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In vitro hydrolysis of blends from enantiomeric poly(lactide)s Part 1. Well-stereo-complexed blend and non-blended films

Hideto Tsuji*

Department of Ecological Engineering, Faculty of Engineering, Toyohashi University of Technology, Tempaku-cho, Toyohashi, Aichi 441-8580, Japan

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Abstract

Well-stereo-complexed 1:1 blend and non-blended films were prepared from PLLA and PDLA both having a medium molecular weight ($M_w = 1.5 \times 10^5$) by solvent evaporation method and their hydrolysis in phosphate-buffered solution (pH = 7.4) at 37°C was investigated up to 30 months using gel permeation chromatography (GPC), tensile tests, differential scanning calorimetry (DSC), scanning electron microscopy (SEM), optical polarizing microscopy, X-ray diffractometry, and gravimetry. The rate of reduction in molecular weight, tensile strength, Young's modulus, melting temperature, and mass remaining of the films in the course of hydrolysis was lower for the well-stereo-complexed 1:1 blend film than for the non-blended films. The induction period until the start of decrease in tensile strength, Young's modulus, and mass remaining was longer for the well-stereo-complexed 1:1 blend film than for the non-blended films. These findings strongly suggest that the well-stereo-complexed 1:1 blend film was more hydrolysis-resistant than the non-blended films. The retarded hydrolysis of the well-stereo-complexed 1:1 blend film compared with that of the non-blended films was ascribed mainly to the peculiar strong interaction between L- and D-lactide unit sequences in the amorphous region and/or the three-dimensional (3D) micro-network structure in the 1:1 blend film formed by stereo-complexation in the course of solvent evaporation. The change in the molecular weight distribution and surface morphology of the 1:1 blend film after hydrolysis revealed that its hydrolysis in phosphate-buffered solution proceeded homogeneously along the film cross-section mainly via the bulk erosion mechanism.

Keywords: Poly(lactic acid); Poly(lactide); Hydrolysis

1. Introduction

The family of poly(lactide)s (PLAs) and their copolymers have been attracting much attention in terms of medical and pharmaceutical applications and environmental protection because they are hydrolyzable in the human body as well as in each environment [1–7]. Blending biodegradable polymers is a commercially advantageous method to prepare biodegradable materials having a wide variety of physical properties and hydrolysis rates [1–7]. Since the study by Cha and Pitt [8] on the hydrolysis of blends from aliphatic polyesters, poly(ϵ-caprolactone), poly(L-lactide) (PLLA), and poly(L-lactide-*co*-glycolide), a great amount of investigations have been performed for PLAs and their copolymers based polymer blends in order to vary their physical properties and biodegradability [1–7].

Blends from enantiomeric PLLA and poly(D-lactide) (PDLA) are different from the other PLAs and their copolymers based blends because stereo-complexation or racemic crystallization occurs in the former blends owing to a strong interaction between L- and D-lactide unit sequences [9,10]. In a previous work, we reported that the mechanical properties of 1:1 blend films from PLLA and PDLA were higher than those of their non-blended films when they were prepared by slow solvent evaporation [10]. The increased mechanical properties of the 1:1 blend films were ascribed to stereo-complexation or formation of stereo-complex microcrystallites composed of L- and D-lactide unit sequences, which caused three-dimensional (3D) gelation in the course of solvent evaporation [9,10]. The 3D gelation will increase tie chain density and suppress the formation of large size spherulites in the 1:1 blend films, resulting in their increased mechanical properties compared with their non-blended films [10].

There is limited information available on the hydrolysis of the blends from PLLA and PDLA. Retarded hydrolysis of the blends was reported in the patent article without detailed estimation of molecular

* Tel.: +81-532-44-6922; fax: +81-532-44-6929.
E-mail address: tsuji@eco.tut.ac.jp (H. Tsuji).

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Table 1
Characteristics of L/D, L and D films before and after hydrolysis in phosphate-buffered solution for 30 months

Sample	$M_w/10^5$ (g/mol)		M_w/M_n		T_g (°C)		$T_{m,H}$ (°C)		$T_{m,S}$ (°C)	
	Before	After	Before	After	Before	After	Before	After	Before	After
L	1.56	0.20	1.8	5.4	66	65	177	156	–	–
D	1.52	0.09	1.6	3.2	66	[a]	178	157	–	–
L/D	1.50	0.80	1.6	3.2	67	65	177	175	225	227

Sample	ΔH_g (J/g)		$x_{c,H}$ (%)		$x_{c,S}$ (%)		SR_m [b] (μm)	
	Before	After	Before	After	Before	After	Before	After
L	3	3	49	69	–	–	100	[c]
D	3	0	52	76	–	–	100	[c]
L/D	3	3	10	14	35	46	<5	[c]

Sample	Tensile strength (kg/mm^2)		Young's modulus (kg/mm^2)		Elongation-at-break (%)	
	Before	After	Before	After	Before	After
L	2.8	0.0	108	0	4.7	0.0
D	2.9	0.0	117	0	4.3	0.0
L/D	2.1	0.5	85	52	13.9	0.7

[a] Glass transition peak was too diffuse to evaluate T_g.
[b] The maximum radius of spherulite estimated for 25 μm-thick film.
[c] No significant change was recognized after hydrolysis for 30 months.

characteristics of the polymers and the content of two crystalline species, stereo-complex crystallites consisting of both L- and D-lactide unit sequences and homo-crystallites composed of either L- or D-lactide unit sequences [11]. Li and Vert found that stereo-complexation occurs during hydrolysis of the poly(L-lactide-*co*-D-lactide) (50/50, 62.5/37.5) prepared by ring-opening polymerization of the mixtures of L- and D-lactides [12,13]. This was ascribed to preferred hydrolysis and removal of the chains having relatively random monomer unit sequences.

The purpose of the present wok is to investigate the in vitro hydrolysis of well-stereo-complexed 1:1 blend and non-blended films from PLLA and PDLA and to find the reason for the difference in hydrolysis behaviors between the well-stereo-complexed 1:1 blend and non-blended films. For this purpose, the films were prepared from PLLA and PDLA both having a medium weight-average molecular weight (M_w) of 1.5×10^5 using solvent evaporation method, because the 1:1 blends from PLLA and PDLA both with a low M_w could not form any films and homo-crystallization of either L- or D-lactide unit sequences occurred predominantly in the blend films from PLLA and PDLA both having a high M_w [9,10]. In this study solvent evaporation was performed rapidly to reduce a shape strain of the 1:1 blend film caused by the growth of stereo-complex crystallites and syneresis after 3D gelation of mixed solutions [9]. Hydrolysis of the 1:1 blend and non-blended films was performed up to 30 months and the hydrolyzed films were studied using gel permeation chromatography (GPC), tensile tests, differential scanning calorimetry (DSC), scanning electron microscopy (SEM), optical polarizing microscopy, X-ray diffractometry and gravimetry.

2. Experimental

2.1. Materials

Synthesis and purification of PLLA and PDLA used in this work were described in detail in previous papers [14–17]. The molecular characteristics of the purified PLLA and PDLA are given in Table 1. The specific optical rotation measured in chloroform at 25°C and at a wave length of 589 nm ($[a]_D^{25}$) was −154 and +155°, respectively, for the purified PLLA and PDLA, in good agreement with the reported values [9,10,18]. The films used for hydrolysis were prepared from the purified PLLA and PDLA by the method described in the previous papers [9,10,16,17]. Each solution of PLLA and PDLA in methylene chloride was separately prepared to have a polymer concentration of 1.0 g/dl. They were admixed with each other equimolarly under vigorous stirring. The solution was cast onto a Petri dish, followed by solvent evaporation at room temperature for approximately 1 day. Solvent evaporation was performed very rapidly compared with that in the previous works (ca. 1 week) [9,10] to avoid the formation of a large shape strain in the 1:1 blend film, which will be caused by the growth of stereo-complex microcrystallites and the syneresis after 3D gelation in the 1:1 mixed solution. The resulting films were dried in vacuo for 1 week prior to hydrolysis. The appearance of the 1:1 blend and the non-blended films was whitish and opaque, respectively. The 1:1 blend and non-blended PLLA and PDLA films are abbreviated L/D, L and D films, respectively.

2.2. Hydrolysis

Hydrolysis of the films (1.8 mm × 3.0 mm × 50 mm or 25 μm) was performed in 10 ml of 0.15 M phosphate-buffered

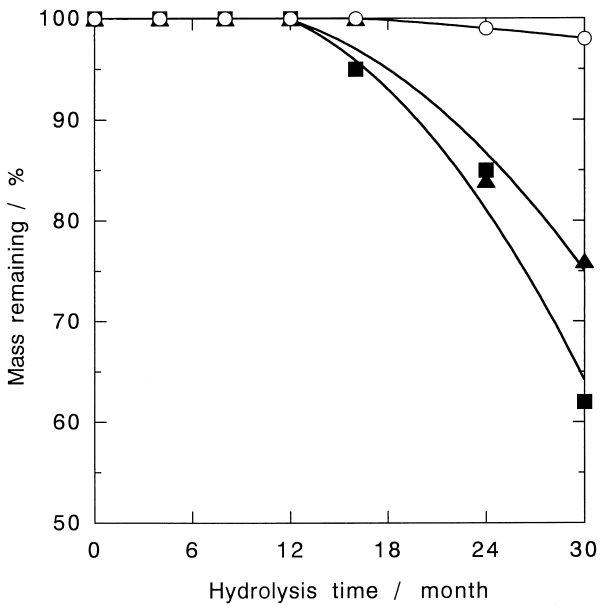


Fig. 1. Mass remaining of L/D (○), L (▲) and D (■) films as a function of hydrolysis time.

solution (pH = 7.4 ± 0.1) at 37°C for predetermined periods of time exchanging the buffered solution once a month. After hydrolysis, the films were washed thoroughly with doubly distilled water at room temperature, followed by drying under a reduced pressure for at least 2 weeks.

2.3. Measurements

M_w and number-average molecular weight (M_n) of the polymers were evaluated in chloroform at 40°C using a Tosoh GPC system with TSK gel columns ($GMH_{XL} \times 2$) and polystyrene as a standard. The solutions of the L/D films before and after hydrolysis were prepared by dissolving them in chloroform at 90°C for 4 min in sealed test tubes, because of their low solubility in chloroform at room temperature. Insignificant change occurred in the molecular weight distributions of the L and D films by heating at 90°C for 4 min in chloroform. The observed molecular weight distribution of the L/D film before hydrolysis was in good agreement with that expected from those of the L and D films before hydrolysis.

The glass transition, crystallizaiton, and melting temperatures (T_g, T_c and T_m, respectively) and the enthalpy of glass transition, crystallization and melting (ΔH_g, ΔH_c, and ΔH_m, respectively) of the films were determined by a Shimadzu DT-50 DSC. The films were heated at a rate of 10°C/min under a nitrogen gas flow of 50 ml/min for DSC measurements. T_g, T_c, T_m, ΔH_g, ΔH_c and ΔH_m were calibrated using tin, indium and benzophenone as standards. The crystallinities ascribed to homo- and stereo-complex crystallites in the films ($x_{c,H}$ and $x_{c,S}$, respectively) were evaluated according to the following equations [16,17,19]:

$$x_{c,H}(\%) = 100(\Delta H_{c,H} + \Delta H_{m,H})/93 \quad (1)$$

$$x_{c,S}(\%) = 100\Delta H_{m,S}/142 \quad (2)$$

where 93 and 142 (J/g of polymer) are ΔH_m of the PLLA (or PDLA) and the stereo-complex crystals having the infinite crystal thickness reported by Fischer et al. [20] and Loomis et al. [21] and $\Delta H_{c,H}$, $\Delta H_{m,H}$ and $\Delta H_{m,S}$ are ΔH_c and ΔH_m of homo-crystallites and ΔH_m of stereo-complex crystallites, respectively, of the films. The peaks of the crystallization and the melting of homo-crystallites and the melting of stereo-complex crystallites appear in DSC thermograms at the temperature range of 80–120, 140–180 and 210–240°C, respectively. The crystallization peak at 80–120°C was assumed to be that of homo-crystallites for simplicity as in a previous paper [22].

Tensile properties of the 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. X-ray diffractometry was performed at 25°C using a Rigaku RINT-2500 equipped with a CuKα source.

2.4. Microscopy

Morphology of the films was studied with a SEM (Hitachi S-2300) and a Zeiss polarizing microscope. The thickness of the films utilized for microscopic observation was 25 μm. The films for SEM observation were coated with carbon to a thickness of about 20 nm.

3. Results

Table 1 tabulates observed values of M_w, M_w/M_n, T_g, $T_{m,H}$, $T_{m,S}$, ΔH_g, $x_{c,H}$, $x_{c,S}$, tensile strength, Young's modulus and elongation-at-break of the films with a thickness of 50 μm and maximum spherulite radius (SR_m) of the films with a thickness of 25 μm before and after hydrolysis in the phosphate-buffered solution for 30 months. Here, $T_{m,H}$ and $T_{m,S}$ are T_m of homo- and stereo-complex crystallites, respectively. The $x_{c,S}$ of the L/D film before hydrolysis is higher than its $x_{c,H}$, meaning that stereo-complexation was prevailing over homo-crystallization during solvent evaporation. The total crystallinity ($x_{c,H} + x_{c,S}$) of the L/D film before hydrolysis is almost identical with the $x_{c,H}$ of the L and D films before hydrolysis. The tensile strength and Young's modulus of the L/D film prepared by rapid solvent evaporation (2.1 and 85 kg/mm^2) are smaller than 4.6 and 150 kg/mm^2 of those prepared by slow solvent evaporation, whereas the initial elongation-at-break is larger for the L/D film prepared by rapid solvent evaporation (13.9%) than for that prepared by slow solvent evaporation (4.0%) [10].

The decrease in M_w is larger for the L and D films than for the L/D film. The M_w/M_n increased for all the films after hydrolysis. The change in T_g and ΔH_g of the L/D and L films is very small, while glass transition was not recognized for the D film after hydrolysis. The decrease in $T_{m,H}$ upon hydrolysis is larger for the L and D films than that for the L/D

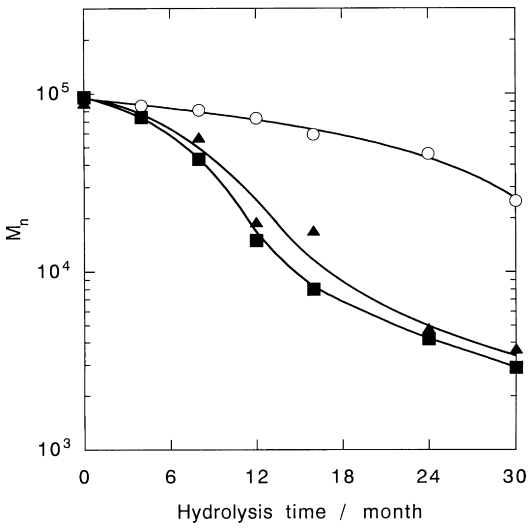


Fig. 2. M_n of L/D, (○), L (▲) and D (■) films as a function of hydrolysis time.

film, while decrease in $T_{m,S}$ of the L/D film is very small compared with that in $T_{m,H}$ of the L and D films. The large decrease in $T_{m,H}$ of the L and D films is suggestive of a significant decrease in the thickness of homo-crystallites, while a very small change in $T_{m,S}$ and $T_{m,H}$ of the L/D film suggests that no significant change occurred in the thickness of stereo-complex and homo-crystallites. The x_c of all the films significantly increased after hydrolysis. The SR_m value was given for the films before hydrolysis alone in Table 1, since no significant change was observed for SR_m after hydrolysis, in agreement with the results for melt-crystallized PLLA films hydrolyzed in alkaline [17] and phosphate-buffered [23] solutions. The L/D film had non-zero tensile strength, Young's modulus and elongation-at-break 30 months after hydrolysis, while these values became practically zero for the L and D films.

3.1. Mass remaining

Fig. 1 shows the mass remaining for the L/D, L and D films as a function of hydrolysis time. The mass loss is an index for the content of water-soluble oligomers formed by hydrolysis and then released from the mother films into the surrounding medium. The induction period until the mass remaining started to decrease is longer for the L/D film (24 months) than for the L and D films (16 months). The mass remaining after hydrolysis for 30 months was 98, 76 and 62% for the L/D, L and D films, respectively. This suggests that a very small amount of water-soluble oligomers were formed in the L/D film even after hydrolysis for 30 months. A slightly different mass loss observed during hydrolysis between the L and D films may be ascribed to the difference in their initial molecular weight distribution.

3.2. Molecular weight

Fig. 2 demonstrates the M_n of the L/D, L and D films as a function of hydrolysis time. The M_n of the L/D film decreased slowly compared with that of the non-blended films. Hydrolytic rate constant (k) was evaluated by the method described by Cha and Pitt [8] using the M_n values of the films hydrolyzed for 0 and 4 months. The estimated k value for the L/D film (0.73×10^{-3} day^{-1}) is one order smaller than that for the L (1.41×10^{-3} day^{-1}) and D (2.14×10^{-3} day^{-1}) films. The k values for the L and D films are in agreement with $k = 2$–3.5×10^{-3} day (0–365 days) for high molecular weight as-cast and melt-crystallized PLLA films ($M_w = 1.2 \times 10^6$, $M_w/M_n = 2.6$) [23,24] but slightly smaller than 6.72×10^{-3} day^{-1} (0–42 days) for low molecular weight compression-moulded PLLA specimens ($M_n = 3 \times 10^4$) found by Cha and Pitt [8]. The k value difference between the non-blended PLLA specimens may be due to the difference in their preparation method and molecular weight distribution.

Fig. 3 shows the GPC curves of the L/D and L films hydrolyzed for different periods of time. The result of the D film is not given in Fig. 3, because its change in GPC curves during the hydrolysis was comparable with that of the L film. Because of the same reason, the result of the D film will not be given in Figs.6, 7, and 9. The molecular weight of the L/D film shifted to lower region on the whole without the formation of any specific peak originating from crystalline residue during hydrolysis up to 30 months. On the contrary, the molecular weight of the L film shifted to lower accompanying specific peak formation around the molecular weight of 4×10^3 when hydrolysis was carried out longer than 24 months. This indicates that the chains in the amorphous region of the L film were hydrolyzed to water-soluble oligomers and then eluted from the mother film, leaving the chains in the crystalline region.

The molecular weight of the specific peak for the L film (4×10^3) was rather smaller than 7.4, 9.3 and 13.9×10^3 reported for the PLLA films prepared by annealing at 120, 140 and 160°C from the melt [25], and 1×10^4 for the PLLA specimens prepared by compression moulding and crystallization at 130°C (Li and Vert) [26] and for as-polymerized PLLA specimens (Pistner et al.) [27]. This is probably due to a small crystalline thickness of the L film compared with those reported earlier.

3.3. Mechanical properties

Fig. 4(a)–(c) demonstrates the change of residual tensile strength, Young's modulus, and elongation-at-break, respectively, for the L/D, L and D films. The tensile properties are indexes for the density of the remaining tie chains in the amorphous region. As evident from Fig. 4(a) and (b), the induction period until a noticeable decrease in the tensile strength and Young's modulus is longer for the L/D film than for the L and D films. It is interesting to note that the L/D film retained its initial tensile strength and Young's modulus for 16 and 24 months, respectively, while the tensile strength and Young's modulus of the L and D films started to

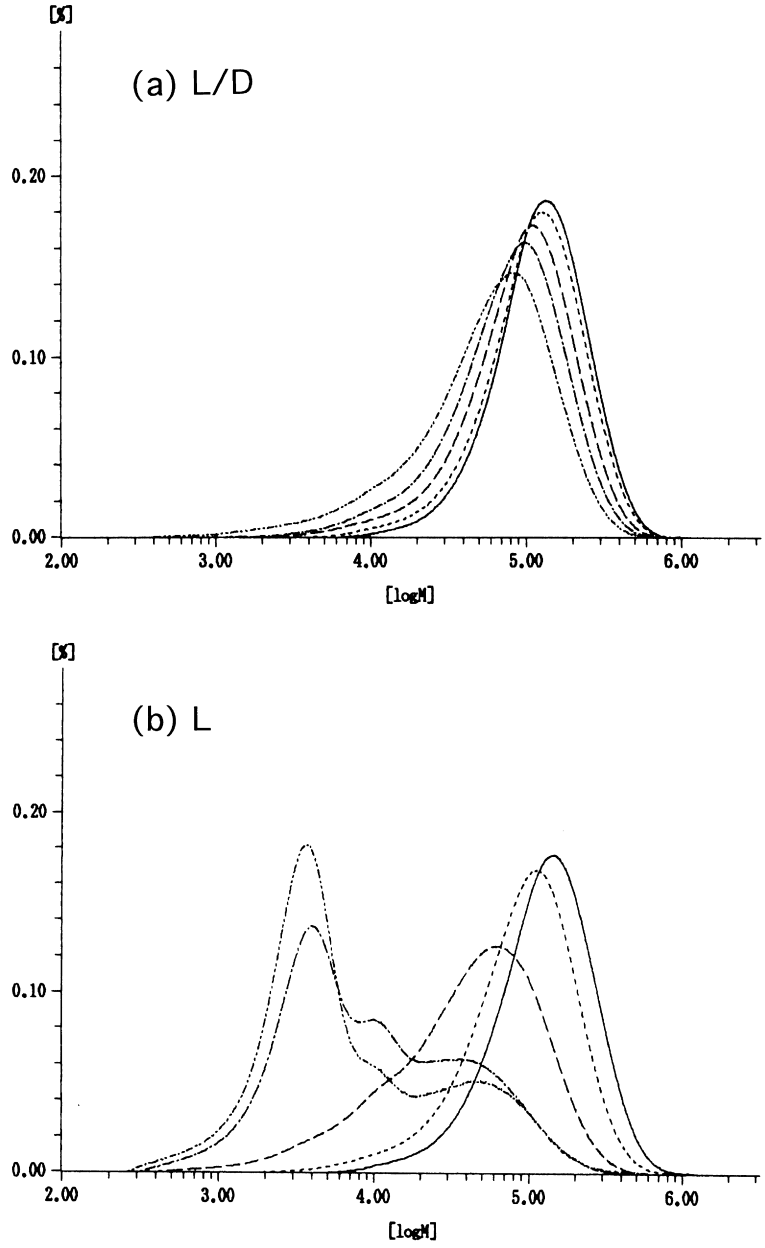


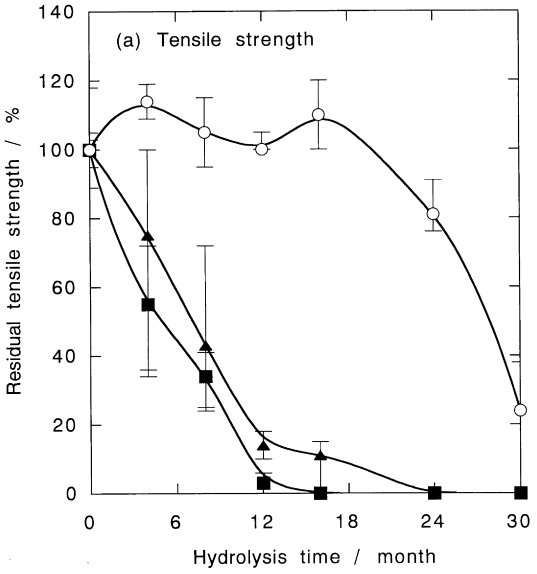
Fig. 3. GPC curves of L/D, (a) and L (b) films after hydrolysis for different times: —: 0 month; ···:8 months; - - - :16 months; -·-·-: 24 months; and -···-: 30 months.

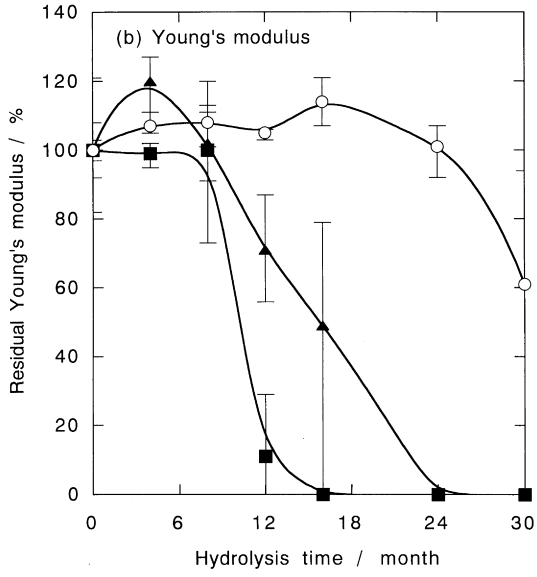
decrease without any induction periods and 12 months after hydrolysis, respectively. The elongation-at-break of the L and D films decreased slowly in the first 8 months but rapidly after hydrolysis time longer than 12 months, while that of the L/D film decreased gradually. The elongation-at-break remaining at hydrolysis time above 12 months is higher for the L/D film than for the L and D films.

3.4. Change in the crystalline region

Fig. 5 shows the DSC thermographs of the L/D, L and D films before and after hydrolysis for 30 months. The melting peak of homo-crystallites of the L and D films, appearing around 180°C before hydrolysis, shifted to lower temperature after hydrolysis for 30 months, accompanying an area increase, in agreement with the reported results for PLLA specimens [17,23–29]. The melting sub peak of homo-crystallites appearing around 170°C for the L film after hydrolysis for 30 months may be ascribed to those crystallized during the DSC measurements. In contrast, the melting peak of homo-crystallites of the L/D film showed a very small change after hydrolysis for 30 months. On the contrary, the melting peak of stereo-complex crystallites in the L/D film, became larger without changing its position after 30 months for hydrolysis.

Fig. 6 demonstrates the X-ray diffraction profiles of the





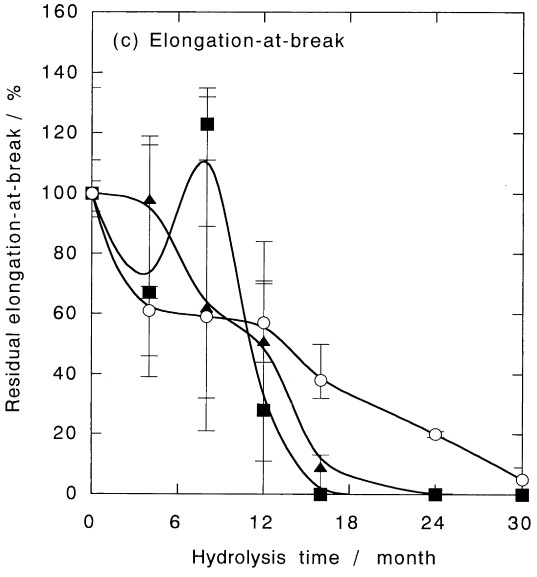


Fig. 4. Residual tensile strength (a), Young's modulus (b) elongation-at-break (c) of L/D (○), L (▲) and D (■) films as a function of hydrolysis time.

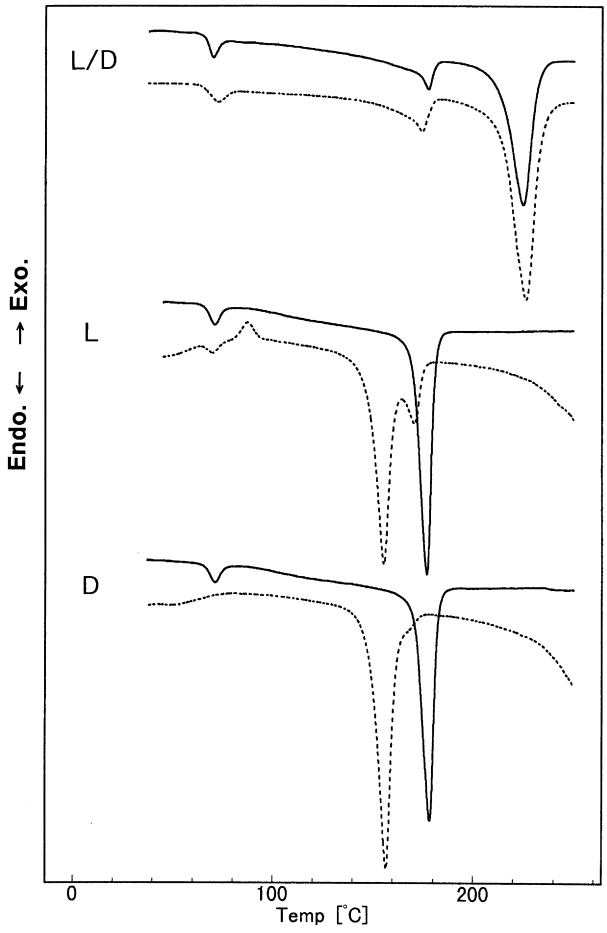


Fig. 5. DSC thermograms of L/D, L and D films before (—) and after (- - -) hydrolysis for 30 months.

L/D, L and D films before and after hydrolysis for 30 months. The most intense peaks of the L/D, films before and after hydrolysis are observed at 2θ values of 12, 21 and 24°, in excellent agreement with the reported results [30–33] for PLA stereo-complex crystallized in a triclinic unit cell of dimensions: $a = 0.916$ nm, $b = 0.916$ nm, $c = 0.870$ nm, $\alpha = 109.2°$, $\beta = 109.2°$, and $\gamma = 109.8°$, in which L-lactide and D-lactide segments are packed parallel taking 3_1 helical conformation [31], while the main peaks of the L films before and after hydrolysis appear at $2\theta = 15$, 17, and 19° [30–33], which are comparable with the α form of PLLA crystallized in a pseudo-orthorhombic unit cell of dimensions: $a = 1.07$ nm, $b = 0.595$ nm, and $c = 2.78$ nm, which contains two 10_3 helices [31]. The peaks observed at 2θ values of 17 and 19° for the L/D films before and after hydrolysis are ascribed to the α form of PLLA or PDLA. These findings indicate that the L/D films contain both stereo-complex and homo-crystallites before and after

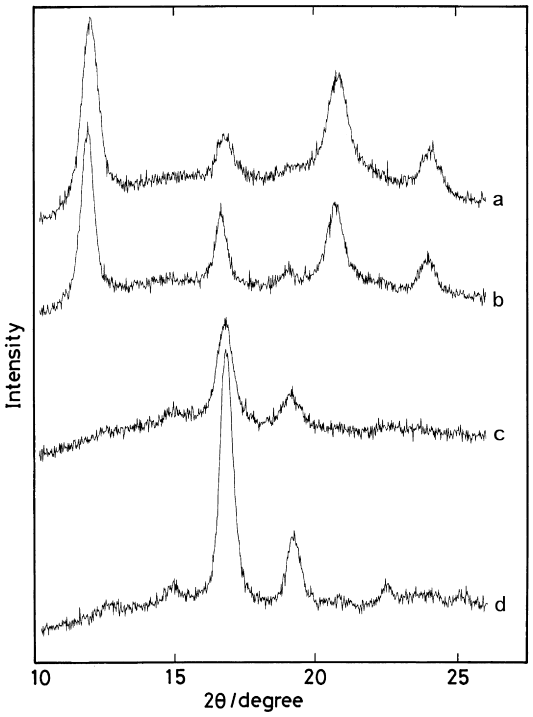


Fig. 6. X-ray diffraction profiles of L/D a,b and L c,d films before a,c and after b,d hydrolysis for 30 months.

hydrolysis, in agreement with the DSC result. The diffraction peaks of stereo-complex and homo-crystallites of the L/D film became sharper after hydrolysis for 30 months, suggesting that their lattice disorder decreased after hydrolysis. The intensity and sharpness of the peaks of the L film dramatically increased after hydrolysis for 30 months. This suggests that its crystallinity increased while the lattice disorder of homo-crystallites decreased after hydrolysis.

3.5. Morphological change

The polarizing optical photomicrographs of the L/D and L films with a thickness of 25 μm before and after hydrolysis for 30 months are shown in Fig. 7. As seen, the L film before hydrolysis is covered with the spherulites with a maximum radius of about 100 μm, while the L/D film before hydrolysis contains a great amount of micro-crystallites but no well-defined spherulites. After 30 months of hydrolysis, many dark lines along the radius direction of the spherulites were formed in the L film, while in the case of L/D film solely an increase in the brightness was observed. A slight decrease in the photographic contrast between bright and dark region in spherulites was recognized for the L film after hydrolysis for 30 months in agreement with that observed for melt-crystallized PLLA films after hydrolysis in alkaline solution for 150 days [17] and after hydrolysis in phosphate-buffered solution for 36 months [23]. This contrast decrease suggests that the L film was hydrolyzed preferentially at the chains in the amorphous region connecting the crystalline lamellae in the spherulites, resulting in a reduced orientation of the lamellae.

The SEM photomicrographs of the L/D and L films before and after hydrolysis for 30 months are shown in Figs. 8 and 9, respectively. Interestingly, 3D micro-network structure is observed for the L/D films before and after hydrolysis. This structure was probably formed by stereo-complexation or formation of stereo-complex microcrystallites, which may have caused 3D gelation and followed by syneresis during solvent evaporation. The 3D micro-network structure is composed of the fibers with diameter ca. 1 μm. As evident from Fig. 8, insignificant change in morphology occurred for the L/D film after hydrolysis for 30 months.

Some protuberances observed on the surface of the L films before and after hydrolysis for 30 months are ascribed to the PLLA spherulites. However, the network structure or

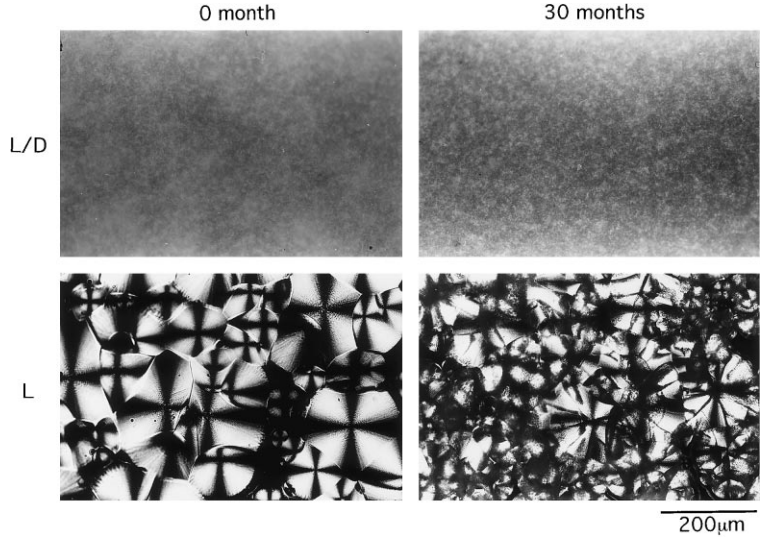


Fig. 7. Polarizing photomicrographs of L/D, and L films before and after hydrolysis for 30 months.

pores were not recognized on the surface of the L films. Hydrolysis for 30 months induced crack formation inside the PLLA spherulites. The dark lines in the PLLA spherulites after hydrolysis for 30 months (Fig. 7) is probably due to this crack formation. Insignificant surface microstructure change other than this crack formation was observed for the L film after hydrolysis for 30 months even when magnification was increased up to 3×10^3 times.

4. Discussion

The initial shift of the whole molecular weight distribution of the L/D, L and D films to lower molecular weight (Fig. 3) and the SEM photographs of the hydrolyzed L/D (Fig. 8) and L (Fig. 9) films demonstrate that the bulk erosion mechanism was dominant for the hydrolysis of the films in phosphate-buffered solution at pH = 7.4. This is in agreement with that reported for the melt-crystallized PLLA specimens hydrolyzed in phosphate-buffered solution [23], but is in contrast to that reported for the melt-crystallized PLLA specimens hydrolyzed in dilute alkaline solution at pH = 12, where the surface erosion mechanism was prevailing [17]. The unvaried mono-disperse GPC curvature of the L/D film during hydrolysis indicates that the L/D, film with thickness below 50 μm underwent homogeneous hydrolysis along the film cross-section, in contrast to the PLA specimens having thickness higher than 2 mm, where hydrolysis was accelerated at the core [26,34].

It is evident from the results obtained by DSC and gravimetry, GPC, tensile tests and SEM that the chains in the crystalline and amorphous regions of the L/D film were more hydrolysis-resistant than the crystalline and amorphous regions of the L and D films, respectively. One probable reason for the high hydrolysis-resistance of the chains in the amorphous region of the L/D film may be the peculiar strong interaction between L- and D-lactide unit sequences in the L/D film than that between either L-lactide unit sequences or D-lactide unit sequences in the L and D films. This strong interaction will delay the diffusion of water molecules into the amorphous region of the L/D film, resulting in the retarded hydrolysis of the chains in the amorphous region as well as those in the crystalline region surrounded by this hydrolysis-resisitant amorphous region. The difference in the chain packing in the amorphous region between the L/D film and the L and D films may be evidenced by the comparison of the density of the PLLA/PDLA blend film containing stereo-complex crystalline and amorphous region (1.24 g/cm^3) [32] with those of the homo-crystalline (1.29 g/cm^3) and amorphous (1.25 g/cm^3) regions of a PLLA specimen [20]. Almost identical total crystallinity among the films before hydrolysis (Table 1) implies that the difference in the crystalline thickness between the films have had some effects on their hydrolytic behavior.

On the contrary, it is well known that low molecular weight oligomers formed by hydrolysis will catalyze the hydrolysis of PLA materials and that hydrolysis rate is proportional to the concentration of carboxyl group of the oligomers and polymers [1–8]. Another reason for the high hydrolysis-resistance of the L/D film may be its 3D micro-network structure, which will reduce the mean distance for the catalytic oligomers to diffuse out from the mother films, resulting in their reduced concentration in the L/D film compared with those in the L and D films. The difference in this mean distance between the films is evident from the comparison of the diameter ca. 1 μm of the network fibers of the L/D film with the bulk thickness 50 or 25 μm of the non-porous L and D films.

Li et al. [26] and Grizzi et al. [34] reported that accelerated hydrolysis occurred at the core part of PLA materials due to the entrapped catalytic oligomers when the material thickness was increased above 2 mm. In this present work, though the apparent thickness of the films was as low as 50 or 25 μm, it is probable that the concentration of catalytic oligomers in the bulky non-porous L and D films was higher than that in the 3D micro-network of the L/D film, resulting in the accelerated hydrolysis of the L and D films. Indeed, Lam et al. reported that a porous PLLA film was more hydrolysis-resistant than a non-porous PLLA film though their thickness (<300 μm) was lower than 2 mm [35]. They concluded that the retarded hydrolysis of the porous PLLA film was owing to a very small amount of catalytic oligomers entrapped in it compared with that in the non-porous bulky PLLA film.

The initial low tensile strength and Young's modulus and high elongation-at-break of the L/D film prepared by rapid solvent evaporation compared with that prepared by slow solvent evaporation for 1 week [10] may be ascribed to the 3D micro-network structure. In the previous work, this 3D micro-network structure was not observed when the L/D film was prepared by slow solvent evaporation [10]. However, large sized pores (10–30 μm) were formed for the L/D film prepared by slow solvent evaporation when M_w of PLLA and PDLA were increased to 2.5 and 1.8×10^5, respectively [10]. This is probably due to the enhanced growth of stereo-complex microcrystallites and syneresis after 3D gelation.

In conclusion, it is assumed from this study that the hydrolysis-resistance of PLA materials can be increased by stereo-complexation between PLLA and PDLA and that biodegradable materials with a wide variety of hydrolysis rate can be manufactured by varying their mixing ratio. The hydrolysis-resistance of the well-stereo-complexed L/D film may be ascribed to the peculiar strong interaction between L- and D-lactide unit sequences in the amorphous region and/or its 3D micro-network structure, which will decrease the diffusion rate of water molecules into the amorphous region and/or the concentration of catalytic oligomers formed by hydrolysis, respectively. The hydrolysis of the L/D film with thickness below 50 μm in phosphate-buffered

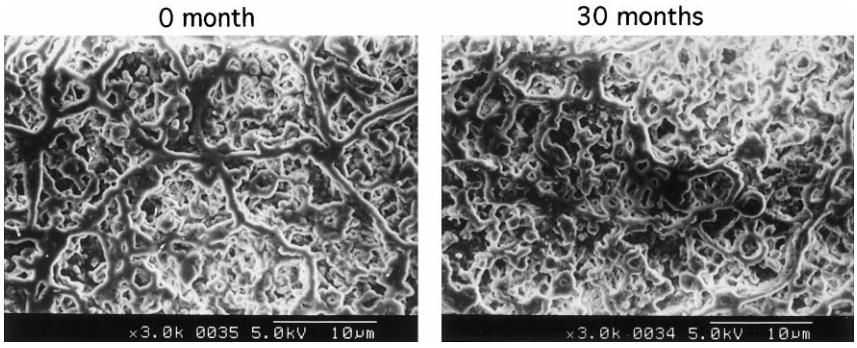


Fig. 8. SEM photomicrographs of L/D, before and after hydrolysis for 30 months.

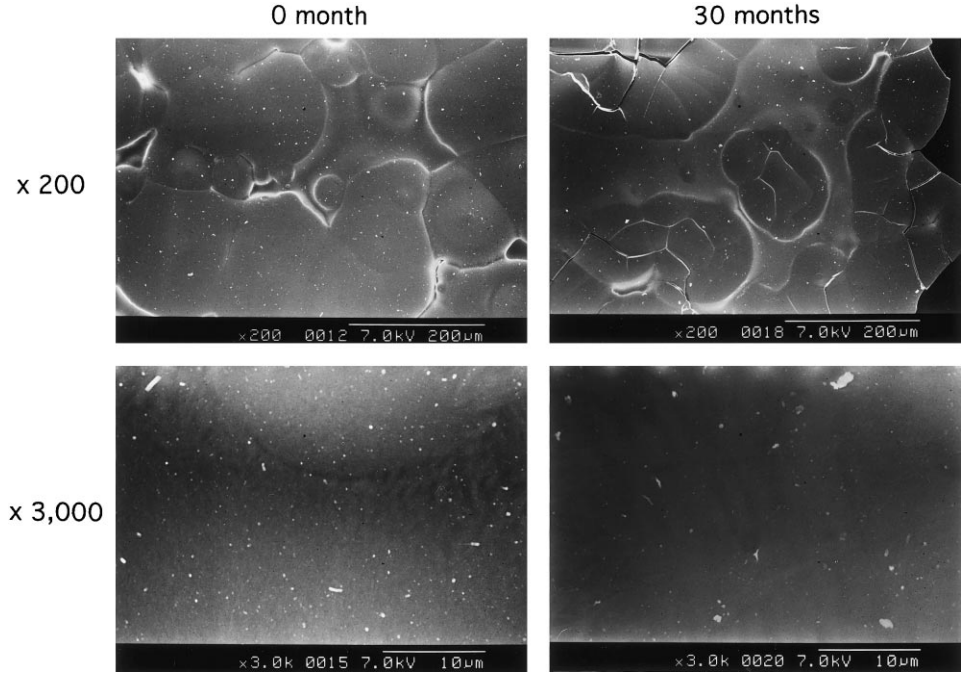


Fig. 9. SEM photomicrographs of L films before and after hydrolysis for 30 months at magnification of 200 and 3000×.

solution proceeded homogeneously along the film cross-section mainly via the bulk erosion mechanism.

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