Poly(L-lactide). IX. Hydrolysis in Acid Media

Hideto Tsuji, Kazumasa Nakahara

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

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ABSTRACT: Amorphous and crystallized poly(L-lactide) (PLLA) films are prepared by quenching and annealing at 140°C for 600 min, respectively, from the melt. Their hydrolysis is investigated at pH 2.0 in HCl and DL-lactic acid (DLLA) solutions (37°C) for up to 300 days, and the results are compared with those obtained for PLLA films hydrolyzed at pH 7.4 (phosphate-buffered solution) and pH 12 (NaOH solution). The changes in the weight loss and molecular weight distribution of the PLLA films during hydrolysis in the acid media reveals that their hydrolysis proceeds homogeneously along the film cross section by mainly a bulk erosion mechanism. Moreover, the durability of PLLA films in the acid media is very similar to that in the neutral medium but higher than that in the alkaline medium. The hydrolysis rate constant values (k) of the initially amorphous PLLA0 film evaluated from the changes in the number-average molecular weight were 3.0 and 2.4×10^{-3} day^{-1} at pH 2.0 in the HCl and DLLA solutions, respectively. These k values are very similar to 2.6×10^{-3} day^{-1} at pH 7.4 in the phosphate-buffered solution. The similar k values and the negligible weight loss after the hydrolysis for 300 days reflect that the hydronium ions and the lactic acid oligomers and monomers have insignificant catalytic effects on the hydrolysis of the PLLA films. Increasing the initial crystallinity of the PLLA film increases the hydrolysis rate in the HCl solution, whereas increasing the initial crystallinity of the PLLA film does not alter the hydrolysis rate in the DLLA solution. The differential scanning calorimetry results show that the crystallization of PLLA chains occurs during the hydrolysis, irrespective of the hydrolysis acid media and the initial crystallinity. © 2002 Wiley Periodicals, Inc. J Appl Polym Sci 86: 186–194, 2002

Key words: annealing; biodegradable; biomaterials; degradation; polyesters

INTRODUCTION

Polylactides, which are poly(lactic acid)s (PLAs), attract much attention because they are producible from renewable resources including starch and are nontoxic and biodegradable in natural environments and the human body.[1–9] Moreover, PLA polymers have mechanical properties comparable with those of commercial polymers such as polyethylene, polypropylene, and polystyrene.[1–9] Among PLA polymers, poly(L-lactide), [i.e., poly(L-lactic acid) (PLLA)] has the best mechanical properties. In previous studies of this series we investigated the effects of structural parameters on the hydrolysis of PLLA films in different media such as a phosphate-buffered solution (pH 7.4),[10–12] an alkaline solution (pH 12),[13] and a proteinase K/Tris-HCl buffer solution system (pH 8.6).[14,15] The following results were obtained from these studies:

1. Hydrolysis of PLLA films proceeds via mainly a surface erosion mechanism in the alkaline solution (pH 12)[13] and the proteinase K/Tris-HCl buffer solution system,[14,15] whereas in phosphate-buffered solution it proceeds homogeneously along the film cross section via mainly a bulk erosion mechanism.[10–12]
2. Hydrolytic scission of PLLA chains occurs predominantly in the amorphous region between the crystalline regions inside and outside the spherulites, irrespective of the hydrolysis media.[10–15]
3. In the alkaline solution[12] and the proteinase K/Tris-HCl buffer solution system[14,15] the overall hydrolysis rate of the PLLA films decreases with the initial crystallinity (X_c), whereas in phosphate-buffered solution it increases with the initial X_c.[10–12]
4. The radius of the spherulites had a practically negligible effect on the hydrolysis of PLLA films, regardless of the hydrolysis media.[11,13]
5. The low molecular weight (LMW) specific peaks in gel permeation chromatography (GPC) curves for the crystallized PLLA films hydrolyzed in the above-mentioned media were ascribed to the PLLA chains of one and several folds in the crystalline region.[10–15] The molecular weight of the

Correspondence to: H. Tsuji (tsuji@eco.tut.ac.jp).

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TABLE I
Characteristics of PLLA Films before and after Hydrolysis at pH 2.0 and 37°C in Acid Solutions

Samples	Hydrolysis media	Hydrolysis time (days)	$M_n \times 10^{-5}$ (g/mol)	M_w/M_n	T_g (°C)	T_c (°C)	T_m (°C)	X_c (%)
PLLA0	—	0	4.4	2.0	56	110	177	0
	HCl solution	300	2.0	1.9	67	96	178	3
	Lactic acid solution	300	2.2	1.8	67	99	178	3
PLLA140	—	0	4.2	2.0	65	—	182	32
	HCl solution	300	1.1	2.0	63	—	178	49
	Lactic acid solution	300	2.2	1.7	66	—	182	45

crystalline residues increases with the annealing temperature applied for specimen preparation from the melt.[11–13]

6. In phosphate-buffered solution the increasing of the hydrolysis temperature does not alter the hydrolysis mechanism of the PLLA films and the effects of the highly ordered structures on the hydrolysis.[12]

On the other hand, Makino et al. studied the effects of pH, inonic strength, and buffer concentration on the hydrolysis of PLLA microspheres.[16] It was suggested that the concentration of hydroxide and hydronium ions in the microspheres has an important role in the hydrolysis when the ζ potential of the microspheres is negative and positive, respectively.

The effects of pH on the hydrolysis of poly(DL-lactide) [i.e., poly(DL-lactic acid) (PDLLA)] were studied by Mason et al.,[17] Makino et al.,[18] Shih,[19,20] and Li and McCarthy.[21] They found that the acid media slightly accelerates the hydrolysis of PDLLA[17,18] and the water absorption of PDLLA hydrolyzed at pH 3.7 was much lower than that hydrolyzed at pH 7.4.[21] Shih revealed that in acid media the hydrolytic scission at the PDLLA chain ends is faster than that of the internal ester bonds and in alkaline media the hydrolysis proceeds by random chain scission.[18,19] However, in acid media the hydrolysis mechanism of PLLA as bulk materials and the effects of highly ordered structures on the hydrolysis were not investigated. Moreover, there is limited information available for the effects of water-soluble lactic acid oligomers and monomers present in the media, the concentrations of which increase during hydrolysis, on the hydrolysis of PLLA materials. On the other hand, the changes in the residual weight, molecular weights, and thermal properties of PLLA film shaped materials by contact with acid media are important to estimate their durability and highly ordered structural changes when they are used as food packages, containers, bottles, and so on. However, such basic information was not reported thus far.

The purposes of this work are to unveil the hydrolysis mechanism of PLLA as bulk materials in acid media, to investigate the effects of an important highly ordered structure (the crystallinity) on the hydrolysis of PLLA films in acid media and the changes in their highly ordered structures during acid hydrolysis, to study the effects of water-soluble lactic acid oligomers and monomers present in the media on the hydrolysis of PLLA materials, and to compare the results obtained for PLLA films hydrolyzed at low pH with those hydrolyzed at medium and high pH. For these purposes we prepared the amorphous and crystallized PLLA films by quenching and annealing, respectively, of solution-cast films from the melt.[22] The acceleration effect of oligomers, which are formed by PLA hydrolysis and trapped at the core of the specimens, was reported by Li et al.[23,24] and Grizzi et al.[25] for specimens with thicknesses above 2 mm. To exclude this effect on the hydrolysis, the thickness of the PLLA films was kept as thin as about 50 μm. The hydrolysis of the PLLA films was carried out in HCl and DL-lactic acid (DLLA) solutions at pH 2.0 for up to 300 days. The hydrolyzed films were studied using gravimetry, GPC, and differential scanning calorimetry (DSC).

EXPERIMENTAL

Materials

The synthesis and purification of PLLA and the preparation of films from the purified PLLA [number-average molecular weight (M_n) = 4.9×10^5, polydispersity index (M_w/M_n) = 2.0, where M_w is the weight-average molecular weight] were performed by the procedure reported previously.[22] Annealing of the PLLA films before hydrolysis was carried out by the following procedure.[22] Each of the PLLA films of 50 $\pm$ 10 μm thickness were placed between two Teflon sheets and sealed in a glass tube under reduced pressure. The sealed PLLA films were melted at 200°C for 5 min and then quenched at 0°C or melted at 200°C for 5 min and then annealed at 140°C for 600 min. The PLLA films quenched at 0°C from the melt and annealed at 140°C from the melt are abbreviated as PLLA0 and PLLA140, respectively.

TABLE II
Characteristics of PLLA Films before and after Hydrolysis at pH 7.4 and 37°C in Phosphate-Buffered Solution

Samples	Hydrolysis time (days)	$M_n \times 10^{-5}$ (g/mol)	M_w/M_n	T_g (°C)	T_c (°C)	T_m (°C)	X_c (%)
PLLA0	0	5.4	2.0	68	110	177	0
	365	2.1	2.0	72	99	178	3
PLLA140	0	5.5	2.1	67	—	185	37
	365	1.6	1.9	68	—	186	43

Adapted from Tsuji et al.[10,11]

Hydrolysis

The hydrolysis of the PLLA films (18 mm × 30 mm × 50 μm) was performed at 37°C and pH 2.0 in 0.01*N* HCl (guaranteed grade, Nacalai Tesque Inc., Kyoto, Japan) and DLLA solutions, at pH 7.4 in a phosphate-buffered solution,[10,11] and at pH 12 in a 0.01*N* NaOH solution.[13] The hydrolysis media containing 0.02 wt % of sodium azide (guaranteed grade, Nacalai Tesque Inc.) were exchanged once a month. The DLLA solution at pH 2.0 was prepared by the dilution of a 90% DLLA solution (Nacalai Tesque Inc.) using distilled water. After the hydrolysis, the PLLA films were washed thoroughly with distilled water at room temperature, followed by drying under reduced pressure for at least 14 days. The distilled water used for dilution of the DLLA solution and washing of the hydrolyzed films was HPLC grade (Nacalai Tesque Inc.).

Measurements and observation

The glass-transition (T_g), crystallization (T_c), and melting temperatures (T_m) and the enthalpies of crystallization (ΔH_c) and melting (ΔH_m) of the PLLA films were determined with a Shimadzu DT-50 differential scanning calorimeter. The PLLA films (sample weight ca. 3 mg) were heated at a rate of 10°C/min under a nitrogen gas flow at a rate of 50 mL/min. The T_c, T_m, ΔH_c, and ΔH_m were calibrated using tin, indium, and benzophenone as standards. The percentage of crystallinity (X_c) of the PLLA films was evaluated according to the following equation:[22]

$$X_c = 100/(\Delta H_m + \Delta H_c)/135 \quad (1)$$

where 135 (J/g polymer) is the enthalpy of melting of the PLLA crystal having infinite crystal thickness as reported by Miyata and Masuko.[26] The 135 J/g of polymer value was used in this study instead of the 93 J/g of polymer utilized earlier,[27] because a previous study found the latter value to be too small to evaluate the crystallinity of PLLA specimens with high crystallinities.[12] By definition, ΔH_m and ΔH_c are positive and negative values, respectively.

The M_n and M_w and the molecular weight distribution (M_w/M_n) of the PLLA films were evaluated in chloroform at 40°C by a Tosoh GPC system (RI-8020 refractive index monitor) with TSK Gel columns (two GMH_{XL}) using polystyrene as a standard. Tables I–III summarize the observed values of the M_w, M_w/M_n, X_c, T_m, and T_g of the PLLA films before and after the hydrolysis at different pHs.[10,11,13]

RESULTS AND DISCUSSION

Weight loss

Figure 1 shows the weight losses of the initially amorphous PLLA0 and crystallized PLLA140 films during hydrolysis at pH 2.0 in the acid media, at pH 7.4 in phosphate-buffered solution, and at pH 12 in NaOH solution. A negligible weight loss was detected for both the PLLA0 and PLLA140 films, even when the hydrolysis at pH 2.0 in HCl and DLLA solutions was continued for 300 days. The insignificant weight loss of the PLLA films at pH 2.0 for the long period of 300 days is in good agreement with the results reported for the PLLA microspheres hydrolyzed at pH 1.2 and 3.2 in acid media for 120 days[16] and with those for the

TABLE III
Characteristics of PLLA Films before and after Hydrolysis at pH 12 and 37°C in NaOH Solution

Samples	Hydrolysis time (days)	$M_n \times 10^{-5}$ (g/mol)	M_w/M_n	T_g (°C)	T_c (°C)	T_m (°C)	X_c (%)
PLLA0	0	5.4	2.0	68	110	177	0
	150	3.6	2.0	69	100	177	6
PLLA140	0	5.5	2.0	67	—	183	37
	150	0.82	8.0	68	—	185	45

Adapted from Tsuji and Ikada.[13]

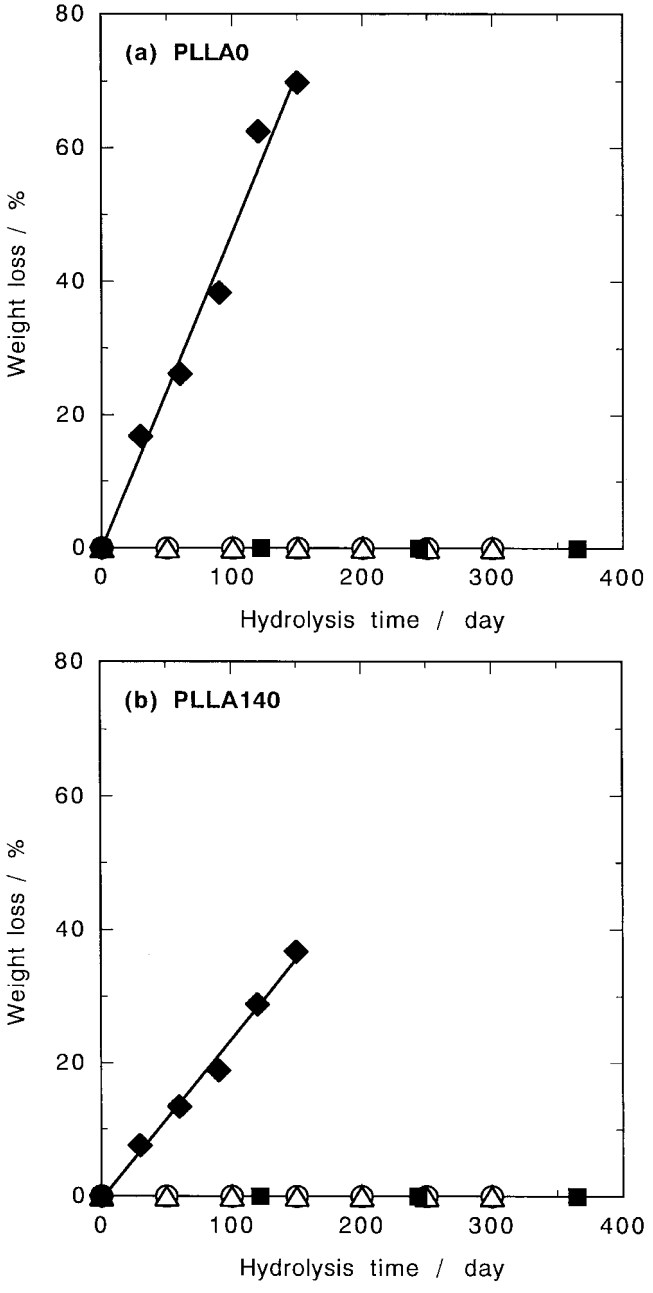

Figure 1 The percentage of weight loss changes of (a) PLLA0 and (b) PLLA140 films during the hydrolysis at pH 2.0 in (○) HCl and (△) DLLA solutions, (■) at pH 7.4 in phosphate-buffered solution, and (♦) at pH 12 in NaOH solution.

PLLA films hydrolyzed at pH 7.4 in a phosphate-buffered solution for 365 days.[10,11] The results obtained here strongly suggest that the hydronium ions from HCl and DLLA have a very small catalytic effect on the hydrolysis of PLLA chains. The weight loss is an index for the content of water-soluble oligomers and monomer formed by hydrolysis and then released from the mother PLLA films into the surrounding media. Therefore, a negligible weight loss means that an insignificant amount of water-soluble oligomers

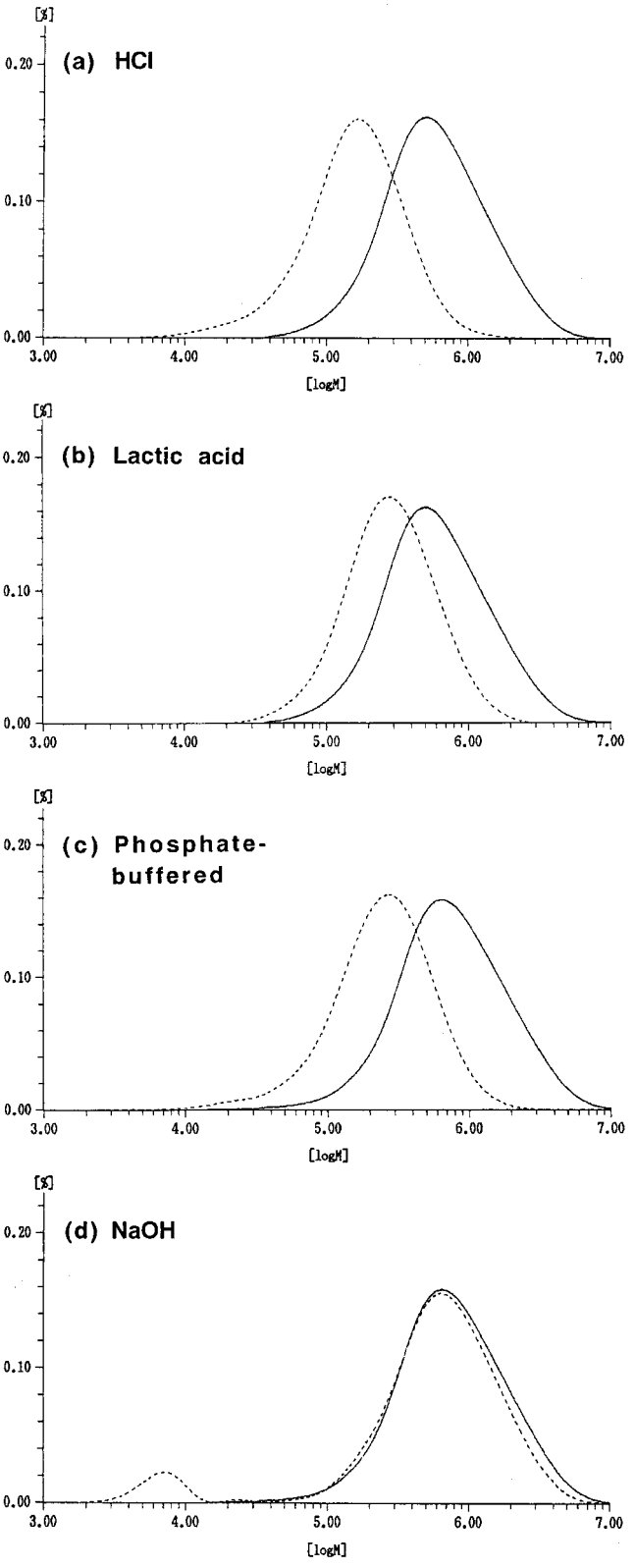

Figure 2 GPC curves of PLLA140 films (—) before and (- - -) after the hydrolysis at pH 2.0 in (a) HCl and (b) DLLA solutions for 300 days, (c) at pH 7.4 in phosphate-buffered solution for 365 days, and (d) at pH 12 in NaOH solution for 120 days.

TABLE IV
Hydrolysis Mechanisms of PLLA Films under Different Conditions

pH	Temp. (°C)	Enzyme	Hydrolysis mechanism	
			Chain cleavage	Material erosion
2.0	37	No	Random in amorphous region	Bulk
7.4			Random in amorphous region	Bulk
12			Random in amorphous region	Surface
7.4	37	Proteinase K	Predominant cleavage at chains with free ends and tie chains in amorphous region	Surface
7.4	97	No	Random in amorphous region	Bulk

and monomer were formed or the formed water-soluble oligomers and monomers were trapped in the films.

However, at pH 12 the weight losses of the PLLA0 and PLLA140 films increased without any induction periods and the final weight loss values at 150 days were 70 and 37%, respectively.[13] This means that the hydroxyl ions have a strong catalytic effect on the hydrolysis and that the water-soluble LMW oligomers and monomer were released from the films. The high weight loss value of the amorphous PLLA0 film compared to that of the crystallized PLLA140 specimens was ascribed to the predominant hydrolysis and removal of the chains in the amorphous region compared to those in the crystalline region.

Molecular weight change

Figure 2 gives the changes in the molecular weight distribution of the crystallized PLLA140 films during the hydrolysis at pH 2.0 in the acid media and those at pH 7.4 and 12. As seen in Figure 2(a–c), the initial peaks of the crystallized PLLA films hydrolyzed at pH 2.0 and 7.4 shift as a whole to a lower molecular weight during the hydrolysis. In addition to the significant induction periods observed for the weight losses of PLLA films hydrolyzed at pH 2.0 and 7.4, these changes confirm that the hydrolysis of the PLLA films at low and medium pH proceeds homogeneously along the film cross section by mainly a bulk erosion mechanism. The negligible shift of the initial main peak of the crystallized PLLA film hydrolyzed at pH 12 for 120 days [Fig. 2(d)], despite the significant weight loss (Fig. 1), reflects that the hydrolysis at high pH takes place mostly via a surface erosion mechanism. It is probable that the hydroxyl ions are entrapped by the ester groups on the film surface, thereby disturbing their diffusion into the specimens. Similar results were reported for the enzyme-catalyzed hydrolysis of PLLA films in the presence of proteinase K, where the hydrolysis proceeds via a surface erosion mechanism.[14,15] The hydrolysis mechanisms of PLLA films under different conditions are summarized in Table IV.

The LMW specific peak ascribed to the crystalline residues,[10–15] which are formed by predominant hydrolysis and removal of the chains in the amorphous region, appears for the crystallized PLLA140 film at a molecular weight of around 6×10^3 when hydrolyzed at pH 12 for 120 days [Fig. 2(d)].[13] In contrast, no such LMW specific peak appears in the molecular weight distributions of the PLLA140 films in the range of 1×10^3 to 3×10^4 when hydrolyzed at pH 2.0 in HCl and DLLA solutions for 300 days [Fig. 2(a,b)] and at pH 7.4 in phosphate-buffered solution for 365 days [Fig. 2(c)].[10,11] The absence of such LMW specific peaks at low and medium pH strongly suggests that the negligible weight loss during the hydrolysis for 300 and 365 days is attributable to insignificant formation of water-soluble oligomers in the films instead of being due to entrapment of the formed water-soluble oligomers in the films. The LMW specific peaks appeared in the molecular weight distributions of the crystallized PLLA films hydrolyzed in the presence of proteinase K for 50 h[14,15] and even in those hydrolyzed at pH 7.4 in the phosphate-buffered solution after the long-term hydrolysis of 730 days.[10,11] Therefore, prolonged hydrolysis of the crystallized PLLA films will yield such specific peaks.

The initially amorphous PLLA0 films at different pH values show GPC profile changes similar to those of the initially crystallized PLLA140 films (data not shown), excluding no specific peak formation at the LMW range for the PLLA0 film hydrolyzed at pH 12 and the difference in the shift rates between PLLA0 and PLLA140 films, which are shown in Figure 3.

Figure 4 presents the changes in the M_n values of the initially amorphous PLLA0 films during the hydrolysis at pH 2.0, 7.4, and 12. The M_n of the PLLA0 films hydrolyzed at pH 2.0 decreases monotonously with hydrolysis time, irrespective of the hydrolysis media. The decrease rates in the M_n of the PLLA0 films hydrolyzed at pH 2.0 in HCl and DLLA solutions are similar to that hydrolyzed at pH 7.4. The hydrolysis rate constant (k) values of the PLLA films were estimated by assuming the exponential decreases in M_n of the films during the hydrolysis and using the following equation[28]:

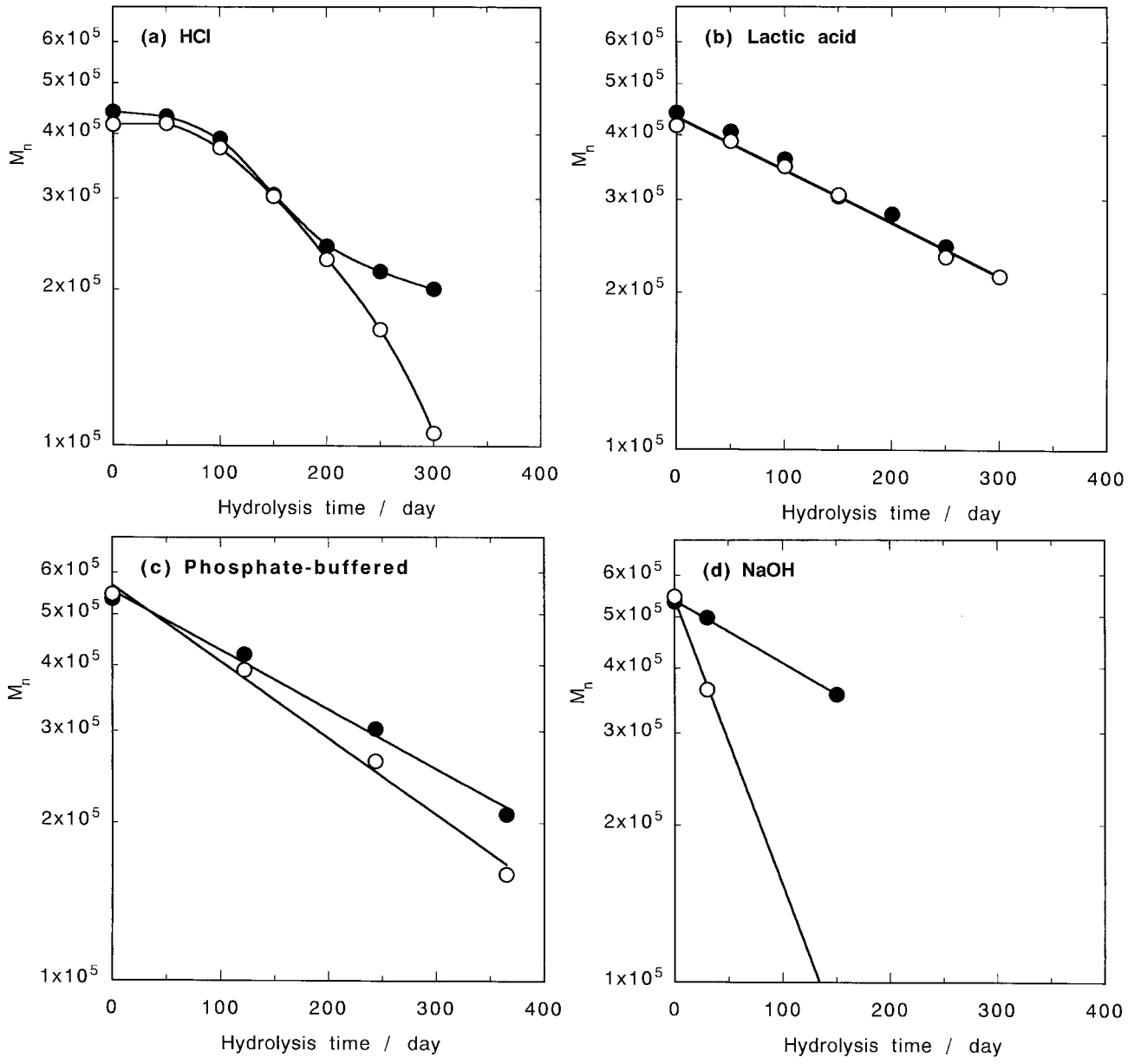

Figure 3 The number-average molecular weight (M_n) changes of (●) PLLA0 and (○) PLLA140 films during the hydrolysis at pH 2.0 in (a) HCl and (b) DLLA solutions, (c) at pH 7.4 in phosphate-buffered solution, and (d) at pH 12 in NaOH solution.

$$\ln M_n\,(t_2) = \ln M_n\,(t_1) - kt \qquad (2)$$

where $M_n(t_2)$ and $M_n(t_1)$ are M_n values at the hydrolysis times of t_2 and t_1, respectively. The obtained k values of 3.0 and 2.4×10^{-3} day^{-1} for the PLLA0 films hydrolyzed at pH 2.0 in the HCl and DLLA solutions are very similar to the k value of 2.6×10^{-3} day^{-1} obtained for the PLLA0 films hydrolyzed at pH 7.4 in the phosphate-buffered solution. The k value for the PLLA0 film hydrolyzed at pH 12 was not evaluated because the release of water-soluble LMW oligomers and monomer at the early stage of the hydrolysis, as evidenced by the significant weight loss, disturbs the utilization of eq. (2).

In addition to the negligible weight loss of the PLLA films hydrolyzed in the acid media, these results indicate that the catalytic effects of hydronium ions from these acids are very small, irrespective of the kind of acids, and the durability of PLLA films in the acid media is very similar to that in the neutral medium but higher than that in the alkaline medium. This can be explained by the hydrolysis mechanism of PLLA chains in acid media proposed by Shih; hydrolytic scission at the chain ends was faster than that of the internal ester bonds.[19,20] The high molecular weight of the PLLA specimens used in this study decreased the terminal group density, resulting in the hydronium ions having insignificant catalytic effects on the hydrolysis.

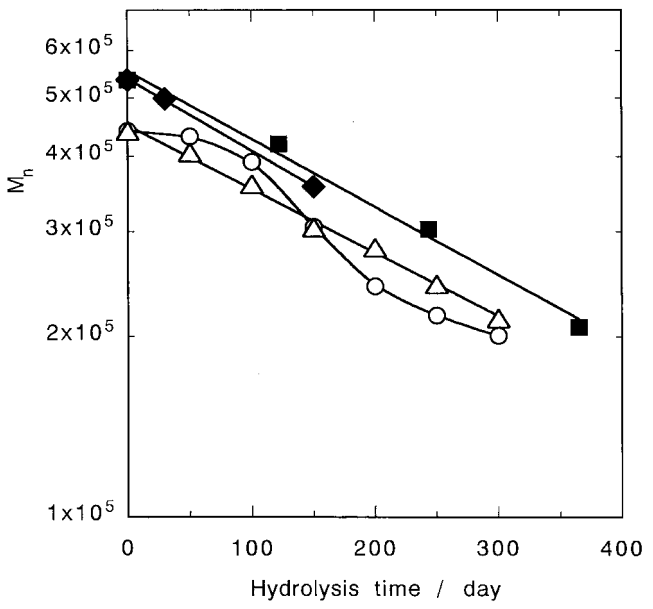

Figure 4 The number-average molecular weight (M_n) changes of PLLA0 films during hydrolysis at pH 2.0 in (○) HCl and (△) DLLA solutions, (■) at pH 7.4 in phosphate-buffered solution, and (♦) at pH 12 in NaOH solution.

The very small differences between the results obtained for the PLLA films hydrolyzed in HCl and DLLA solutions (Figs. 1, 2) show that the catalytic effects of the lactic acid oligomers and monomers present in the DLLA solution was negligibly small, although those formed by hydrolysis of thick PLA specimens and trapped there inside are reported to accelerate the autocatalytic hydrolysis at the specimen core.[23–25] The effects of oligomers and monomers on the hydrolysis of PLA chains may differ, depending on their average molecular weights. It is probable that the LMW water-soluble oligomers and monomers present in the DLLA solution have an insignificant catalytic effect on the hydrolysis whereas the entrapped medium molecular weight, water-insoluble oligomers formed by the hydrolysis accelerate the hydrolysis. Another probable explanation is that LMW water-soluble oligomers and monomers present in the DLLA solution cannot diffuse into the PLLA specimens.

Figure 3 shows the changes in the M_n of the initially amorphous PLLA0 and crystallized PLLA140 films during the hydrolysis at pH 2.0 in the acid media, together with those at pH 7.4 and 12. In the HCl solution [Fig. 3(a)] the decrease profile of the M_n of the PLLA140 film is very similar to that of the PLLA0 film in the first 200 days, but the decrease rate of the M_n is much higher for the PLLA140 film than for the PLLA0 film for the hydrolysis period of longer than 200 days. The rapid hydrolysis of the crystallized PLLA film compared to that of the amorphous PLLA film at hydrolysis times exceeding 200 days is similar to the results at pH 7.4 in the phosphate-buffered solution [Fig. 3(c)] and can therefore be explained by the same mechanism proposed previously for the PLLA films hydrolyzed in the phosphate-buffered solution.[10,11] In the crystallized PLLA film the densities of the terminal carboxyl and hydroxyl groups in the amorphous region between the lamellae were increased by their exclusion from the crystalline region during crystallization. As a result, the increased density of catalytic carboxyl groups and the high water concentration due to the increased hydrophilic terminal groups may have enhanced hydrolysis of the chains in the amorphous region in the crystallized PLLA film, resulting in the rapid decrease of its M_n.

In DLLA solution the decreases in the M_n for the PLLA0 and PLLA140 films are very similar [Fig. 3(b)]. This means that the X_c has a negligible effect on the hydrolysis of PLLA films in the DLLA solution. However, prolonged hydrolysis may cause the hydrolysis rate difference between the two different PLLA specimens.

On the other hand, at pH 12 the decrease rate in the M_n is higher for the PLLA140 film than for the PLLA0 film [Fig. 3(d)]. This is attributable to the predominant hydrolysis and removal of the chains in the amorphous region on the surface of the crystallized PLLA film, followed by the accumulation of LMW PLLA chains in the crystalline residues as shown in Figure 2(d). Such an accumulation did not occur in the amorphous PLLA film. These LMW components of the crystalline residues must have caused the large decrease in the M_n of the crystallized PLLA film compared to that of the amorphous PLLA film.

Change in crystalline region

Figure 5 gives the changes in the X_c of the PLLA films during the hydrolysis at pH 2.0 in the acid media and those at pH 7.4 and 12 in the other solutions. The X_c values of all the PLLA films become higher during the hydrolysis, irrespective of the pH of the media. This reflects the fact that the amount of the crystalline region per unit weight increased during the hydrolysis. The negligible weight loss for the PLLA films hydrolyzed at pH 2.0 for 300 days and at pH 7.4 for 365 days is evidence that the crystallization of the PLLA chains increased the X_c values but the selective hydrolysis and subsequent removal of the chains in the amorphous region had no significant contribution to the increased X_c values. However, the significant weight losses of the initially crystallized PLLA films hydrolyzed at pH 12 at the early stage of the hydrolysis shows that the occurrence of selective hydrolysis and subsequent removal of the chains in the amorphous region, as well as the crystallization during the hydrolysis, increased the X_c values.

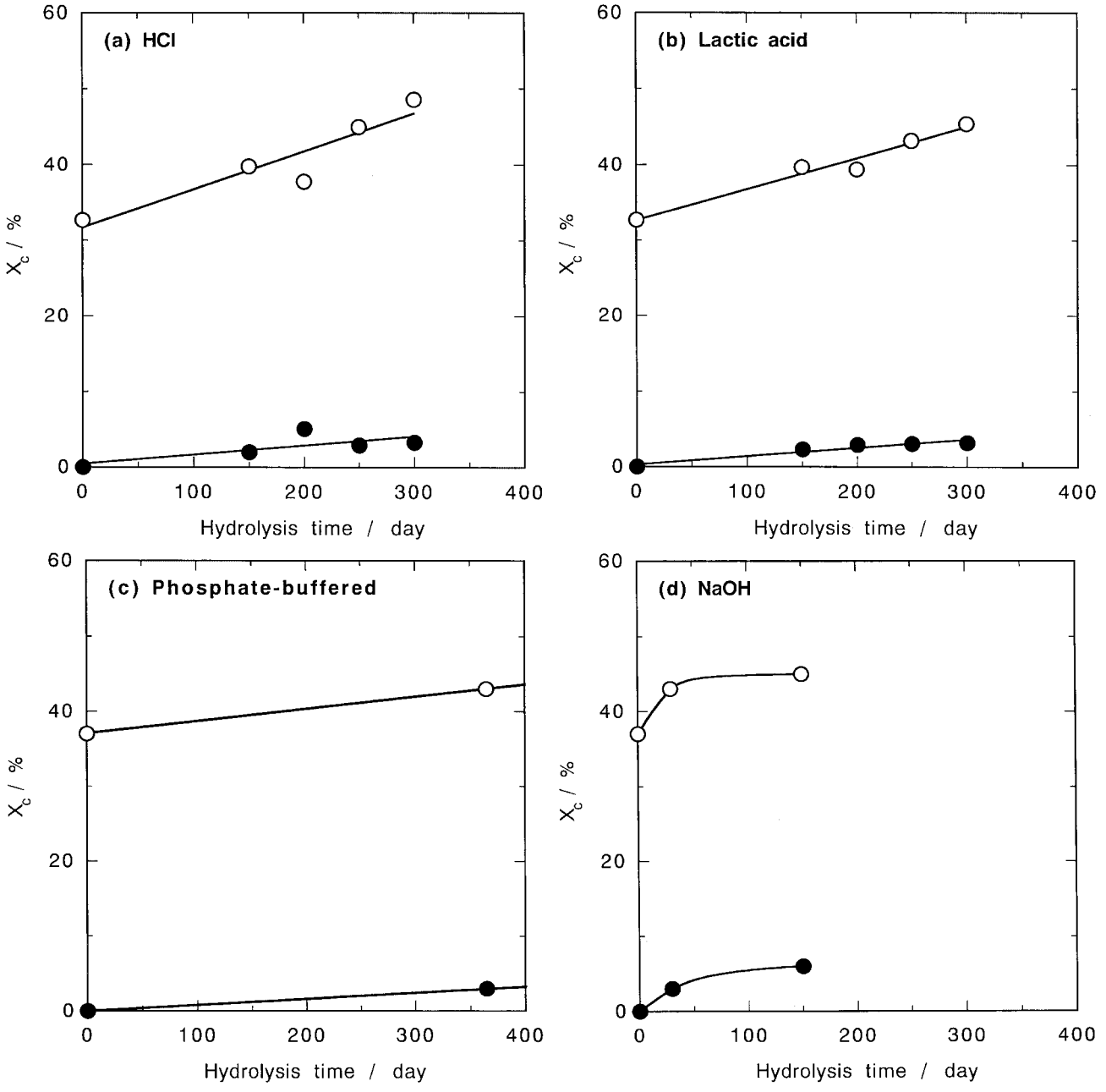

Figure 5 The crystallinity (X_c) of (●) PLLA0 and (○) PLLA140 films hydrolyzed at pH 2.0 in (a) HCl and (b) DLLA solutions, (c) at pH 7.4 in phosphate-buffered solution, and (d) at pH 12 in NaOH solution as a function of the hydrolysis time.

The changes in the T_m of the PLLA films before and after the hydrolysis at different pH values are shown in Tables I–III. The T_m values of the initially amorphous PLLA0 films are for the crystallites formed during DSC heating and therefore do not reflect the crystalline thickness of the specimens. As is evident from these tables, all of the crystallized PLLA140 films, excluding that hydrolyzed at pH 2.0 in the HCl solution, increased slightly after the hydrolysis, showing the increased crystalline thicknesses of the PLLA films after the hydrolysis. On the other hand, the T_m value of the PLLA140 film hydrolyzed at pH 2.0 in HCl decreased significantly from 182 to 178°C. Decreased T_m values were observed for the PLLA specimens at the late stage of hydrolysis[10–15,24,28–31] and reflect the decreased crystalline thickness or the structural change at the crystallite surfaces of the PLLA140 film during the hydrolysis in the HCl solution.

CONCLUSIONS

From the results described above the following conclusions can be derived for the hydrolysis of PLLA films in acid media at pH 2.0 and 37°C:

1. The hydrolysis of the PLLA films proceeds homogeneously along the film cross section by mainly the bulk erosion mechanism.
2. The durability of PLLA films in the acid media is very similar to that in the neutral medium but higher than that in the alkaline medium.
3. The k values of the initially amorphous PLLA films were 3.0 and 2.4 $\times$ 10^{-3} day^{-1} in HCl and DLLA solutions, respectively, and 2.6 $\times$ 10^{-3} day^{-1} at pH 7.4 in phosphate-buffered solution. The very similar k values and the negligible weight loss with the hydrolysis period of 300 and 365 days reflect that the hydronium ions and lactic acid oligomers and monomers present in the DLLA solution have no significant catalytic effects on the hydrolysis of the PLLA chains.
4. In HCl solution the increasing of the initial X_c of PLLA films increased the hydrolysis rate, whereas in DLLA solution the increasing of the initial crystallinity of the PLLA film did not affect the hydrolysis rate.
5. The crystallization of PLLA chains occurred during the hydrolysis, irrespective of the hydrolysis acid media and the initial crystallinity.

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