 5\text{ mm} \times 240\text{ }\mu\text{m}$  in 10 mL of a phosphate-buffered solution (0.1M  $\text{KH}_2\text{PO}_4$ , 0.1M NaOH) of pH 7.4 at  $50^{\circ}\text{C}$  for 4 weeks. The phosphate-buffered solution of all the samples was renewed every week. The film samples were immersed in a phosphate-buffered solution and were periodically recovered for the water uptake determination. The water on the film surface was removed with absorbent paper and the films were weighed every day during the hydrolysis. The amount of the water uptake was calculated using the following equation:

$$\% \text{ H}_2\text{O uptake} = 100 \times (W_{\text{wet}} - W_{\text{in}}) / W_{\text{in}} \quad (1)$$

where  $W_{\text{wet}}$  and  $W_{\text{in}}$  are weights of the wet and dried films.

### Intrinsic viscosity

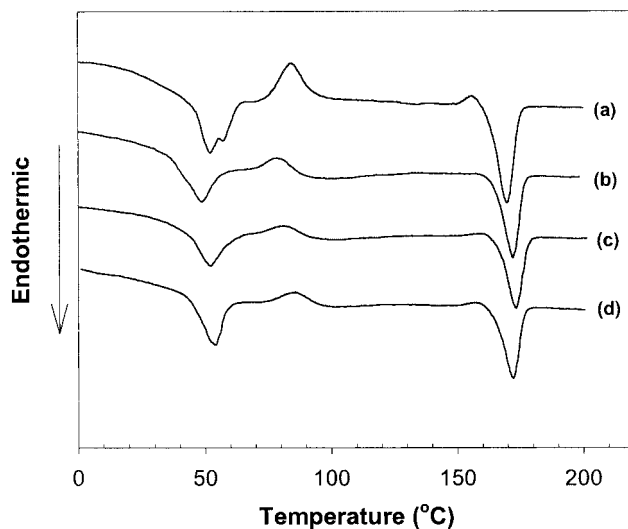
The intrinsic viscosity was measured with an Cannon-Fenske viscometer on the polymer solution in chloroform (0.006 g/10 mL) at  $30^{\circ}\text{C}$ . The viscosity-average molecular weight ( $M_v$ ) of the PLLA was determined from their intrinsic viscosity  $[\eta]$  by using the following equation<sup>16</sup>:

$$[\eta] = 5.45 \times 10^{-4} \times M_v^{0.73} \quad (2)$$

## RESULTS AND DISCUSSION

### Compatibility of PCL and PLLA in the blend with and without containing P(LLA-co- $\epsilon$ CL)

Figure 2 shows the DSC thermograms of the PLLA/PCL (70/30) blends compatibilized with various amount of P(LLA-co- $\epsilon$ CL); results are summarized in Table I. The peak temperature of an endotherm for the dispersed PCL domains and the PLLA matrix in the blend does not change significantly with the addition of P(LLA-co- $\epsilon$ CL). However, it is found that the addition of the compatibilizing agent into the PLLA/PCL



**Figure 2** DSC thermograms of the PLLA/PCL (70/30) blends with various amounts of P(LLA-co- $\epsilon$ CL): (a) 0 phr; (b) 5 phr; (c) 10 phr; (d) 15 phr.

blend slightly reduced the area of the endothermic peak of the dispersed PCL domains, as shown in Table I. This result implies that the crystallinity, one of the important factors in the hydrolysis of polymer, is decreased with the addition of P(LLA-co- $\epsilon$ CL).

Figure 3 shows the SEM micrographs of the fractured cross section of the blend film from which the dispersed PCL domains were extracted. It is found that the addition of the P(LLA-co- $\epsilon$ CL) into the PLLA/PCL blend significantly reduces the size of the dispersed PCL domains from  $\sim 10\text{ }\mu\text{m}$  to  $\sim 3\text{ }\mu\text{m}$ . This indicates that P(LLA-co- $\epsilon$ CL) used as a compatibilizer can contribute to the enhancement of the compatibility between the dispersed PCL domains and the PLLA matrix. It is also found that, for the PLLA/PCL blends compatibilized with P(LLA-co- $\epsilon$ CL), the size of the dispersed PCL domain is significantly reduced with addition of the compatibilizer; however, it is not further reduced by increasing the concentration of the compatibilizer over 5 phr. Similar results on the polystyrene/ethylene-propylene rubber blends compatibilized with poly(styrene/ethylene-butylene) diblock copolymer have already been reported by Polizu and Favis.<sup>17</sup> The excess of P(LLA-co- $\epsilon$ CL) seems to be dissolved in the PLLA matrix rather than at the interface between the dispersed PCL domains and the PLLA matrix. To investigate the miscibility of the PLLA matrix with P(LLA-co- $\epsilon$ CL), the PLLA/P(LLA-co- $\epsilon$ CL) binary blend film was prepared and the blend morphology was investigated. Figure 4 shows the SEM images of the fractured surface of the binary blend films after P(LLA-co- $\epsilon$ CL) was etched with THF. As shown in Figure 4, the P(LLA-co- $\epsilon$ CL) domain is not observed and thus the P(LLA-co- $\epsilon$ CL) is considered to be mis-

TABLE I  
DSC Results of the PLLA/PCL (70/30) Blends with Various Amount of Compatibilizer

Compatibilizer (phr)	PCL		PLLA	
	$T_m$ (°C)	$\Delta H_m$ (J/g)	$T_m$ (°C)	$\Delta H_m$ (J/g)
P(LLA- <i>co</i> - $\epsilon$ CL)				
0	57 $\pm$ 0.2	22.1	172.5 $\pm$ 0.05	22.4
5	49 $\pm$ 0.09	16.9	170 $\pm$ 0.1	16.8
10	50 $\pm$ 0.15	15.3	172 $\pm$ 0.08	16.5
15	51 $\pm$ 0.12	14.6	171 $\pm$ 0.1	16.2
P(LLA- <i>b</i> - $\epsilon$ CL)				
0	57 $\pm$ 0.2	22.1	172.5 $\pm$ 0.05	22.4
5	50 $\pm$ 0.07	21.7	173.0 $\pm$ 0.03	17.6
10	48 $\pm$ 0.02	17.5	172.4 $\pm$ 0.09	15.4
15	51 $\pm$ 0.16	19.0	173.2 $\pm$ 0.11	16.9

cible with the PLLA matrix. The miscibility between PLLA and P(LLA-*co*- $\epsilon$ CL) was also supported by DSC experiment. As shown in Figure 5, all the binary blends of PLLA and P(LLA-*co*- $\epsilon$ CL) studied exhibit single glass transition temperature.

#### Compatibility of PCL and PLLA in the blend with and without containing P(LLA-*b*- $\epsilon$ CL)

Figure 6 shows the DSC thermograms of the PLLA/PCL (70/30) blends compatibilized with P(LLA-*b*- $\epsilon$ CL), and the results are summarized in Table I. It is found that the endothermic peak area of the dispersed PCL phase in the blends decreases with the addition of P(LLA-*b*- $\epsilon$ CL) up to 10 phr and slightly increases above 10 phr. The incorporation of the appropriate

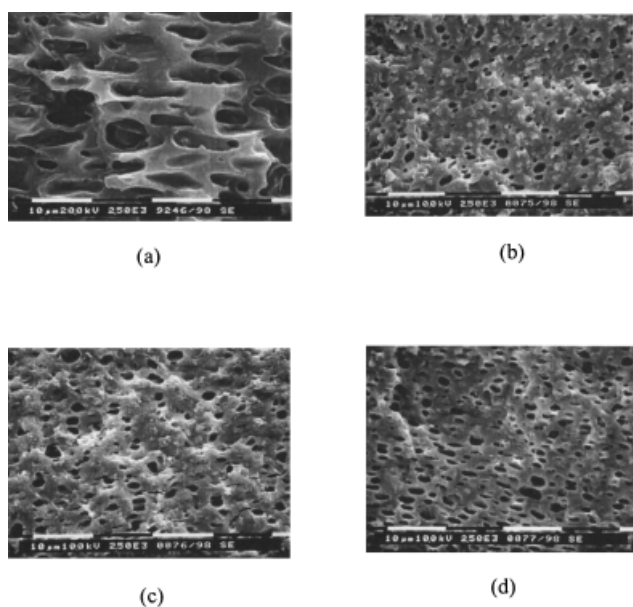
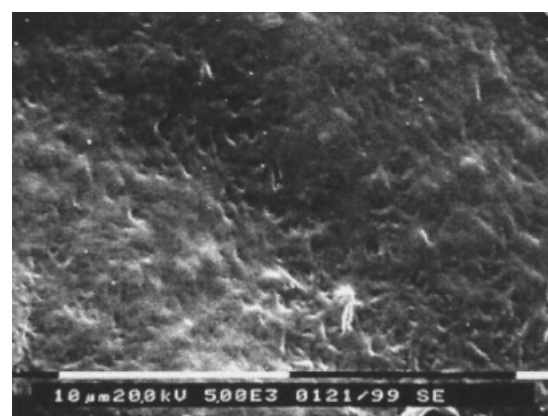
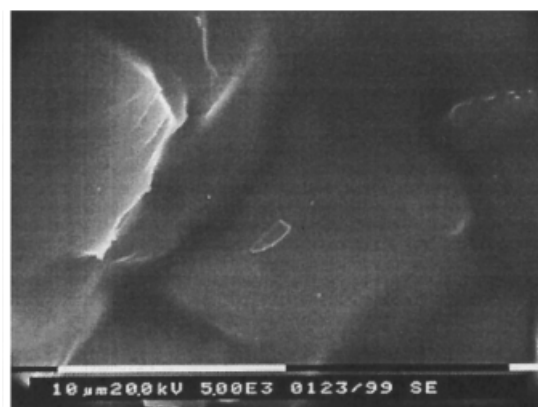


Figure 3 SEM image of the fractured surface of the PLLA/PCL (70/30) films from which the PCL domains were extracted with change of the amount of P(LLA-*co*- $\epsilon$ CL) added: (a) 0 phr; (b) 5 phr; (c) 10 phr; (d) 15 phr.

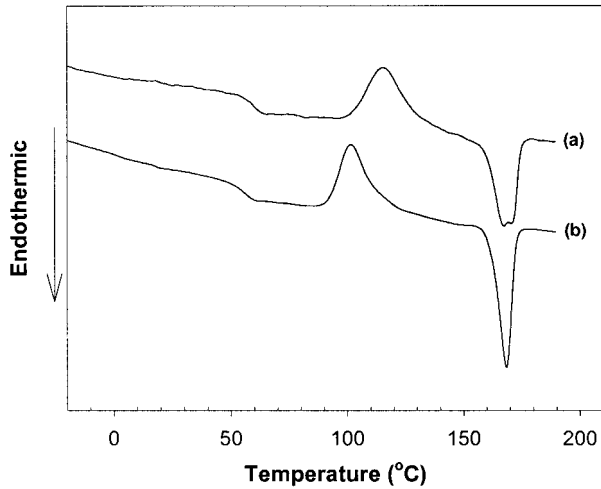


(a)



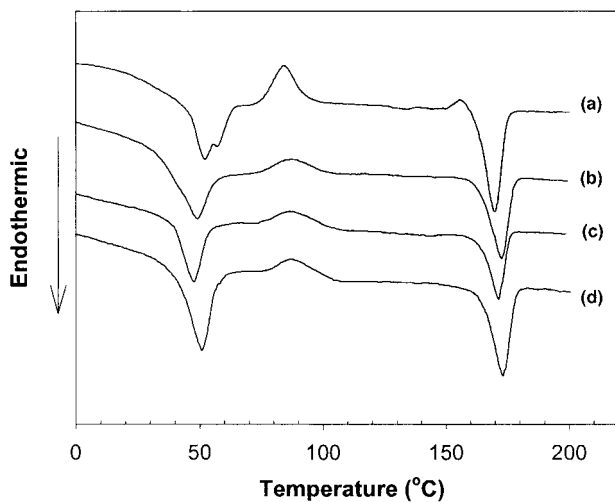
(b)

Figure 4 SEM image of the fractured surface of the binary blend films from which P(LLA-*co*- $\epsilon$ CL) was extracted: (a) PLLA/P(LLA-*co*- $\epsilon$ CL) (70/5); (b) PLLA/P(LLA-*co*- $\epsilon$ CL) (70/10).

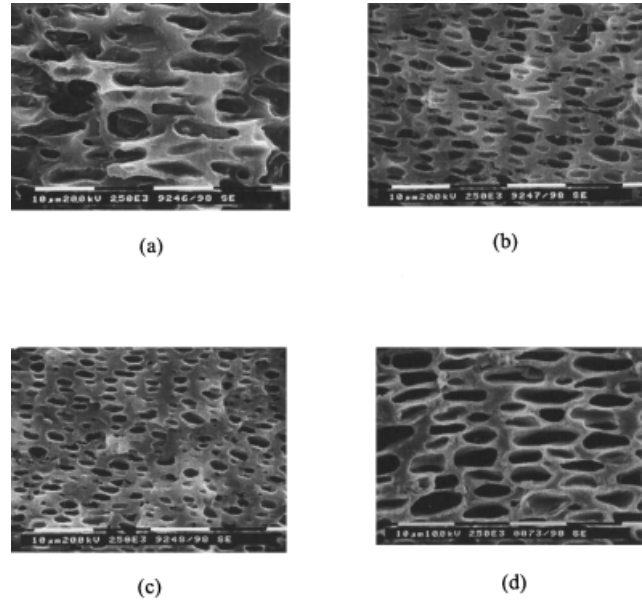


**Figure 5** DSC thermograms of the PLLA/P(LLA-co-εCL) binary blend: (a) PLLA/P(LLA-co-εCL) (70/5); (b) PLLA/P(LLA-co-εCL) (70/10).

amount of the diblock copolymer into the blend could lead to a suppression of the crystallization of the dispersed PCL domains in the blend but the excess amount of asymmetric diblock copolymer seems to increase the crystallization of PCL. The endothermic peak area of the PLLA matrix was not changed with an increase in the P(LLA-*b*-εCL) content. Figure 7 shows the SEM micrographs of the compatibilized PLLA/PCL. The dispersed domain size is found to decrease with an increase of the compatibilizer content up to 10 phr. It implies that the P(LLA-*b*-εCL) added in the blend seems to be located at the interface of the PLLA matrix and the dispersed PCL domains. However, the addition of 15 phr diblock copolymer increased the dimension of the dispersed PCL domains,



**Figure 6** DSC thermograms of the PCL/PLLA (30/70) blends with various amounts of P(LLA-*b*-εCL): (a) 0 phr; (b) 5 phr; (c) 10 phr; (d) 15 phr.



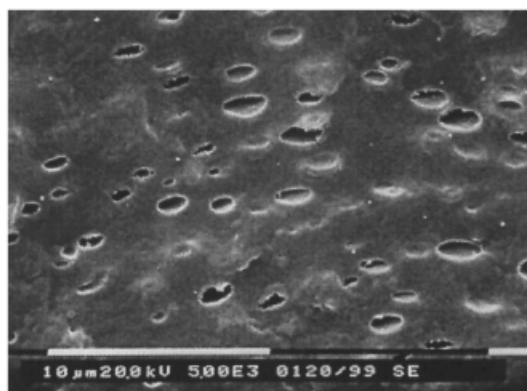
**Figure 7** SEM images of the fractured surface of the PLLA/PCL (70/30) films from which the PCL domains were extracted with change of the amount of P(LLA-*b*-εCL) added: (a) 0 phr; (b) 5 phr; (c) 10 phr; (d) 15 phr.

as shown in Figure 7(d). According to the previous study of Brown et al.,<sup>18</sup> the excess diblock copolymer formed the micelles in the PS/PMMA blend and the micelles were in the PMMA phase because the PMMA segment in the copolymer was richer. Because the PCL segments of P(LLA-*b*-εCL) used in this study are richer, the excess P(LLA-*b*-εCL) in the PCL/PLLA blend seems to form micelles without being located at the interface. These micelles may be located in the dispersed PCL domains rather than in the PLLA matrix. If the micelles are present in the PLLA matrix, the micelles should be the type of PCL core and PLLA shell and the micelle domains with a size of 1–2 μm, which has been observed from the SEM micrographs of the blend of PLLA with diblock copolymer, as shown in Figure 8, should be observed in the PLLA matrix of the blend compatibilized with P(LLA-*b*-εCL). However, the micelle domains with a size of 1–2 μm were not observed in the PLLA matrix, as shown in Figure 7(d). The micelles formed by the diblock copolymer may be of the type of PLLA core and PCL shell and the micelles would dissolve in the dispersed PCL domains. Because the excess of the diblock copolymer tends to form the micelles, the addition of an excess amount of the asymmetric diblock copolymer into the blends can make the compatibility of PLLA/PCL blend poorer.

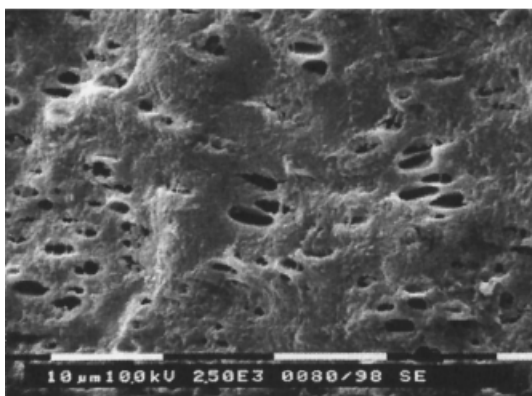
#### Molecular weight change during the hydrolysis

The studies on the hydrolysis of the PLLA matrix in the PLLA/PCL blend were conducted by immersion

of the blend film into the phosphate buffer of pH 7.4 at 50°C. The hydrolysis rate is known to be proportional to water and ester concentrations and to be autocatalyzed by the generated carboxylic end groups. The change of water uptake content during hydrolysis was almost same among all the samples studied. Mass loss becomes detectable only when water-soluble oligomers are formed upon hydrolysis or eluted into the surrounding medium. During the hydrolysis performed at 50°C for 4 weeks, mass loss was not observed. Figure 9 shows the change of viscosity-average molecular weight against hydrolysis time for PLLA matrix in the blend compatibilized with P(LLA-co- $\epsilon$ CL) or P(LLA-*b*- $\epsilon$ CL). The viscosity-average molecular weight of PLLA in the blend films compatibi-

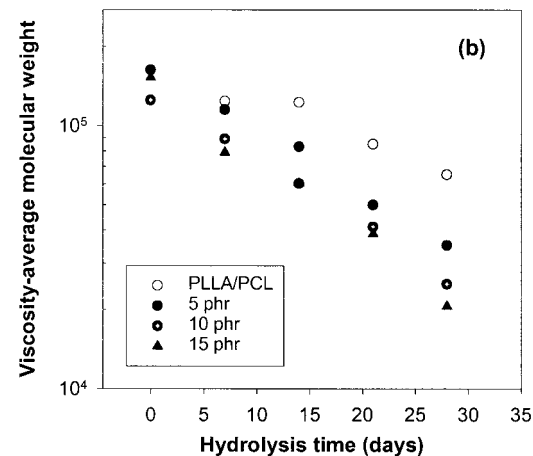
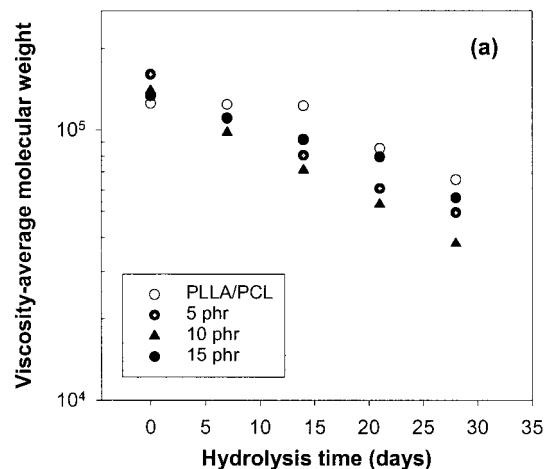


(a)



(b)

**Figure 8** SEM image of the fractured surface of the PLLA/P(LLA-*b*- $\epsilon$ CL) films from which P(LLA-*b*- $\epsilon$ CL) domains were extracted: (a) PLLA/P(LLA-*b*- $\epsilon$ CL) (70/5); (b) PLLA/P(LLA-*b*- $\epsilon$ CL) (70/10).



**Figure 9** The viscosity-average molecular weight change of the PLLA/PCL (70/30) blend films with various amounts of compatibilizer during the hydrolysis: (a) P(LLA-*b*- $\epsilon$ CL); (b) P(LLA-*co*- $\epsilon$ CL).

lized with P(LLA-*co*- $\epsilon$ CL) or P(LLA-*b*- $\epsilon$ CL) was decreased during the hydrolysis. The decrease of the molecular weight seems to be mainly influenced by the concentration of the terminal carboxyl group because the crystallinity of the PLLA matrix in the blend does not change with the content of the added P(LLA-*co*- $\epsilon$ CL). The PLLA matrix of the blend films compatibilized with excess amount of P(LLA-*co*- $\epsilon$ CL) contains some amount of P(LLA-*co*- $\epsilon$ CL), as has already been described in the previous section. The PLLA matrix and P(LLA-*co*- $\epsilon$ CL) dissolved in the PLLA matrix will be degraded by the hydrolysis. The degradation of P(LLA-*co*- $\epsilon$ CL) with low molecular weight ( $M_w = 51,000$ ) greatly decreases the intrinsic viscosity of the PLLA matrix due to the increase of the concentration of the terminal carboxyl group. Therefore, as shown in Figure 9, the decrease in the molecular

weight of the blend films compatibilized with P(LLA-co- $\epsilon$ CL) is much more significant than that of the blend films compatibilized with P(LLA-*b*- $\epsilon$ CL).

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