

Blends of Crystalline and Amorphous Poly(lactide).

III. Hydrolysis of Solution-cast Blend Films

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ABSTRACT: Hydrolysis of blend films prepared from amorphous poly(DL-lactide) (a-PLA) and isotactic crystalline poly(D- or L-lactide) (c-PLA) having different c-PLA contents [$X = \text{c-PLA}/(\text{a-PLA} + \text{c-PLA})$] was performed in phosphate buffered solution of pH 7.4 at 37°C. The blend films before and after hydrolysis were studied using gel permeation chromatography, tensile testing, differential scanning calorimetry (DSC), and optical rotation. The mass of the blend films remaining after hydrolysis of longer than 20 months was larger with the increasing initial X . The tensile strength of the blend films remained unchanged in the early stage of hydrolysis, followed by a rapid decrease with time, the duration of period for the tensile strength remaining unchanged was longer for the blend films of smaller X . The change in crystallinity, molecular weight, and specific optical rotation during hydrolysis of the blend films revealed that degradation took place preferentially in the amorphous region than in the crystalline region of the blend films. A double melting peak was observed in the DSC spectra of blend films with $X = 0.75$ and 0.5 after hydrolysis for 20 months. The time difference in the induction of reduction between the tensile strength and the mass due to hydrolysis of the blend films increased with an increase in X . © 1997 John Wiley & Sons, Inc. *J Appl Polym Sci* **63**: 855–863, 1997

Key words: hydrolysis; poly(lactide); polymer blends

INTRODUCTION

Polymer degradation is increasingly becoming very important because of at least two reasons: the serious problem of plastic wastes and effective medical application of biodegradable polymers.¹ Although polymer degradation induced by ultraviolet rays, ionizing radiation, heating, and chemical oxidation has been extensively studied for a long time, hydrolytic degradation of polymers has attracted less attention except for their enzymatic degradation. In contrast to other degradations, polymer hydrolysis needs water molecules, which

are required to come in contact with hydrolytically labile bonds in the polymer by diffusion through the polymer matrix. Therefore, hydrolysis of a polymeric material in the solid state must greatly depend on the phase structure because water penetration through the polymeric material will proceed at a higher rate in the amorphous region than in the crystalline region. Indeed, a large number of studies have been concerned with the influence of phase structure of polymers on their hydrolysis even for the limited family of poly(lactide) (PLA).^{2–11}

In this work, we select PLA as the polymer for hydrolysis study because the PLA family includes different kinds of polymers with respect to optical purity and stereoregularity.^{12–15} Among them are homopolymers of L-lactide (or L-lactic acid), DL-

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lactide (or DL-lactic acid), meso-lactide, and their copolymers.^{12–15} Poly(L-lactide) and poly(D-lactide) are enantiomeric with each other, both being optically pure, isotactic, and crystalline.^{12–15} Poly(L-lactide) has the same properties as poly(D-lactide), except for optical rotation.¹⁶ Here, we call poly(L-lactide) and poly(D-lactide) c-PLA. On the other hand, poly(DL-lactide) is racemic and amorphous^{12–15} and, hence, here called a-PLA. Among the PLA family, c-PLA and a-PLA have been most extensively studied,^{2–15,17–28} as they are commercially available or can be readily synthesized by polymerization of the corresponding monomers.

Key factors in both medical and industrial applications of degradable polymers may be their mechanical property and degradation rate. In some applications, a rapidly degradable material with high initial strength is needed, while other applications require a high strength and slow degradation material. A major disadvantage of c-PLA and a-PLA is slow degradation and poor mechanical property, respectively. It seems likely that blending of c-PLA and a-PLA yields products with mechanical properties and degradation rates varying over a wide range because total crystallinity can be changed readily by altering their blending ratio. The present work was undertaken to study the effects of blending of c-PLA and a-PLA on the degradation and physical properties before and after hydrolysis. The polymer specimens to be used in the present study were prepared by casting PLA blend solutions to have a film form. Hydrolysis of the films was carried out in phosphate buffered solution of pH 7.4 at 37°C. It is well known that *in vitro* hydrolysis of PLA gives results quite similar to those of *in vivo* hydrolysis.^{20,25} As the results obtained for poly(L-lactide) were almost identical with those of poly(D-lactide), this study describes only the results obtained using poly(D-lactide) as c-PLA.

EXPERIMENTAL

Materials

c-PLA and a-PLA were synthesized with the method previously reported.^{29–31} Ring-opening polymerization of lactides was performed for each lactide in bulk at 140°C for 10 h using stannous octoate (0.03 wt %) as a polymerization catalyst.³⁰ The resulting polymers were purified by reprecipitation using methylene chloride for c-PLA and ac-

etone for a-PLA as solvents and methanol as a precipitant. a-PLA synthesized from DL-lactide or 1 : 1 mixture of D- and L-lactide is reported to have tetrad sequence distribution between Bernoullian pair and single additions.^{32–35}

Blend films used for hydrolysis experiments were obtained by the following procedure. Mixed methylene chloride solutions of c- and a-PLA with different c-PLA contents were prepared to have a total polymer concentration of 1 g/dL. The solutions were cast onto flat glass plates, and the solvent was allowed to evaporate at room temperature for approximately one week, then dried *in vacuo* for two weeks before being subjected to hydrolytic degradation. The blend films were aged for more than one month at room temperature to approach the equilibrium state. Films with a thickness of about 200 μm were used, except for a morphological study (25 μm) and dynamic mechanical study (50 μm).

Hydrolysis

A blend film (30 mm \times 5 mm \times 200 μm) was hydrolyzed in 10 mL of 0.15M phosphate buffered solution of pH 7.4 at 37°C for given periods of time. The thickness of starting films was kept smaller than 300 μm to avoid inhomogeneous degradation along the film cross-section, which was expected to occur when the film thickness was above 2 mm.²⁸ Hydrolyzed films were washed twice and extracted with distilled water for one day at room temperature, then dried *in vacuo* for two weeks.

Physical Measurements

Intrinsic solution viscosity ($[\eta]$) of PLA was measured in chloroform at 25°C. M_w of the polymers was evaluated in chloroform with a Tosoh GPC system (TSK Gel GMHXL \times 2) using polystyrene as a standard.

Mechanical properties of the initial and hydrolyzed films were measured at 25°C and 50% relative humidity using a tensile tester at a cross-head speed of 100%/min. The initial length of the specimen was always kept at 20 mm. Dynamic mechanical analyses for the initial films with a thickness of 50 μm were performed using Orientec Rhovibron DDV-01FP at 35 Hz and a heating rate of 4°C/min.

The melting temperature (T_m) and enthalpy of fusion (ΔH_m) of the initial and hydrolyzed films were determined with a Shimadzu DT-50 differ-

ential scanning calorimeter. Dried blend samples were heated under a nitrogen gas flow at a fixed rate of 10°C/min. Higher heating rates, such as 20°C/min, induced a T_m shift to higher temperature, and lower rates, such as 5°C/min, resulted in thermal degradation of PLA due to long exposure to high temperature. T_m and ΔH_m were calibrated using indium as a standard. The crystallinity of blends (x_c) with different c-PLA contents (X) was calculated from the following equations without excluding the a-PLA part:

$$x_c(\%) = 100 \cdot \Delta H_m / 93 \quad (1)$$

$$X(w/w) = \text{c-PLA} / (\text{a-PLA} + \text{c-PLA}) \quad (2)$$

where ΔH_m (J/g of polymer) is the enthalpy of fusion estimated from differential scanning calorimetry (DSC) thermograms. The value of 93 (J/g of polymer) is the enthalpy of fusion of the c-PLA crystal having the infinite size reported by Fischer et al.² The observed enthalpy of fusion may contain the crystallization enthalpy of crystallizable phases, but no independent crystallization peak was observed in our study. X-ray diffraction was not utilized to estimate the crystallinity.

Morphology of films before degradation was studied with a Zeiss polarizing microscope. Films of 25 μm thickness were used for the microscopic observation since photographic contrast became extremely low when their thickness was greater than 50 μm .

The specific optical rotation ($[\alpha]$) of polymers was measured in chloroform at a concentration of 1 g/dL and 25°C using JASCO DIP-140 at a wavelength of 589 nm.

RESULTS

Before Hydrolysis

Molecular and physical properties of the PLA specimens before hydrolysis are summarized in Table I. Shown in Table I, $[\alpha]_D^{25}$ values before degradation are approximately +156 degrees for c-PLA, and 0 degrees for a-PLA, in good agreement with the literature values.^{33,36} The optical purity of c-PLA and a-PLA was 100 and 0%, respectively, when evaluated from $[\alpha]_D^{25}$.^{31,33} The c-PLA and a-PLA specimens from which blends were prepared to have different compositions were selected from each of polymer homologue stocks so as to have similar molecular weights. The c-PLA and a-PLA

molecules seem to be homogeneously mixed at least in the solution and molten state because the intrinsic viscosity ($[\eta]$) of the blends practically obeyed the arithmetic addition rule of the viscosity.

However, microphase separation will occur in the PLA blends when polymer molecules of the blends are no more in the mobile state as a result of solvent evaporation of the blend solutions or cooling of the molten blends because these processes will bring about crystallization of c-PLA. Indeed, polarizing microscopy revealed that spherulitic assemblies were formed in the continuous black phase of a-PLA even at $X = 0.3$. With the increasing X , the amorphous black phase disappeared, resulting in full spherulitic assemblies. Typical spherulite morphology appeared at X ranging between 0.6 and 0.8. The spherulite radius became maximum at $X = 0.8$ (ca. 50 μm) and decreased when X deviated from 0.8. As X approached unity, the spherulite morphology became obscure, probably because of formation of a larger number of nucleus for spherulite. The a-PLA chains must have been present somewhere in the amorphous region, being excluded from the crystalline region, as suggested in previous papers.^{37,38}

The microphase separation is also supported by the viscoelastic property of the PLA blends. Their storage modulus (G') and loss tangent ($\tan \delta$) values are represented in Figure 1. Apparently, the phase transition temperatures are virtually not influenced by X unless it is smaller than 0.5. The temperature dependence of G' and $\tan \delta$ for $X = 0.3$ is similar to that of $X = 0$, suggesting that the a-PLA phase composes the continuous matrix. The transition temperature around 50°C can be assigned as the glass transition of a-PLA,³⁹ while the transition around 50 and 150°C as the glass transition and melting of c-PLA, respectively.³⁹⁻⁴¹ G' of the blends with X above 0.5 for the temperature range between T_g and T_m increased with the increasing X . No remarkable dependence of transition temperatures on the blend composition also supports the occurrence of microphase separation in the PLA blends, in good agreement with the results reported by Jorda and Wilkes.⁴²

In spite of microphase separation of c-PLA and a-PLA, mechanical properties such as tensile strength (σ_B) and elongation-at-break (ϵ_B) of blends have intermediate values between c-PLA and a-PLA. Probably due to microphase separation of c-PLA and a-PLA, x_c of the blends increases linearly with the increasing X without changing

Table I Molecular Characteristics and Physical Properties of the PLA Films before Hydrolysis

<i>X</i>	Molecular Characteristics			Physical Properties			
	$[\eta]$ (dL/g)	M_w (g/mol)	$[\alpha]_D^{25}$ (deg.)	σ_B (kg/mm ²)	ϵ_B (%)	T_m (°C)	x_c (%)
0 (a-PLA)	3.42	7.2×10^5	0	4.0	15	—	0
0.25	3.98	7.4×10^5		4.8	9	177	9
0.5	4.47	7.3×10^5	+78	4.2	11	178	25
0.75	4.80	7.5×10^5		4.8	9	179	38
1 (c-PLA)	5.11	7.4×10^5	+156	5.4	4	179	55

T_m , as shown in Table I, suggesting that the relative ratio of crystalline region to amorphous region can be readily controlled by changing X without the altering crystalline size of c-PLA.

After Hydrolysis

When PLA molecules undergo hydrolysis, mass loss of PLA takes place, in addition to the change of the molecular and physical properties. Figure

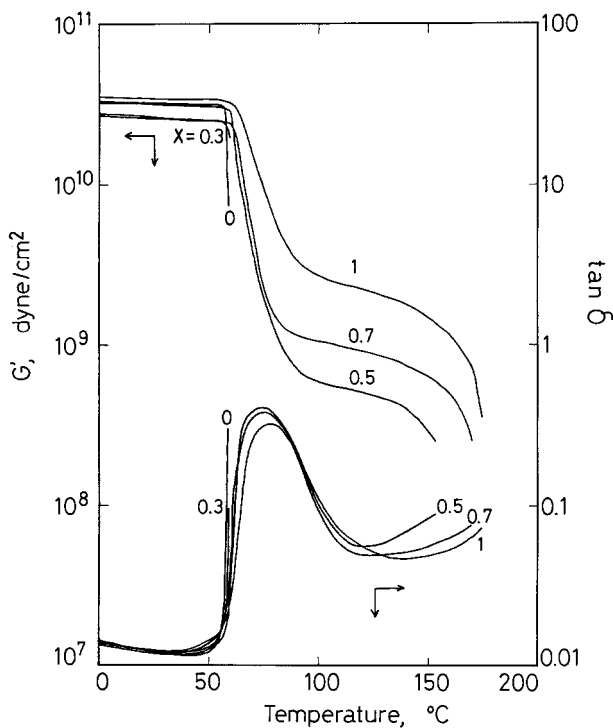


Figure 1 Storage modulus (G') and loss tangent ($\tan \delta$) as a function of temperature for the PLA films with different X before hydrolysis.

2 shows the mass loss of PLA blends as a function of hydrolysis time. Obviously, the a-PLA film ($X = 0$) first gradually loses its mass in the early stage, but very rapidly after 12 months; whereas the mass loss of c-PLA ($X = 1$) proceeds much more slowly for a longer time, similar to the initial x_c dependence of c-PLA on degradation time.^{4,9-11} Other blend films exhibit intermediate time courses of the loss between a-PLA and c-PLA. The mass remaining after hydrolysis for longer than 16 months increases with the increasing X or initial x_c of the blend films. There is a probability that the initial slight mass loss observed for a-PLA was due to removal of solvent residues during the hydrolysis test.

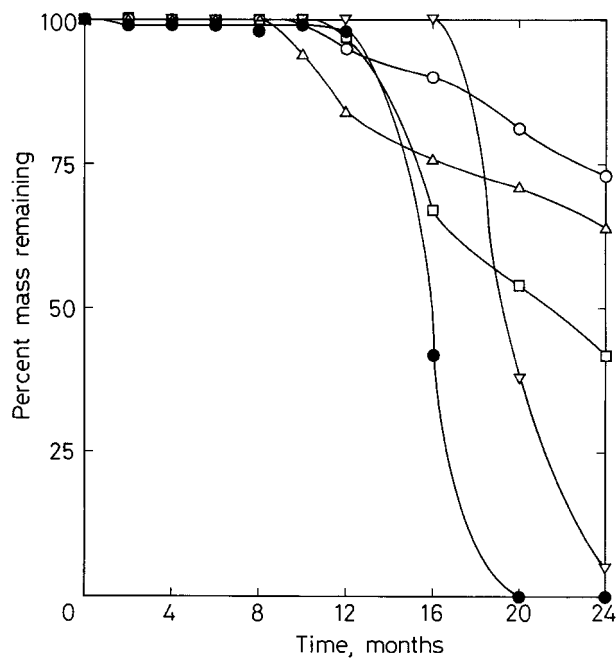


Figure 2 Mass remaining for the PLA films with different X as a function of hydrolysis time: $X = (\bullet)$ 0, (∇) 0.25, (\square) 0.5, (\triangle) 0.75, and (\circ) 1.

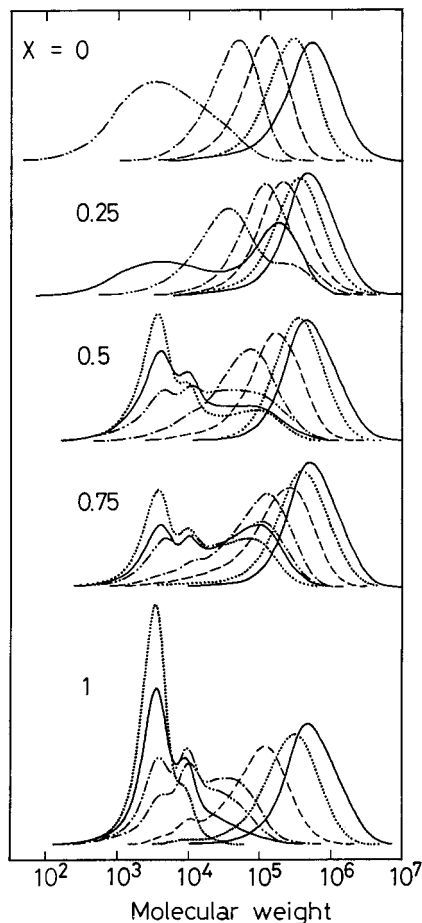


Figure 3 Molecular weight distribution of the PLA films with different X for different hydrolysis times: —, 0 month; ·····, 4 months; - - - - - , 8 months; - · - · - · - , 12 months; - - - - - , 16 months; —, 20 months; ·····, 24 months.

Hydrolysis of ester bonds must be occurring on PLA molecules prior to the start of mass loss. It will become detectable only when degradation by-products that are soluble in the surrounding aqueous medium are yielded as a result of extensive hydrolysis. The degradation reaction occurring before the onset of mass loss can be studied from the molecular weight change of the PLA specimen remaining hydrolysis. Figure 3 shows the molecular weight of the PLA remaining after different hydrolysis times. The a-PLA always exhibits molecular weight distributions with a single peak, regardless of the hydrolysis time, and all of the distribution curves shift to lower molecular weight with hydrolysis. This suggests that hydrolysis of a-PLA takes place homogeneously throughout the film cross-section without any significant induction period for degradation. On the

other hand, the c-PLA subjected to hydrolysis has double or triple peaks in the molecular weight distribution. Obviously, degradation of c-PLA does not proceed from the film surface to the bulk because the main peak of all the distribution curves shifts again to lower molecular weight with hydrolysis. If hydrolysis starts from the film surface and then goes into the core with the degradation time, the main peak of the molecular weight distribution would remain at the initial position with a reduced peak area. It is seen that accumulation of low molecular weight fractions becomes more remarkable with the prolonged hydrolysis of c-PLA, while the double peak around 1×10^4 and 5×10^3 remains unchanged. A similar specific peak was also reported for c-PLA hydrolyzed in phosphate buffered solution^{4,7} and L-lactide-rich PLA hydrolyzed in alkaline medium.² PLA blend films show an intermediate molecular weight change between those of a-PLA and c-PLA. The specific peak formation of the blend films with $X = 0.5$ and 0.75 during hydrolysis must be due to the crystalline region of c-PLA in the blend films. The very broad molecular weight distribution of the blend with $X = 0.25$ after 20 months of hydrolysis compared to that after 16 months may be due to selective removal of degradation products of the a-PLA component as will be mentioned below.

DSC charts before and after hydrolysis of PLA for 16 months (a-PLA) and 20 months (blends and c-PLA) are shown in Figure 4. It has been already established that the endothermic peak around 60°C observed for a-PLA before hydrolysis is due to the glass transition,³⁹ while the single peak around 180°C for c-PLA before hydrolysis is assigned to melting of the crystalline region.^{16,39-41} As is obvious from Figure 5, the glass transition of a-PLA becomes almost undetectable after hydrolysis for 16 months, while the peak due to melting of crystallites of c-PLA shifts from 180 to 160°C upon hydrolysis for 20 months. Interestingly, the melting of crystallites in the blends produces a double peak except for the blend with $X = 0.25$. It seems probable that the endotherm observed at the higher temperature around 175°C for the blends with $X = 0.5$ and 0.75 corresponds to that of the blend with $X = 0.25$, while the endotherm appearing at the lower temperature around 160°C is similar to that of the c-PLA after hydrolysis. Another remarkable finding is the larger area of the endotherm assigned to the crystalline melting after hydrolysis for 20 months than that before hydrolysis. It follows that the crystallinity of the

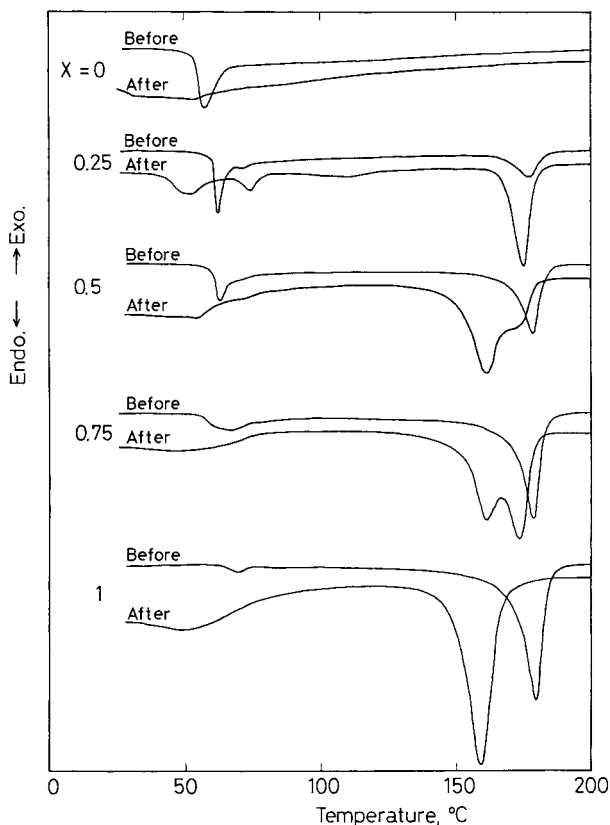


Figure 4 DSC thermograms of the PLA films with different X before and after 20 months of hydrolysis (The PLA film with $X = 0$ was subjected to hydrolysis for 16 months).

hydrolyzed PLA films becomes higher than that of PLA films before hydrolysis. The melting temperature reduction and the increase in x_c by hydrolysis have been reported for c-PLA.^{4,5,7,9} Figure 5 shows the change of crystallinity (x_c) of the blends estimated from DSC charts. x_c of the blends, as well as c-PLA, gradually increased within the initial eight months. This must be ascribed to further c-PLA crystallization during hydrolysis, not preferential removal of hydrolyzed PLA chains in the amorphous region, since an insignificant mass loss occurred within this period as seen from Figure 2, revealing that further crystallization of c-PLA occurs even in the presence of a-PLA by decreased PLA molecular weight and water molecules penetration into amorphous region. On the other hand, x_c of the blend films increases rapidly for the hydrolysis time longer than eight months, while that of c-PLA remained unchanged. This must be due to the preferential removal of a-PLA from the blend films. The $[\alpha]_D^{25}$ of c-PLA decreased from +156 to +148 degrees,

probably due to increased density of terminal group after 16 months of hydrolysis, while that of the blend with $X = 0.5$ increased from +78 to +124 degrees. This finding gives evidence for the preferential scission and removal of a-PLA chains from the blend films. Otherwise, $[\alpha]_D^{25}$ of the blend with $X = 0.5$ would not increase from +78 to +124 degrees upon hydrolysis, but would decrease from +78 degrees.

Figure 6 demonstrates the change of tensile strength (σ_B) of the PLA films plotted against the hydrolysis time. Again, blend films show intermediate tensile strengths between a-PLA and c-PLA during hydrolysis. Unexpectedly, the mechanical strength of crystalline c-PLA became lower than that of amorphous a-PLA in the course of degradation, although the c-PLA film initially had a higher strength than the a-PLA. The duration of period for the tensile strength remaining unchanged was longer for the blend films of smaller X or initial x_c .

DISCUSSION

The hydrolysis results of blends have revealed that controlling the initial x_c by altering the mixing ratio of crystalline and amorphous PLA pro-

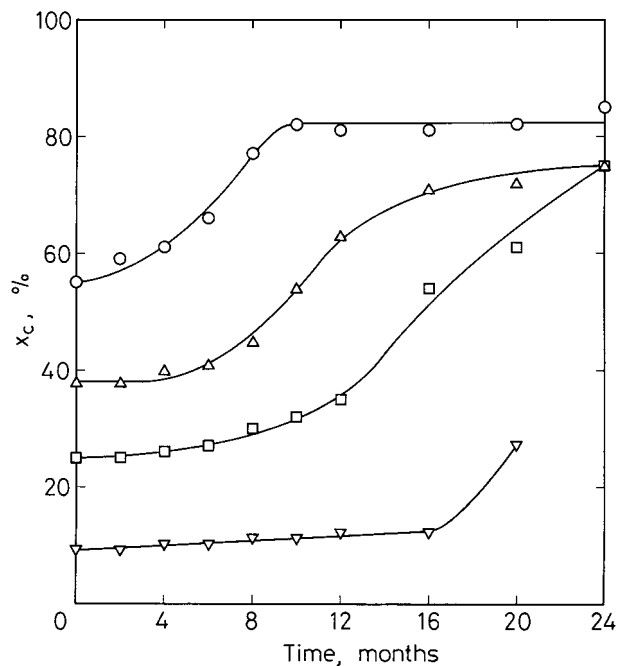


Figure 5 Crystallinity (x_c) of the PLA films with different X as a function of hydrolysis time: $X = (\nabla)$ 0.25, (\square) 0.5, (\triangle) 0.75, and (\circ) 1.

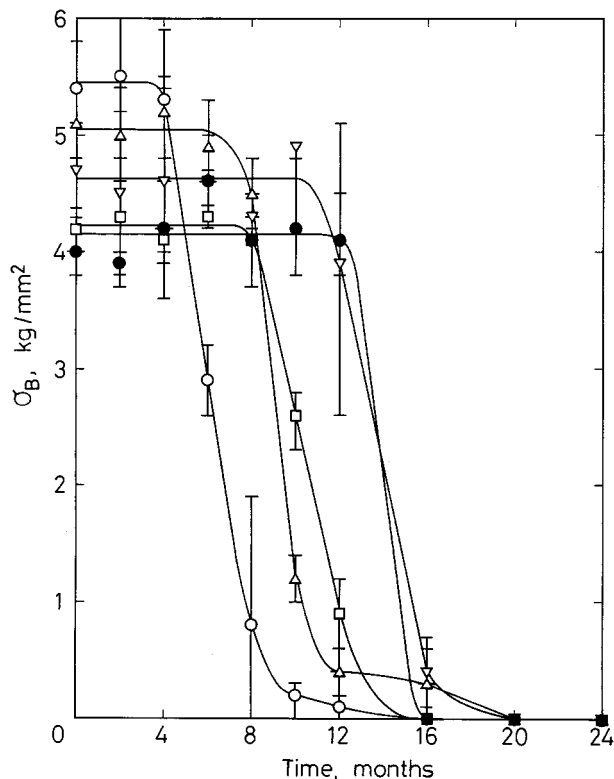


Figure 6 Tensile strength (σ_B) of the PLA films as a function of hydrolysis time: (●) $X = 0$, (▽) 0.25, (□) 0.5, (△) 0.75, and (○) 1.

vides us with a variety of materials with respect to degradation behavior, such as the decrease in total mass, molecular weight, and tensile strength. The hydrolytic behavior of the blend with $X = 0.5$ was intermediate between those of c-PLA and a-PLA, while the behavior of the blends with $X = 0.25$ and 0.75 approached to that of their major components, a-PLA and c-PLA, respectively.

A most interesting finding in this study may be the dependence of the tensile strength of PLA films on hydrolytic degradation, as demonstrated in Figure 6. The c-PLA film had the highest tensile strength before hydrolysis among the polymers used simply because it has the highest crystallinity, while a-PLA is a completely amorphous polymer. It is noteworthy that the a-PLA film maintains the initial strength for such a long time as 12 months in water, whereas c-PLA retains the initial strength only for two months. The blend film with $X = 0.5$ shows a tensile strength as low as that of a-PLA and retains its initial strength only for almost half the time of a-PLA. The difference in the strength retention time between a-

PLA and c-PLA may be explained in terms of tie molecules connecting microcrystallites in crystalline polymers and are, therefore, responsible for the ultimate tensile strength of crystalline polymers. When a certain fraction of tie molecules undergoes main-chain scission by random hydrolysis, a detectable reduction in the tensile strength will begin, as proposed by Chu and Campbell.⁴³ On the contrary, amorphous polymers with polar groups such as a-PLA have no microcrystallites, and each molecule is bound to the neighbors by the van der Waals force at temperatures below T_g . In other words, all the constituent polymer chains may be considered as "tie molecules" in the case of polar amorphous polymers at temperature below T_g . As a result, a considerably large number of chain scissions will be required for a-PLA to exhibit a noticeable reduction in the tensile strength.

As shown in Figure 2, approximately 75% of the initial mass of c-PLA film still remains even after 24 months of hydrolysis, although 100% of mass has disappeared for the a-PLA film. Such very slow degradation of c-PLA is undoubtedly ascribed to the large crystalline region where water diffusion is strongly prevented. If long-term retention of mechanical strength such as 12 months is required, a-PLA seems to be more suitable than c-PLA. The initial poor mechanical property of the amorphous polymer may be improved by forcing the polymer chains to align to a fixed direction.

The polymer fraction that disappeared from the mother PLA samples during hydrolysis and caused the mass loss is soluble in the hydrolytic medium. The GPC charts shown in Figure 3 allow us to estimate roughly the molecular weight of the soluble fraction. Extrapolation of the maximum slope of the lowest molecular weight side of the GPC peak for the PLA films with the largest mass loss to the baseline will give the highest molecular weight of the water-soluble fraction. The estimated molecular weight referred to polystyrene standards is approximately 300 for a-PLA and the blend of $X = 0.25$. This means that biodegradation products with molecular weights below 300 have been eluted from the PLA films into the surrounding medium.

Two modes have been proposed for inhomogeneous hydrolysis of polymeric materials: one is hydrolysis that proceeds gradually from the surface into the film (surface erosion); the other hydrolysis takes place preferably in bulk phase as Vert et al. reported for thick PLA sam-

ples.^{4,14,15,25,26,28,44,45} The results of GPC as well as DSC measurements reveal that neither the main GPC nor the melting DSC peak remains at the initial position after hydrolysis. This fact denies such a surface erosion mode that should leave a fraction of intact polymer in the degradation residue. It seems probable for the present samples that water-soluble degradation products with molecular weights lower than 300 have rapidly diffused out into the outer aqueous medium since the sample films are as thin as 200 μm .²⁸ A plausible reason for the appearance of low molecular weight peaks in Figure 3 for films containing c-PLA is selective scission of polymer chains in the amorphous region, leaving the crystalline region unattacked.² If this is the case, the molecular weight of folded polymer chains in the crystalline region should be 5×10^3 . The two times larger molecular weight (1×10^4) may be due to linking of two folded chains that have not yet received hydrolytic scission.

The double peak observed for the melting DSC endotherm of the blend films with $X = 0.5$ and 0.75 after hydrolysis is another interesting finding, similar to the double peak in the GPC after long-term hydrolysis. A slight shift of the melting DSC peak to lower temperature may be explained in terms of the dependence of melting temperature on the molecular weight of polymer, as reported in a previous study.³⁹ However, this cannot explain why a double peak appeared at 161 and 174°C in the melting DSC endotherm of two blend films after hydrolysis. A well-known explanation for such a multiple peak is melting–recrystallization–melting of crystallites during DSC scanning.^{46–48} However, this cannot explain why recrystallization did not occur for films with $X = 0.25$ and 1 . A possible explanation for that is the presence of two different environments surrounding the spherulitic crystallites of c-PLA component in the blend films after hydrolysis. One is the continuous a-PLA phase similar to the environment of the blend film of $X = 0.25$, which has a single melting peak at 175°C. The other environment is the c-PLA phase, which shows a melting peak shift from 180 to 159°C upon hydrolysis. As mentioned above, this shift may result from the reduction in the molecular weight by hydrolysis.

Finally, it should be mentioned that any trace of stereocomplexation between D-rich and L-rich biodegradation products was not found in this study, in contrast with that reported by Li and Vert.^{27,49} This might be due to different film prepara-

tion and initial molecular characteristics of PLA used.

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