Blends of Aliphatic Polyesters. II. Hydrolysis of Solution-Cast Blends from Poly(L-lactide) and Poly(ε-caprolactone) in Phosphate-Buffered Solution

HIDETO TSUJI,[1] YOSHITO IKADA[2]

[1] Department of Ecological Engineering, Faculty of Engineering, Toyohashi University of Technology, Tempaku-cho, Toyohashi, Aichi 441, Japan

[2] Research Center for Biomedical Engineering, Kyoto University, 53 Kawahara-cho, Shogoin Sakyo-ku, Kyoto 606, Japan

ABSTRACT: Blend films were prepared from poly(L-lactide)(PLLA) and poly(ε-caprolactone)(PCL) with different PLLA contents [X_{PLLA} (w/w) = PLLA/(PCL + PLLA)] by the solution-casting method and their hydrolysis behaviors were investigated up to 20 months in a phosphate-buffered solution of pH 7.4 at 37°C by gel permeation chromatography, tensile testing, differential scanning calorimetry, and gravimetry. Polarizing microscopic observation and dynamic mechanical analysis revealed that PCL and PLLA were phase-separated in blend films before hydrolysis. The mass remaining, molecular weight, and tensile strength of the blend films with X_{PLLA} of 0.5 and 0.75 decreased more rapidly by hydrolysis than those of the nonblended PLLA, while the elongation at break of the blend film of X_{PLLA} = 0.25 decreased the slowest. The rate constant for hydrolysis (k) calculated from the M_n change during hydrolysis was higher for blend films of X_{PLLA} = 0.5 and 0.75 than those expected from k of nonblended PLLA and PCL. The melting temperature (T_m) of PLLA in the blend and nonblended films of X_{PLLA} = 0.5, 0.75, and 1 decreased from 179 to 161, 160, and 175°C upon hydrolysis for 20 months, respectively, while that for X_{PLLA} = 0.25 slightly increased from 176 to 177°C. On the other hand, T_m and the crystallinity of PCL was significantly increased by hydrolysis for 20 months, irrespective of X_{PLLA}. © 1998 John Wiley & Sons, Inc. J Appl Polym Sci **67:** 405–415, 1998

Key words: polylactide; polycaprolactone; polymer blends; hydrolysis

INTRODUCTION

Aliphatic polyesters such as poly(L-lactide)(PLLA), poly(D-lactide), poly(DL-lactide)(PDLLA), polyglycolide, poly(β-hydroxybutyrate) (PHB), and poly(ε-caprolactone)(PCL) and their copolymers have been used in surgical, pharmaceutical, and industrial applications due to their biodegradability in the human body as well as in the environ-ment.[1–9] The key basic properties required to these biodegradable polyesters include degradation kinetics, initial mechanical properties, and a balanced time course between the degradation and its strength change, which are dependent on the application purpose of the biodegradable polymers and the environment to which they are exposed during or after their practical use.

The conventional means employed for fabricating biodegradable products possessing optimal physical properties are monomer synthesis, molecular weight adjustment, copolymerization, and blending. Especially, the last two, copolymerization and blending, have been widely utilized for

improving the performance of biodegradable aliphatic polyesters which have attracted much more interest than have other synthetic and natural polymers. For instance, we demonstrated that biodegradable materials with a wide variety of mechanical properties can be prepared by simple blending of glassy amorphous PDLLA with rubbery crystalline PCL without using a copolymerization technique and, in addition, the initial mechanical properties of the blends prior to hydrolysis can be predicted from those of the constituent homopolymers, even though the two polymers are phase-separated.[10] Recently, Hiljanen-Vainio et al. demonstrated that copolymerization of DL-lactide with a small amount of ε-caprolactone yielded a biodegradable product possessing unique properties quite different from those of the DL-lactide homopolymer.[11]

The present study describes the hydrolysis results of blends between crystallizable glassy PLLA and crystallizable rubbery PCL as a model of phase-separated aliphatic polyester blends. The glass transition temperature (T_g) of PLLA is around 60°C, while that of PCL is around -60°C. The crystallizable glassy PLLA is more convenient than is the amorphous glassy PDLLA for hydrolysis study,[10] because the melting temperature (T_m) and crystallinity (x_c) of PLLA is available from differential scanning calorimetry (DSC). Physical properties and degradation behaviors of copolymers from L-lactide and ε-caprolactone will be published in the near future.

EXPERIMENTAL

Materials

The synthesis and characteristics of PLLA and PCL used in this work were described in previous articles.[10,12,13] Ring-opening polymerization of L-lactide and ε-caprolactone was performed in bulk at 140°C for 10 and 72 h, respectively, using stannous octoate (0.03 wt %) as a polymerization catalyst.[14] The molecular characteristics of PLLA and PCL obtained are listed in Table I. The blend films used for the hydrolysis study were prepared by the method described in a previous article.[10] Briefly, methylene chloride solutions of different PLLA and PCL concentrations were prepared at a total polymer concentration of 1.0 g/dL and then cast onto flat glass plates, followed by solvent evaporation at room temperature for approximately 1 week. To avoid reaching a dried state of

quasi-equilibrium, solvent evaporation was performed very slowly as reported in previous articles.[10,15–17] The resulting films were dried *in vacuo* for 1 week and stored at room temperature for more than 1 month to allow equilibrium to be attained. DSC, tensile testing, and dynamic mechanical relaxation measurements were performed on the blend films of 50 μm thickness, because Grizzi et al. reported that inhomogeneous hydrolysis occurred in a phosphate-buffered solution when the film thickness surpassed 2 mm.[18] A morphology study was performed on films of 25 μm thickness.

Hydrolysis

Hydrolysis was performed using films of 1.8 mm $\times$ 3.0 mm $\times$ 50 μm in 20 mL of a 0.15M phosphate-buffered solution of pH 7.4 at 37°C for a predetermined period of time. After hydrolysis, films were washed twice and immersed in double-distilled water at room temperature, followed by drying *in vacuo* for at least 2 weeks.

Measurements

The crystallization temperature (T_c), T_m, and the enthalpy of crystallization and melting (ΔH_c and ΔH_m, respectively) of the blend films were determined by a Shimadzu DT-50 differential scanning calorimeter. Films were heated under a nitrogen gas flow at a rate of 10°C/min. DSC results were calibrated using indium as the standard. The crystallinity of PCL ($x_{c,\mathrm{PCL}}$) in the blend films before hydrolysis was calculated under the assumption that the enthalpy of the glass transition of PLLA in the blend films ($\Delta H_{g,\mathrm{PLLA}}$) was constant, irrespective of the mixing ratio of the two polymers, and the same as that of the nonblended PLLA film before hydrolysis ($\Delta H_{g,\mathrm{PLLA}} = 3$ J/g of PLLA). Under this assumption, the x_c of PLLA, PCL, and the total polymer in the films ($x_{c,\mathrm{PLLA}}$, $x_{c,\mathrm{PCL}}$, and $x_{c,\mathrm{tot}}$, respectively) were calculated for the blend films with different PLLA contents (X_{PLLA}) by the following equations[10,12]:

$$x_{c,\mathrm{PLLA}}(\%) = 100 \times (\Delta H_{m,\mathrm{PLLA}} + \Delta H_{c,\mathrm{PLLA}})/(X_{\mathrm{PLLA}} \cdot 93) \quad (1)$$

$$x_{c,\mathrm{PCL}}(\%) = 100 \cdot (\Delta H_t - \Delta H_{g,\mathrm{PLLA}} \cdot X_{\mathrm{PLLA}})/[(1 - X_{\mathrm{PLLA}}) \cdot 142] \quad (2)$$

Table I   Characteristics of Blend Films Before and After Hydrolysis for 20 Months

X_{PLLA}	Hydrolysis Time (Months)	Characteristics and Properties of Blend Films								
		M_w ($\times 10^5$)	M_w/M_n	$T_{m,PCL}$ (°C)	$x_{c,PCL}$ (%)	$T_{m,PLLA}$ (°C)	$x_{c,PLLA}$ (%)	x_c,t_{ot} (%)	σ_B (kg/mm^2)	ε_B (%)
0	0	2.63	2.0	65.0	67			67	1.1	245
0.25	0	4.01	2.5	64.8	68	176	17	55	1.7	50
0.5	0	5.50	2.7	64.6	55	179	47	51	1.4	34
0.75	0	7.95	3.1	64.5	54	179	52	53	4.0	393
1	0	11.88	2.6			179	51	51	4.9	23
0	20	0.59	2.2	65.3	73			73	0.4	1
0.25	20	0.94	3.7	65.3	a	177	a	a	0[b]	1
0.5	20	0.48	4.6	65.2	a	161	a	a	0	0
0.75	20	0.21	7.3	64.8	a	160	a	a	0	0
1	20	0.75	4.1			175	72	72	0	0

[a] Not estimated because real X_{PLLA} values were not evaluated after hydrolysis.
[b] Between 0 and 0.1.

$$x_{c,tot}(\%) = x_{c,PLLA} \cdot X_{PLLA}$$
$$+ x_{c,PCL} \cdot (1 - X_{PLLA}) \quad (3)$$
$$X_{PLLA}(w/w) = PLLA/(PCL + PLLA) \quad (4)$$

where ΔH_t (J/g of the polymer) is the enthalpy of the overall transition including $\Delta H_{g,PLLA}$ and ΔH_m of PCL appearing around 60°C. The $\Delta H_{c,PLLA}$ (J/g of the polymer) is the ΔH_c of PLLA around 100°C, while 93 J/g of PLLA and 142 J/g of PCL is the enthalpy of fusion of PLLA and PCL crystals having the infinite crystal thickness reported by Fischer et al.[19] and Crescenzi et al.,[20] respectively.

Tensile properties of the blend films were measured at 25°C and 50% relative humidity using a tensile tester at a crosshead speed of 100%/min. The initial length of specimens was always kept at 20 mm. Dynamic mechanical analysis of the blend films was performed using an Orientec Rheovibron DDV-01F at 35 Hz and a heating rate of 4°C.

The molecular weight distribution of the blend polymers was evaluated in chloroform at 40°C by a Tosoh GPC system with TSK gel columns (GMH$_{XL} \times 2$) using polystyrene as the standard. The morphology of the blend films of a thickness of 25 μm was studied with a Zeiss polarizing microscope.

RESULTS AND DISCUSSION

Before Hydrolysis

Crystalline Structure

As demonstrated in Table I, both $T_{m,PCL}$ and $T_{m,PLLA}$ before hydrolysis are constant at X_{PLLA} be-

tween 0.25 and 0.75 except for $T_{m,PLLA}$ at X_{PLLA} = 0.25, suggesting that the crystallite thickness of the crystallizable components, which is closely related to T_m,[21] is identified by the presence of the other crystallizable component. On the other hand, a significant reduction of $x_{c,PCL}$ for X_{PLLA} = 0.5 and 0.75 and $x_{c,PLLA}$ for X_{PLLA} = 0.25 is noticed. This indicates that the nucleation of crystallites rather than crystallite growth of one component is disturbed by the other crystallizable component. The observed decrease in T_m and x_c suggests that the components which have first crystallized during solvent evaporation are PCL and PLLA for X_{PLLA} = 0.25 and X_{PLLA} = 0.5 and 0.75, respectively. The previous finding that $x_{c,PCL}$ was constant for blends solution-cast from crystallizable PCL and amorphous PDLLA, irrespective of the polymer mixing ratio,[10] must be due to no effect of the noncrystallizable PDLLA on the crystallization of PCL. The present result that $T_{m,PLLA}$ slightly decreased at X_{PLLA} = 0.25 whereas $T_{m,PCL}$ remained unvaried for X_{PLLA} between 0 and 0.75 indicates that the disturbance by the other crystallizable component on crystallite growth is weaker for PCL than for PLLA, probably due to higher molecular mobility of PCL ($T_g = -60°C$)[22,23] than that of PLLA ($T_g = 60°C$)[24,25] at room temperature. The $x_{c,tot}$ of the blend films with X_{PLLA} = 0.25, 0.5, and 0.75 is 8, 8, and 2% smaller, respectively, than those expected if PCL and PLLA molecules crystallized independently from each other as in nonblended films. If PCL and PLLA have been phase-separated before their crystallization starts, such a decrease in $x_{c,PCL}$, $x_{c,PLLA}$, $x_{c,tot}$, and $T_{m,PLLA}$ in the blend films would

not occur. Therefore, it is likely that at least before crystallization PCL and PLLA probably are not completely phase-separated in the presence of solvent molecules and have some interaction with each other as in the case of blends from PCL and PDLLA.[10] However, as will be mentioned below, PCL and PLLA undergo phase separation after completion of solvent evaporation.

Morphology

Figure 1 shows polarizing optical photomicrographs of films with different X_{PLLA}. Spherulites with the maximum radius of 400 μm and periodical extinction bands along the radial direction are noticed for the nonblended PCL, while periodical extinction becomes disordered when X_{PLLA} increases to 0.3. The morphological disorder observed for PCL spherulites at $X_{PLLA} = 0.3$ strongly suggests that spherulite formation and crystallization have first occurred for PCL in precedence of PLLA crystallization, probably because PLLA molecules have been trapped in the PCL spherulites. The blend film of $X_{PLLA} = 0.25$ seems to be composed of PCL spherulites containing a small-sized PLLA phase. As a result, crystallization of PLLA may be hindered, as is evident in Table I from the decrease in $T_{m,PLLA}$ and $x_{c,PLLA}$ for $X_{PLLA} = 0.25$. When X_{PLLA} increases to 0.4, normal PCL spherulites no longer appear, indicating strong interference of PCL crystallization by coexisting PLLA molecules. At $X_{PLLA} = 0.5$, a complicated phase-separated morphology is observed. It is likely that simultaneous crystallization of PCL and PLLA has taken place, followed by subsequent phase separation. Assemblies of small crystallites noticed for X_{PLLA} between 0.6 and 0.8 suggest that predominant spherulite formation has not occurred for either of the crystallizable components. However, in spite of a very disordered morphology for X_{PLLA} between 0.6 and 0.8, $T_{m,PLLA}$ and $x_{c,PLLA}$ for $X_{PLLA} = 0.75$ were almost the same for $X_{PLLA} = 1$. This implies that microscopic crystallization of PLLA was not strongly disturbed by the presence of PCL molecules. When X_{PLLA} increases to 0.9, spherulite formation is observed for PLLA, but the morphology is a little disturbed by the presence of PCL molecules. They may be trapped in the PLLA spherulites as a dispersed phase. The nonblended PLLA ($X_{PLLA} = 1$) shows normal spherulites with a radius of 20 μm.

Phase Structure

The phase separation of PCL and PLLA in the blend films can be evidenced by the viscoelastic properties of the films. Their storage modulus (G') and loss tangent (tan δ) are presented in Figure 2. Apparently, the phase-transition temperatures including $-60°C$ (T_g of PCL[22,23]), 60°C (T_m of PCL,[22,23] and T_g of PLLA[24,25]) and 170°C (T_m of PLLA[12,24]) of the blend films virtually are not influenced by varying the X_{PLLA} of the blends. The temperature dependence of G' and tan δ for $X_{PLLA} = 0.3$ is similar to that for $X_{PLLA} = 0$ (nonblended PCL) while the temperature dependence of G' and tan δ for $X_{PLLA} = 0.5$ and 0.7 is similar to that for $X_{PLLA} = 1$ (nonblended PLLA), suggesting that the PCL and the PLLA phases compose the continuous phase in the blend films for $X_{PLLA} = 0.3$ and for $X_{PLLA} = 0.5$ and 0.7, respectively. The G' of the blend films at temperatures between -60 and 60°C increases with an increase in X_{PLLA} when compared at the same temperature, while the G' of blend films of X_{PLLA} above 0.5 increases with the increasing X_{PLLA} for the temperature range between 60 and 150°C. No remarkable dependence of the transition temperatures on the blend composition also supports the occurrence of phase separation in the blends. This is in good agreement with the results of compression-molded blends from PCL and poly(L-lactide-co-glycolide)(83/17) reported by Cha and Pitt[26] and from PDLLA and PCL by us.[10]

Mechanical Properties

Mechanical properties before hydrolysis are summarized in Table I. It is seen that the tensile strength (σ_B) of the blend films is practically unchanged when X_{PLLA} is between 0 and 0.5, but increases dramatically at X_{PLLA} above 0.75. The blend film with $X_{PLLA} = 0.25$ has low elongation at break (ε_B) compared to the nonblended PCL, whereas the blend film with $X_{PLLA} = 0.75$ exhibits a high ε_B in contrast to that of the nonblended PLLA film. Such a σ_B and ε_B dependence on X_{PLLA} is in agreement with that observed for blend films from glassy PDLLA and rubbery PCL.[10] This nonlinear dependence of mechanical properties on X_{PLLA} strongly supports the occurrence of phase separation in the blend films from PCL and PLLA.

After Hydrolysis

Mass Remaining

When the blend films undergo hydrolysis of the main chain of the polymers, the mass loss of the films will take place, in addition to a change in the molecular and mechanical properties. Mass
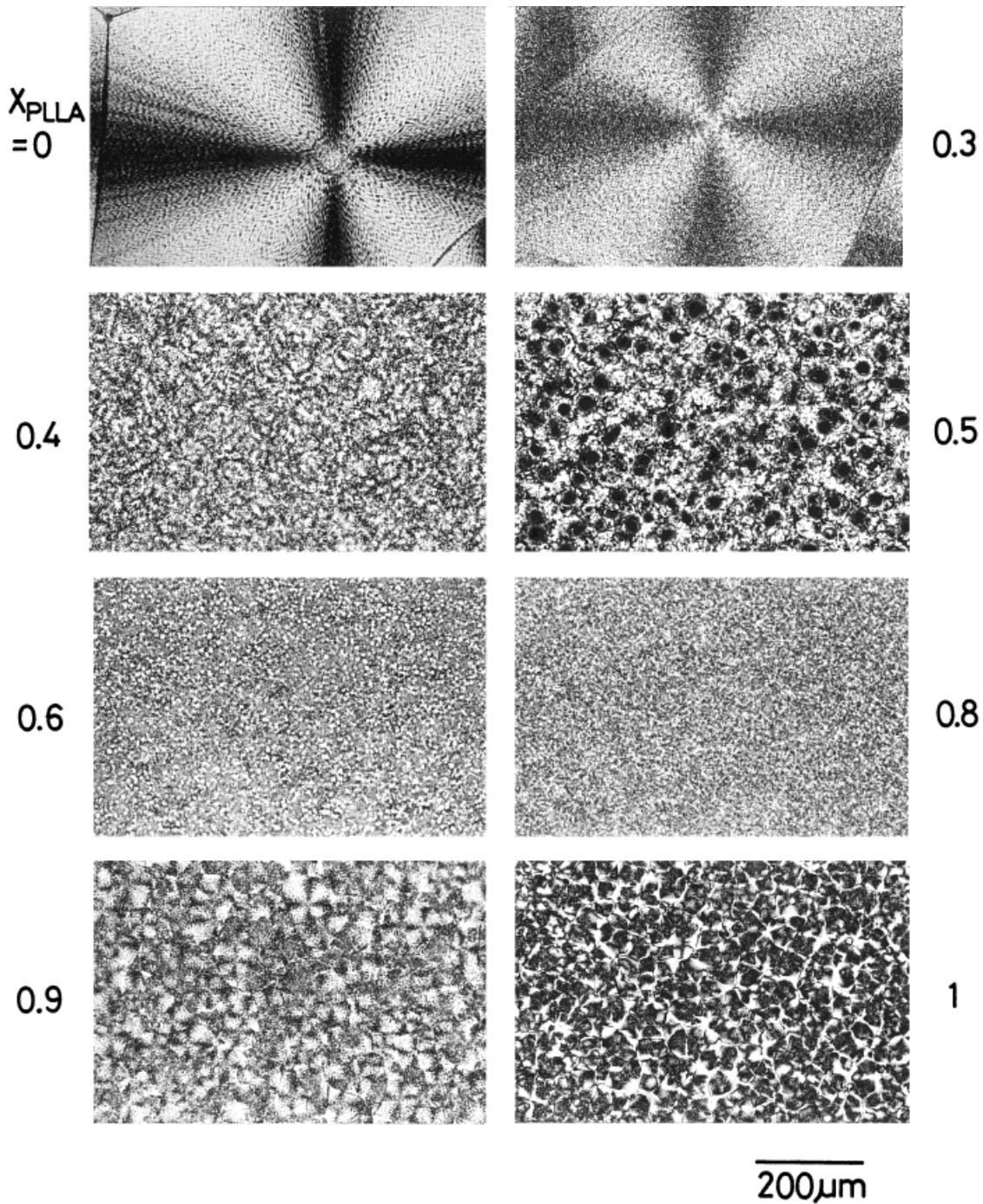
Figure 1 Polarizing photomicrographs of blend films with different X_{PLLA} before hydrolysis.

loss becomes detectable only when water-soluble oligomers are formed upon hydrolysis are eluted into the surrounding medium. Figure 3 shows the film weight remaining after hydrolysis performed for different times. At a hydrolysis time of 12 months, the weight of nonblended PCL (X_{PLLA} = 0), nonblended PLLA (X_{PLLA} = 1), and the blend film of X_{PLLA} = 0.25 remains unchanged, while blend films of X_{PLLA} = 0.5 and 0.75 lose their weight upon hydrolysis. At 20 months, the nonblended PCL and PLLA films lose only a very small amount (1%) of their initial mass, whereas
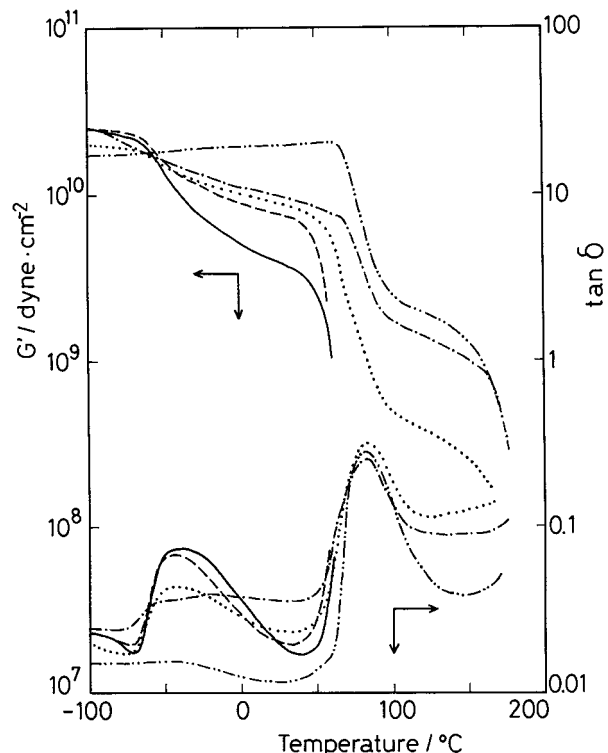
Figure 2 Storage modulus (G') and loss tangent ($\tan \delta$) for blend films as a function of temperature: (——) $X_{PLLA} = 0$; (----) 0.3; (· · · ·) 0.5; (— · — · —) 0.7; (— · · —) 1.

blend films of X_{PLLA} = 0.25, 0.5, and 0.75 lose 2, 8, and 19% of the initial mass, respectively. This suggests that the blending of PLLA with PCL accelerates the hydrolysis of PLLA and PCL molecules to form water-soluble oligomers, resulting in a rapid decrease in mass. It seems that $x_{c,tot}$ has only a small effect on the decrease of the mass remaining. If it depended strongly on $x_{c,tot}$, the decrease in the mass remaining for the non-blended PLLA film and the blend of $X_{PLLA} = 0.5$ (initial $x_{c,tot} = 51\%$) would be larger than that of the blend film with $X_{PLLA} = 0.75$ (initial $x_{c,tot} = 53\%$) after hydrolysis for 20 months.

Molecular Weight Change

Figure 4 shows a semilogarithmic plot of M_n against hydrolysis time for the blend films. It is seen that the M_n of the blend and the nonblended films decreases linearly with hydrolysis time, independent of X_{PLLA}. The slope of the lines for blends of $X_{PLLA} = 0.5$ and 0.75 is larger than that expected from their nonblended films. The rate constant for hydrolysis (k) was calculated according to the following procedure:
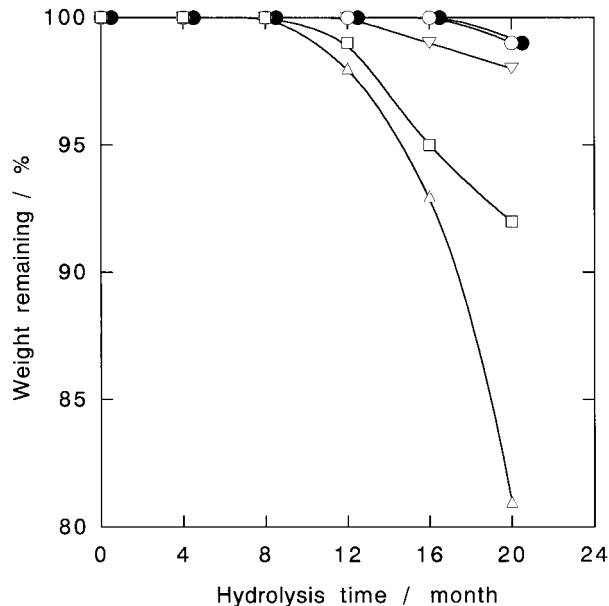

Figure 3 Mass remaining for blend films as a function of hydrolysis time: (●) $X_{PLLA} = 0$; (▽) 0.25; (□) 0.5; (△) 0.75; (○) 1.

The kinetic equation expressing the scission of molecular chains during hydrolysis can be derived under the assumption that scission is autocatalyzed by the terminal carboxyl groups of the polyester chains with the hydrolysis rate proportional to the water and ester concentrations[26]:
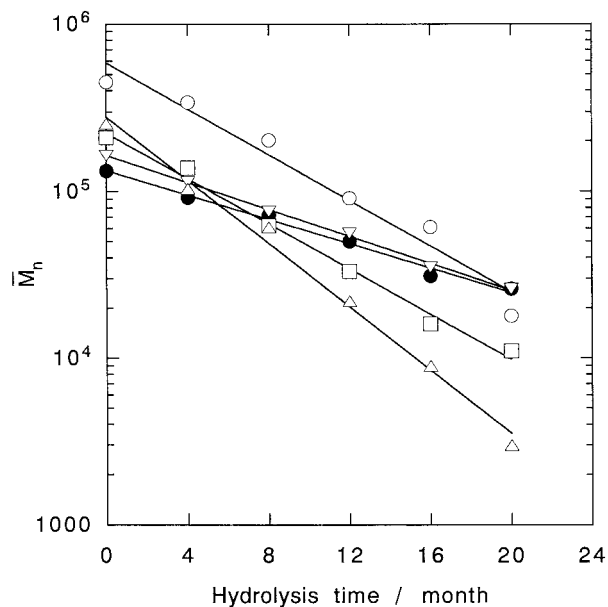
Figure 4 A semilogarithmic plot of M_n against hydrolysis time for blend films: (●) $X_{PLLA} = 0$; (▽) 0.25; (□) 0.5; (△) 0.75; (○) 1.
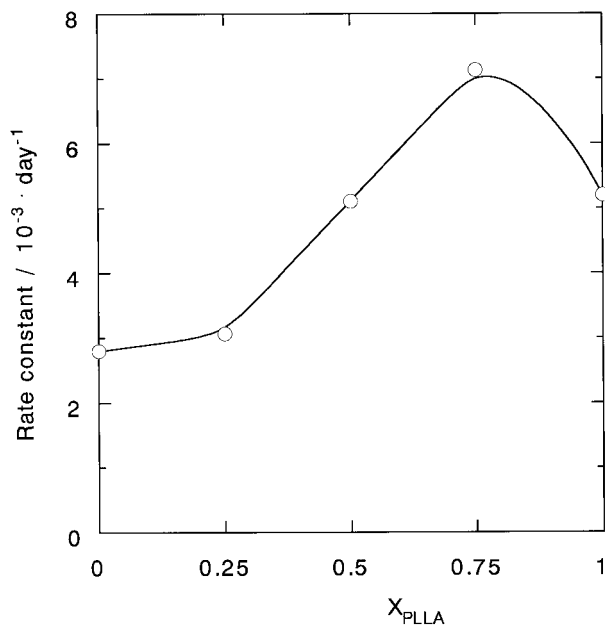
Figure 5 Hydrolysis rate constant (k) obtained from Figure 4 as a function of X_{PLLA}.

$$d[COOH]/dt = k'[COOH][H_2O][ester] \quad (5)$$

where $[COOH]$ is the concentration of the terminal carboxyl group. If $[H_2O][ester]$ is assumed to be constant, integration of eq. (5), coupled with the relationship $[COOH] \propto \bar{M}_n^{-1}$, will give eq. (6):

$$\bar{M}_{n,t} = \bar{M}_{n,0}\exp(-kt) \quad (6)$$

where $\bar{M}_{n,t}$ and $\bar{M}_{n,0}$ are the number-average molecular weight at hydrolysis time $= t$ and 0, respectively, and k is equal to $k'[H_2O][ester]$. Equation (6) can be converted to eq. (7):

$$\ln \bar{M}_{n,t} = \ln \bar{M}_{n,0} - kt \quad (7)$$

Thus, k values can be evaluated from its tangent of the straight lines in Figure 4. The observed values are plotted as a function of X_{PLLA} in Figure 5. The k values of 3.07×10^{-3} and 5.20×10^{-3} day^{-1} for the nonblended PCL and PLLA, respectively, are comparable with 4.08×10^{-3} and 6.72×10^{-3} day^{-1} found for the compression-molded nonblended PCL and PLLA, respectively. The little lower k values observed by our study may be due to the higher crystallinity of the solution-cast specimens than that of the compression-molded. In contrast, the k values for the blend films of $X_{PLLA} = 0.5$ and 0.75 are much higher than those

expected if the hydrolysis of PLLA and PCL molecules takes place independently from each other.

The molecular weight distribution shown in Figure 6 provides us with further information concerning the hydrolysis of the blend films. As is evident, the distribution curves of the nonblended PCL and PLLA shift to lower molecular weight with a single peak for hydrolysis up to 20 months. This indicates that hydrolysis has occurred homogeneously along the cross section of the film without selective removal of any water-soluble fractions from the amorphous region. Low molecular weight peaks observed around 1×10^4 and 5×10^3 for the blend films of $X_{PLLA} = 0.5$ and 0.75 at 16 and 20 months suggest that PCL or PLLA molecules in these blend films are more quickly hydrolyzed than are those in the nonblended PCL and PLLA. Since the hydrolysis of films with a thickness below 2 mm proceeds homogeneously along the cross section of the film,[18] the secondary peaks formation around 1×10^4 and 5×10^3 in the molecular distribution curves in these blends
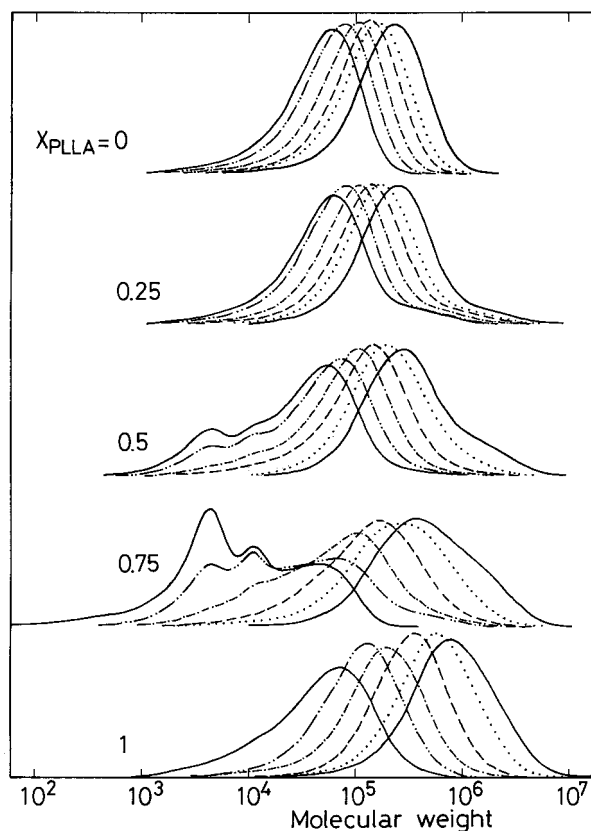

Figure 6 Molecular weight distribution of blend films subjected to hydrolysis for different times: (——) 0 month; (· · · ·) 4 months; (----) 8 months; (– · – · –) 12 months; (– · · –) 16 months; (——) 20 months.

may be due to the removal of water-soluble fractions predominantly formed in the amorphous region, leaving crystalline lamella. The peak formation at specific molecular weights during *in vitro* hydrolysis is in agreement with that reported for crystalline PLLA or poly(D-lactide): compression-molded crystalline PLLA,[27] as-polymerized crystalline PLLA,[28] and solution-cast crystalline PLLA or poly(D-lactide).[29] The specific molecular weights around 1×10^4 and 5×10^3 observed in Figure 6 are in good agreement with those found for solution-cast crystalline PLLA or poly(D-lactide).[29] This result suggests that the rapidly hydrolyzed species in the blend films of $X_{PLLA} = 0.5$ and 0.75 is not PCL but PLLA.

The hydrolysis of blend films seems to be affected by at least three factors: (1) the miscibility of the two homopolymers, (2) the relative molecular weight of the two homopolymers or relative concentration of terminal carboxyl group of the two homopolymers, and (3) the relative hydrophilicity of the two homopolymers or the diffusion rate of water molecules through them. In addition, in the case of phase-separated blends, the domain size and surface area of the two polymer phases must be influential to hydrolysis. Similar to our blends of $X_{PLLA} = 0.5$ and 0.75, the hydrolysis of high molecular weight PDLLA[30] and PCL[26] was accelerated upon addition of low molecular weight PDLLA and poly(L-lactide-*co*-glycolide), respectively. The former blend was homogeneously miscible,[30] while the latter phase-separated.[26] The accelerated hydrolysis of relatively high molecular weight polyesters in the blends may be ascribed to increased hydrophilicity and concentration of the terminal carboxyl group by addition of low molecular weight polyesters as proposed by Mauduit et al.[30] It should be noted that accelerated hydrolysis of relatively high molecular weight aliphatic polyesters occurred, irrespective of the mixing ratio of two polyesters, even when the two components were phase-separated. The reason why the terminal carboxyl group of low molecular weight PCL has a catalytic effect on the PLLA hydrolysis in spite of phase separation may be that the terminal carboxyl group of the PCL molecules trapped in the PLLA-rich phase as well as those of PCL chains from the PCL-rich phase in contact with PLLA-rich phase will catalyze the hydrolysis of high molecular weight PLLA.

Crystalline Structure Change

It has been reported that, when hydrolysis occurs in the crystalline region of degradable polymers
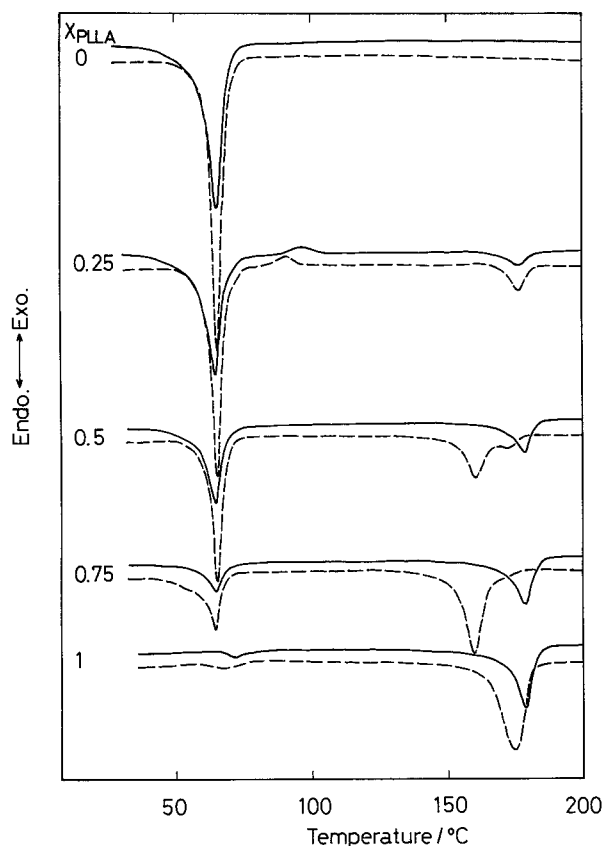
Figure 7 DSC thermograms of blend films before and after hydrolysis for 20 months: (——) before; (----) after.

at the late stage of hydrolysis, the decrease in melting temperature of them was observed in the chart of DSC.[27,28] On the contrary, no significant decrease or a slight increase of melting temperature will appear in the chart of DSC if hydrolysis takes place solely in the amorphous region, resulting in crystallite growth at the initial stage of hydrolysis.[27,28] DSC thermograms of the blend films before and after hydrolysis for 20 months are shown in Figure 7. Table I gives the characteristic values evaluated from the DSC measurements. Evidently, from Figure 7, the melting peak of PCL appearing around 65°C becomes larger after 20 months with a very small increase in peak temperature, irrespective of X_{PLLA}. An increase in the melting peak area (crystallinity) of PCL in the blend films as well as in the nonblended PCL film indicates that crystallization or recrystallization of PCL occurs by the scission of chains in the amorphous region.

The very slight increase in the melting temperature of PCL for all the blend films means that

the PCL crystalline thickness slightly increased during hydrolysis. On the other hand, the lowering of the PLLA melting peak for the blend films of X_{PLLA} = 0.5, 0.75, and 1 from 179 to 161, 160, and 175°C, respectively, upon hydrolysis for 20 months suggests a decrease in PLLA crystalline thickness with a large molecular weight decrease of PLLA. An increase in the PLLA melting peak area (crystallinity) of blend films of X_{PLLA} = 0.5, 0.75, and 1 strongly denotes the subsequent crystallization and recrystallization of PLLA with the removal of water-soluble fractions from the amorphous and crystalline regions of the PLLA-rich phase. As shown in Table I, the decrease in melting temperature is larger for blend films of X_{PLLA} = 0.5 and 0.75 than for the nonblended PLLA, implying that hydrolysis of PLLA was accelerated by the addition of a small amount of PCL. Moreover, if the rapidly degraded and removed species in the blend of X_{PLLA} = 0.75 containing 25 wt % PCL was PCL, the melting peak area of PCL would dramatically decrease at 20 months as 19% weight loss had occurred. However, the melting peak area of PCL increased after hydrolysis for 20 months. These DSC results revealed that the rapidly hydrolyzed species in the blend films of X_{PLLA} = 0.5 and 0.75 was not PCL but PLLA.

On the other hand, the unvaried melting temperature of PLLA in the blend with X_{PLLA} = 0.25 before and after hydrolysis suggests that hydrolysis of PLLA was retarded in the blend film of X_{PLLA} = 0.25, compared to that of the nonblended PLLA. This retardation may be due to the prevention of water diffusion into the dispersed PLLA-rich phase by the hydrophobic continuous PCL-rich phase. In this case, the increased concentration of the terminal carboxyl group of PCL may not play an important role in the hydrolysis of PLLA molecules because of a very low concentration of water in the blends. A small crystallization peak of PLLA is observed around 100°C for the blend of X_{PLLA} = 0.25 both before and after hydrolysis during DSC scanning above the melting temperature of PCL. This strongly suggests that crystallization of PLLA is hindered to some extent by the presence of PCL in this blend even after hydrolysis for 20 months. Probably, a large amount of PLLA molecules trapped in the PCL-rich phase of this blend could not crystallize, while a small amount of PCL in the PLLA-rich phase must have hindered the nucleation of PLLA.

Mechanical Properties' Changes

Figure 8 shows the residual tensile strength of blend films hydrolyzed for different times. Unex-
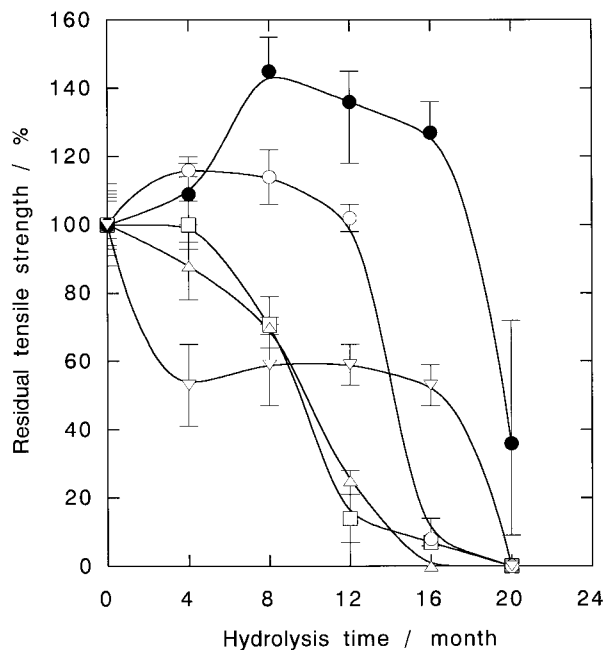
Figure 8   Residual tensile strength of blend films subjected to hydrolysis for different times: (●) X_{PLLA} = 0; (▽) 0.25; (□) 0.5; (△) 0.75; (○) 1.

pectedly, the tensile strength of the nonblended PCL and PLLA increases upon hydrolysis, and after passing through the maximum, it decreases gradually, followed by a rapid decrease. This increased mechanical strength may be explained in terms of the annealing effect of the reorganization of the chains in the amorphous region to a more stable state at 37°C in the presence of water molecules. On the other hand, blend films of X_{PLLA} = 0.5 and 0.75, where the PLLA-rich phase forms the continuous phase, lose most of the initial tensile strength after 16 months, while the blend film of X_{PLLA} = 0.25, where the PCL-rich phase forms the continuous phase, retains half of the initial strength up to 16 months. The initial rapid decrease in the tensile strength of the blend film of X_{PLLA} = 0.25 in the first 4 months may be ascribed to crack formation at the interface between the rubbery PCL-rich and the glassy PLLA-rich phase caused by a difference in size change by the absorption of water molecules.

Figure 9 shows the residual elongation-at-break of blend films as a function of hydrolysis time. The elongation-at-break of blend films of X_{PLLA} = 0.5 and 0.75 decreases monotonously but more rapidly than that of the nonblended PLLA, indicating that an addition of a small amount of PCL accelerates the hydrolysis of PLLA chains in the blend films of X_{PLLA} = 0.5 and 0.75. On the
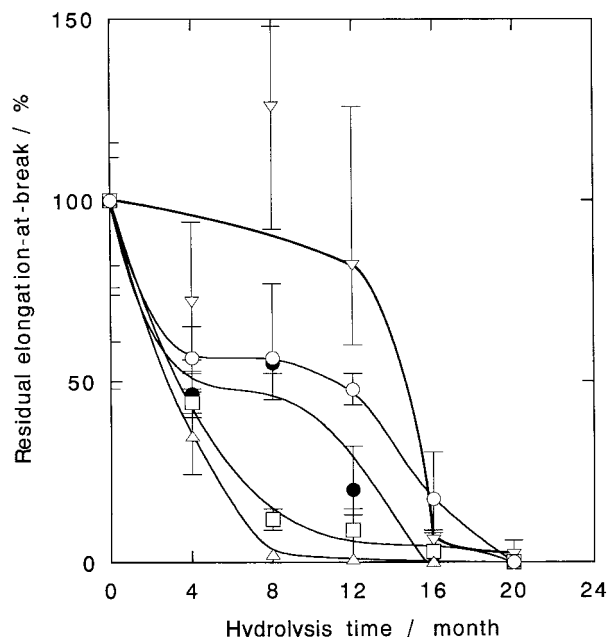
Figure 9 Residual elongation-at-break of blend films subjected to hydrolysis for different times: (●) X_{PLLA} = 0; (▽) 0.25; (□) 0.5; (△) 0.75; (○) 1.

other hand, elongation-at-break of the blend film of X_{PLLA} = 0.25 shows a different pattern, retaining a higher value up to 12 months than that of the nonblended PCL, followed by a rapid decrease starting from 12 months.

Thus, it is obvious that the hydrolysis of PLLA molecules can be accelerated or retarded, depending on the amount of PCL added. A rapid decrease in tensile strength and elongation-at-break for blend films of X_{PLLA} = 0.5 and 0.75 upon hydrolysis may be due mainly to the presence of low molecular weight PCL having a high density of the terminal carboxyl group present in the continuous PLLA-rich phase in the blend films. When the PCL-rich phase forms the continuous phase as in the blend of X_{PLLA} = 0.25, elongation-at-break remains unchanged for a long time, compared to that of the nonblended PCL. This may be ascribed to the retarded hydrolysis of PCL molecules caused by an addition of high molecular weight PLLA molecules having a much lower density of the terminal carboxyl group.

CONCLUSION

In summary, it may be concluded that PLLA and PCL molecules are phase-separated in the blend films. The accelerated hydrolysis of high molecu-

lar weight PLLA in the blend films of high PLLA contents, where the continuous phase consists of PLLA, may be ascribed to the increased concentration of the terminal carboxyl group by addition of low molecular weight PCL. On the other hand, hydrolysis of the high molecular weight PLLA in the blend films of high PCL contents, where the PCL-rich phase forms the continuous phase, may be retarded due to the prevention of water diffusion into the dispersed PLLA-rich phase by the hydrophobic PCL-rich phase. The hydrolysis of PCL molecules was not strongly influenced by the presence of PLLA.

REFERENCES

1. M. Vert, P. Christel, F. Chabot, and J. Leray, In *Macromolecular Materials,* G. W. Hasting and P. Ducheyne, Eds., Boca Raton, Florida, CRC Press, 1984, p. 119–142.
2. M. Vert, S. M. Li, G. Spenlehauer, and P. Guerin, *J. Mater. Sci., Mater. Med.,* **3,** 432 (1992).
3. M. Vert, S. M. Li, and H. Garreau, *Clin. Mater.,* **10,** 3 (1992).
4. *Biodegradable Polymers and Plastics,* M. Vert, J. Feijen, A. Albertsson, G. Scott, and E. Chiellini, Eds., The Royal Society of Chemistry, Cambridge, 1992.
5. G. B. Kharas, F. Sanchez-Riera, and D. K. Severson, In *Plastics from Microbe,* D. P. Mobley, Ed., Hanser Publishers, New York, 1994, pp. 93–137.
6. *Biodegradable Plastics and Polymers,* Y. Doi and K. Fukuda, Eds., Elsevier, Amsterdam, 1994.
7. M. Vert, G. Schwarch, and J. Coudane, *J. Macromol. Sci., Pure Appl. Chem.,* **A32,** 787 (1995).
8. *Biogradable Polymers. Principles and Application,* G. Scott and D. Gilead, Eds., Chapman & Hall, London, 1995.
9. *Studies in Polymers Science 12, Biomedical Applications of Synthetic Biodegradable Polymers,* J. O. Hollinger, Ed., CRC Press, Boca Raton, New York, 1995.
10. H. Tsuji and Y. Ikada, *J. Appl. Polym. Sci.,* **60,** 2367 (1996).
11. M. P. Hiljanen-Vainio, P. A. Orava, and J. V. Seppälä, *J. Biomed. Mater. Res.,* **34,** 39 (1997).
12. H. Tsuji and Y. Ikada, *Polymer,* **36,** 2709 (1995).
13. W. R. Sorensen and T. W. Campbell, In *Preparative Methods of Polymer Chemistry,* Wiley, New York, 1961.

14. S.-H. Hyon, K. Jamshidi, and Y. Ikada, In *Polymers as Biomaterials,* S. W. Shalaby, A. S. Hoffman, B. D. Ratner, and T. A. Horbett, Eds., Plenum, New York, 1984, pp. 51–65.
15. H. Tsuji, S.-H. Hyon, and Y. Ikada, *Macromolecules,* **24,** 5651 (1991).
16. H. Tsuji and Y. Ikada, *Macromolecules,* **25,** 5719 (1992).
17. H. Tsuji and Y. Ikada, *J. Appl. Polym. Sci.,* **53,** 1061 (1994).
18. I. Grizzi, H. Garreau, S. M. Li, and M. Vert, *Biomaterials,* **16,** 305 (1995).
19. E. W. Fischer, H. J. Sterzel, and G. Wegner, *Kolloid-Z.u.Z. Polym.,* **251,** 980 (1973).
20. V. Crescenzi, G. Manzini, G. Calzolari, and C. Borri, *Eur. Polym. J.,* **8,** 449 (1972).
21. See for example, U. W. Gedde, *Polymer Physics,* Chapman & Hall, London, 1995, Chapters 7 and 8.
22. J. V. Koleske and R. D. Lundberg, *J. Polym. Sci., Part A-2,* **7,** 897 (1969).
23. R. Wada, S.-H. Hyon, and Y. Ikada, *Pharm. Res.,* **8,** 1292 (1991).
24. K. Jamshidi, S.-H. Hyon, T. Nakamura, and Y. Ikada, *Polymer,* **29,** 2229 (1988).
25. A. Celli and M. Scandola, *Polymer,* **33,** 2699 (1992).
26. Y. Cha and C. G. Pitt, *Biomaterials,* **11,** 108 (1990).
27. S. M. Li, H. Garreau, and M. Vert, *J. Mater. Sci., Mater. Med.,* **1,** 198 (1990).
28. H. Pistner, D. R. Bendix, J. Mühling, J. F. Reuther, *Biomaterials,* **14,** 291 (1993).
29. H. Tsuji and Y. Ikada, *J. Appl. Polym. Sci.,* **63,** 855 (1997).
30. J. Mauduit, E. Pérouse, and M. Vert, *J. Biomed. Mater. Res.,* **30,** 201 (1996).