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Hydrolytic degradation of poly(D,L-lactide) as a function of end group: Carboxylic acid vs. hydroxyl

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Abstract

D,L-Lactide was initiated with 1,4-butanediol in the presence of stannous octoate catalyst to provide hydroxyl-terminated poly(D,L-lactide) at 5000 and 20,000 g/mol. Portions of these materials were reacted with succinic anhydride in the presence of 1-methylimidazole to convert the hydroxyl functionality to succinic acid-terminated polymers in relatively high yield. The four materials were placed in a 7.4 pH buffered saline solution at 37 °C and monitored up to 180 days for their relative moisture uptake and weight loss behaviors. Carboxylic acid functionality displayed a dramatic effect on the moisture uptake behaviors for the 5000 and 20,000 g/mol polymers when compared to their respective hydroxyl functional materials. Carboxylic acid functionality significantly increased the hydrolytic degradation rate and mass loss behavior for the 5000 g/mol material, but did not affect the hydrolytic degradation rate for the higher molecular weight sample. These results suggest that moisture uptake is not the rate limiting step for the hydrolytic degradation high molecular weight poly(D,L-lactide).

Keywords: Poly(D,L-lactide); Hydrolytic degradation; Carboxylic and functionality

1. Introduction

Biodegradable polyesters and co-polyesters have been the focus of extensive research for several decades as a result of their ease of manufacturing and desirable characteristics. Their ranges of physical properties and hydrolytic degradation profiles have made them attractive candidates for use in a variety of biomedical products such as degradable sutures [1], temporary orthopedic fixtures [2] and controlled pharmaceutical delivery matrices [3,4].

Degradation mechanisms vary among biodegradable polyesters as a function of chemical composition, and are typically categorized as hydrolytic and/or microbial. Factors that influence degradation rate include material hydrophilicity, morphology, crosslink density, and surface chemistry. Additives such as monomers, acidic or basic compounds, superoxide ions, drug composition, and catalysts have all been shown to affect degradation kinetics [5].

Polymer endgroups and endgroup modifications have also been shown to influence degradation. In general, these studies have shown that the presence of free carboxylic acid moieties, whether on the endgroup of the polymer or blended into the sample as an additive or active ingredient, will accelerate the hydrolytic degradation rates of polyesters [5–7]. An additional study has shown that polymers blended with an acidic component show a higher degradation rate than the unmodified material in an acidic aqueous environment [8]. This result implies that carboxylic acid modifications to a biodegradable polymer have a greater influence on degradation than the acidity of the external aqueous environment.

In this paper, we report our study of the moisture absorption and degradation kinetics of poly(D,L-lactide) as a function of carboxylic acid vs. hydroxyl endgroups. Some applications may benefit from the moisture uptake rate and degradation profiles of carboxylic acid-terminated poly(D,L-lactide) homopolymer. The investigation focused on two molecular weight ranges to provide insights regarding endgroup concentration.

2. Experimental

2.1. Materials

The following reagents were used without further purification: D,L-lactide (Ortec, Easley, SC); succinic anhydride, 99+%, 1-methylimidazole, 99+%, 1,2-dichloroethane, anhydrous, 99.8%, 1,4-butanediol, 99+%, sodium sulfate, powder,

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99 + %, tin(II) 2-ethylhexanoate, triethylamine, 99.5%, and chloroform-*d*, 99.8%, 1% TMS (all Sigma–Aldrich); pentane, hydrochloric acid 12.1 N, methanol, 99.9%, tetrahydrofuran, and potassium phosphate monobasic—sodium hydroxide buffer, 7.4 pH, 0.05 M (all Fisher); chloroform (EM Science).

2.2. Synthesis of hydroxyl-terminated poly(D,L-lactide)

A representative procedure for a 20,000 g/mol poly(D,L-lactide) diol was as follows: to a dry 500 mL 3-neck round-bottom flask, contained within a dry-nitrogen-purged glove box, were charged 0.048 g tin(II)-ethylhexanoate, 0.522 g 1,4-butanediol, and 115.320 g D,L-lactide. The reactor was immersed into a 130 °C preheated silicone oil bath and mechanically stirred for 300 min. The reactor was removed from the glove box, and the product was dissolved in approximately 200 mL of hot (70 °C) chloroform. The polymer solution was dripped into a stirred solution of 261 g methanol and 39 g of aqueous HCl at 50 °C over a period of 0.25 h. The resulting turbid polymer solution was precipitated into 2500 mL of cold (<5 °C) pentane with magnetic stirring. The liquid phase was decanted, and the polymer product was redissolved in 300 mL of chloroform. The solution was transferred to a dry 1000 mL round-bottom flask, and the solvent was removed by vacuum stripping. The polymer was further dried in a vacuum oven at <1 in. Hg for 48 h at 50 °C.

2.3. Synthesis of carboxylic acid-terminated poly(D,L-lactide)

To a dry 250 mL 3-neck round-bottom flask were charged 46.830 g (2.3 mmol) poly(D,L-lactide) diol, 125 mL 1,2-dichloroethane, 0.570 g (5.6 mmol) succinic anhydride and 0.386 g (4.7 mmol) 1-methylimidazole. The reactor was equipped with a magnetic stirring device, a heating mantle, N_2 inlet/outlet, and a West condenser utilizing recirculating chilled ethylene glycol (15 °C) coolant. The reactor contents were gently reacted at 65 °C under dry nitrogen for 16 h and then cooled to RT. The polymer solution was washed three times with 200 mL of 10 wt% aqueous HCl, and then twice with 200 mL of distilled water. It was dried for 4 h over approximately 30 g of sodium sulfate using magnetic stirring, filtered, and concentrated utilizing a Brinkman Model RE111 Rotavapor. The sample was transferred immediately into a vacuum oven and held at <1 in. Hg for 48 h at 50 °C. Sample discs for hydroxyl and acid terminated polymers ($d=2.54$ cm, thickness $\cong 1$ mm) were prepared by melt pressing at 100 °C for 15 min and then stored under vacuum at room temperature for approximately 1 week when the final mass of each disc was recorded to the nearest 0.1 mg.

2.4. Gel permeation chromatography

Molecular weights (M_n and M_w) and polydispersity index (PDI) were determined on melt-pressed starting materials using a gel permeation chromatography (GPC) system equipped with a Waters Alliance 2690 separation module, a Waters 484 tunable absorbance detector operating at 265 nm, an on-line multiangle laser light scattering (MALLS) detector fitted with a Gallium arsenide laser (power 20 mW) operating at 690 nm (MiniDawn, Wyatt Technology Inc.), an interferometric refractometer (Optilab DSP, Wyatt Technology Inc.) operating at 35 °C and 690 nm, and two PLgel (Polymer Laboratories Inc.) Mixed E GPC columns (pore size range 50–10^3 Å, 3 μm bead size) connected in series. THF was used as the mobile phase at a flow rate of 1 mL/min. Sample concentrations were approximately 5–10 mg/mL in freshly distilled THF, with an injection volume of 100 μL. Detector signals were simultaneously recorded, and absolute molecular weights and PDIs were calculated using ASTRA 4.0 software (Wyatt Technologies Inc.).

2.5. ^{13}C NMR spectroscopy

Solution ^{13}C NMR spectra were obtained from melt-pressed polymer discs on Varian 200 and 500 MHz spectrometers using 5 mm o.d. tubes with sample concentrations of 20–25% (w/v) in deuterated chloroform containing tetramethylsilane (TMS) as an internal reference. Chemical shifts are given in ppm relative to $CHCl_3$ or TMS.

2.6. Differential scanning calorimetry (DSC) measurements

DSC was used to determine the glass-transition temperature (T_g) for melt-pressed polymer disc starting materials and for wet samples after varying amounts of immersion time. The measurements were performed on approximately 10 mg samples using a TA Instruments DSC Q100. Samples were quenched to −50 °C, ramped at 10 °C/min to 150 °C, cooled 10 °C/min to −50 °C, and re-heated at 10 °C/min to 150 °C. The reported T_g values represent the mid-point temperature for the glass-transition of the second heating cycle.

2.7. Degradation studies

Poly(D,L-lactide) diols and diacids having molecular weights of approximately 5000 and 20,000 g/mol were degraded by exposure to phosphate-buffered aqueous solution (7.4 pH, 0.05 M) at 37 °C. Polymer discs were placed in 100 mL of buffer solution contained within a 125 mL clear glass Fisherbrand jar fitted with a Teflon face-lined cap. The jars were stored at 37 °C in a Fisher Scientific Model 146E incubator. When calculating percent change in mass (water uptake), two discs of a given polymer sample were removed from solution, carefully patted dry with a Kimwipe and weighed to the nearest 0.1 mg and averaged. The % change in mass for each disc was calculated as follows:

$$\%\text{Change in mass} = \frac{m_h - m_i}{m_i} \times 100 \qquad (1)$$

where m_h is the hydrated mass and m_i is the initial mass. After weighing, the discs were placed into a dry 25 mL glass evaporation dish fitted with a teflon liner and stored in a VWR Scientific Model 1410 vacuum oven at room temperature and <1 in. Hg. Each disc was then weighed, periodically, over an

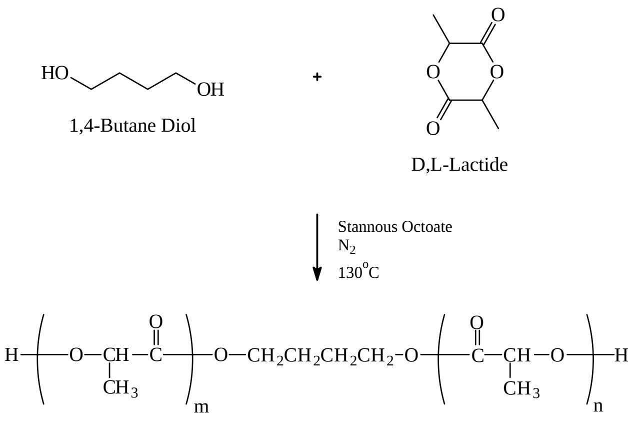

Fig. 1. Synthesis of poly(D,L-lactide) diol.

approximate 2-week period until a constant weight (±0.2 mg) was maintained for 72 h. Remaining mass (%) (dry weight) was calculated as follows:

$$\text{Remaining mass (\%)} = \frac{m_\mathrm{d}}{m_\mathrm{i}} \times 100 \tag{2}$$

where m_d and m_i are the dry and initial weights, respectively.

For the purpose of this work, we elected to measure water uptake daily until we could approximate the % change in mass for each polymer formulation. We then adjusted the measurement periods for each formulation to capture sufficient data to properly determine t_on (onset of degradation) for each material. We elected to exchange the buffer solution at a constant time interval of 15 days throughout the experiment for each formulation, and monitored solution pH on a continual basis in order to effectively determine t_on. This procedure proved to be adequate for determining t_on, and describing the general degradation behavior of the materials.

3. Results and discussion

As shown in Fig. 1, 1,4-butanediol was used to initiate the polymerization of D,L-lactide monomer in the presence of stannous octoate catalyst to produce the hydroxyl-telechelic polyester. The polymers were dissolved in hot $CHCl_3$ and dripped into a mixture of methanol and aqueous HCl to assure the complete exchange of residual stannyl ether catalytic endgroups to hydroxyl functionality. Hydroxyl-terminated polymers with target molecular weights of approximately 5000 and 20,000 g/mol were synthesized using this method.

As shown in Fig. 2, portions of the hydroxyl-terminated polymers were reacted with succinic anhydride in the presence of 1-methylimidazole to convert the hydroxyl end groups to carboxylic acid end groups. The hydroxyl-terminated reactants and carboxylic acid-terminated products were analyzed by GPC to assure polyester main-chain stability under the prescribed reaction and post-reaction washing conditions. The GPC chromatograms shown in Fig. 3 confirm that the primary polyester backbone was essentially unaffected by the reaction conditions. Any observed changes in moisture uptake and degradation behavior between the hydroxyl- and acid-terminus polymers have been attributed to the conversion of endgroup moieties.

^{13}C NMR spectroscopy was used to monitor the diol to diacid conversion. Fig. 4 shows the ^{13}C NMR spectra of the 1,4-butanediol-initiated, 5000 g/mol poly(D,L-lactide) diol and the corresponding di-carboxylic acid. These spectra confirm the conversion of hydroxyl to succinic acid end groups in relatively high yield. Fig. 5 shows an expanded view of the ^{13}C NMR spectra for the diol and diacid between the range of 18 and 67 ppm. For the diol, the ultimate lactide methyl carbon (peak *h*) appears at 20.5 ppm, and the ultimate lactide methine carbon (peak *g*) appears at 66.7 ppm. These ultimate methyl and methine peaks essentially disappear upon conversion to the free acid, indicating that they become indistinguishable from their respective backbone resonances. Minor resonances associated with peaks *h* and *g* are present in the acid-terminated product, which indicates that some unreacted hydroxyl endgroups are still present after the conversion. Peaks *a*/*i* at 25.1 ppm and peaks *b*/*j* at 65.1 ppm remain unchanged during the conversion and are assigned to the methylene groups of the 1,4-butanediol initiator. The methylene carbons associated with the succinic acid endgroups of the polymer coincidentally appear as a single resonance at 28.5 ppm on the 200 MHz NMR. Further, examination of this resonance using a 500 MHz

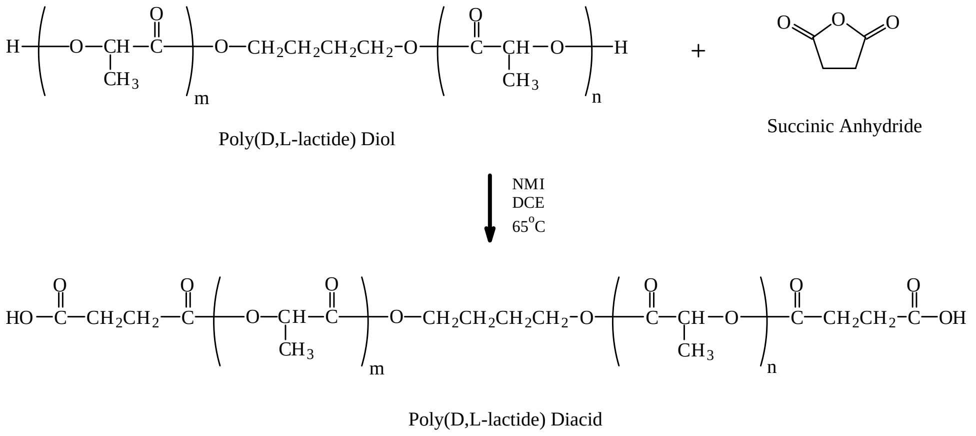

Fig. 2. Synthesis of poly(D,L-lactide) diacid.

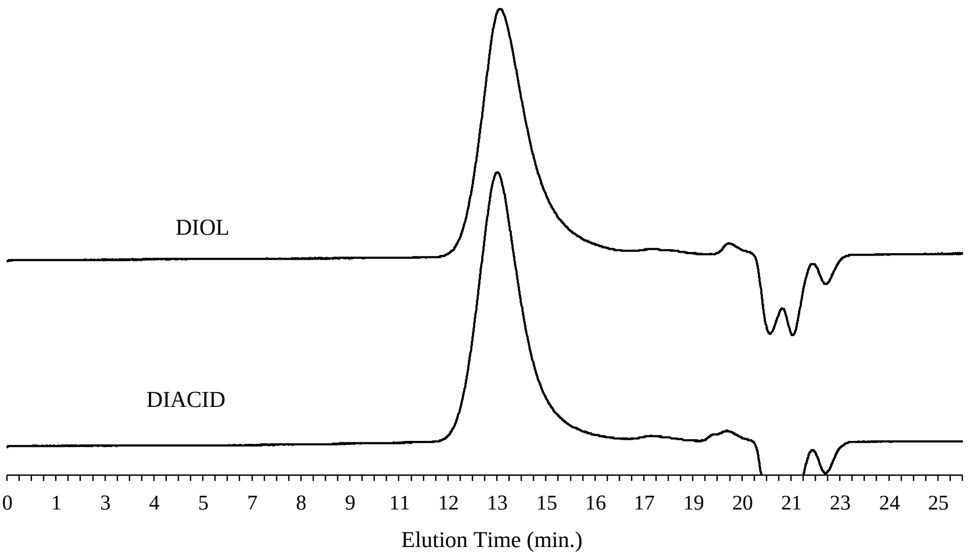

Fig. 3. GPC chromatogram of poly(D,L-lactide) diol and diacid.

spectrometer allowed the individual methylene peaks to be resolved and assigned, as shown in Fig. 6.

Change in mass percent vs. time of immersion in 7.4 pH buffered saline solution at 37 °C is shown in Fig. 7 for 5000 g/mol diol and di-carboxylic acid poly(D,L-lactide)s. The carboxylic acid-terminated polymer showed dramatically higher rate and extent of water uptake compared to the hydroxyl-terminated polymer. The acid-terminated polymer displayed a rapid gain in weight with time over the first 22 days of immersion, after which the weight peaked at around 170% increase above its original weight. Afterward, the sample rapidly lost weight. In contrast, no significant mass change was observed for the hydroxyl-terminated polymer until 40–50 days of immersion. This curve peaked at about 20% increase above the original sample weight, and then displayed gross mass loss between 75 and 95 days of immersion. With

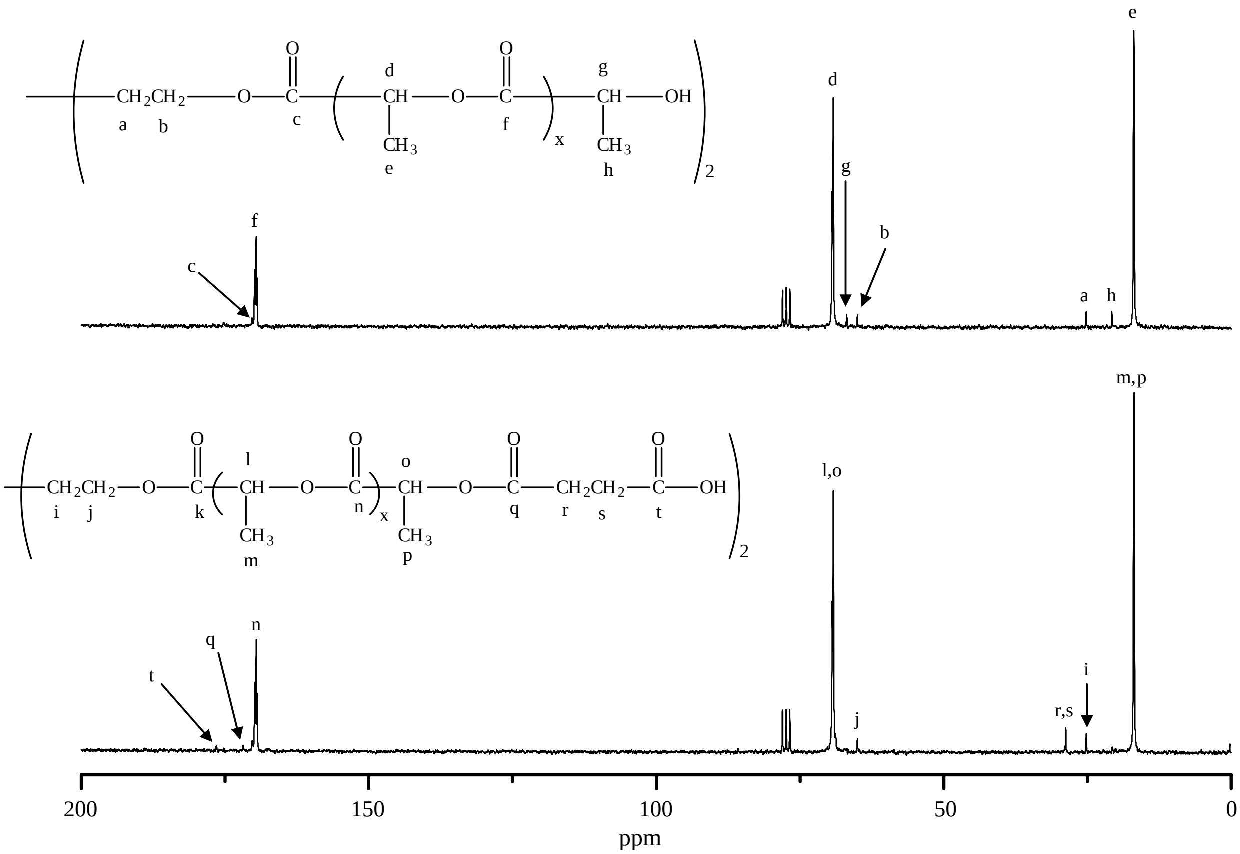

Fig. 4. Two hundred megahertz ^{13}C NMR spectra (0–200 ppm) for poly(D,L-lactide) diol and diacid.

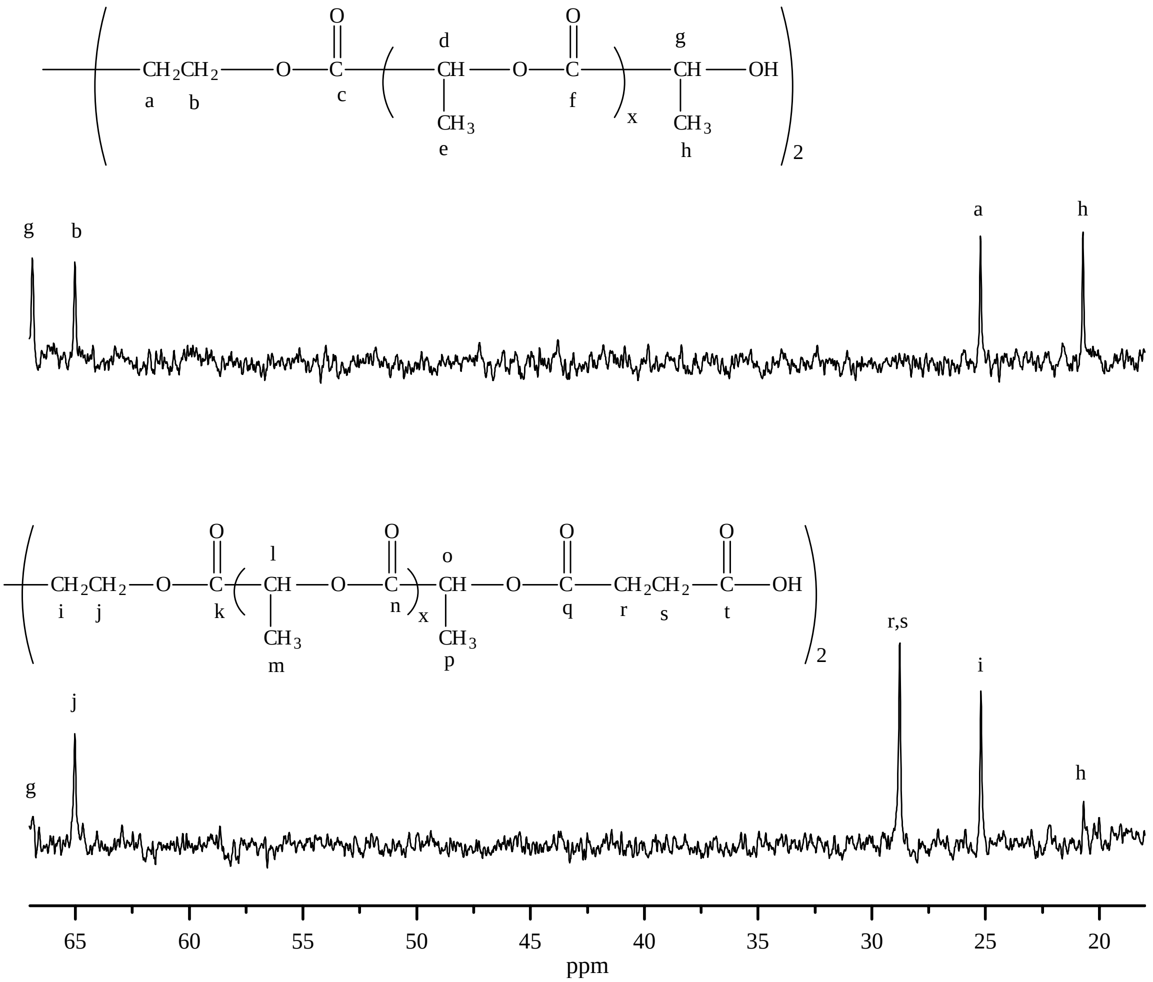

Fig. 5. Two hundred megahertz ^{13}C NMR spectra (18–67 ppm) for poly(D,L-lactide) diol and diacid.

reference to the diacid polymer, it must be assumed that some mass loss took place during the first 22 days of immersion, since change in mass percent as defined herein is actually the net weight including both mass loss and water uptake. The decrease in mass percent during the post-22 day period is due to the steady loss of low molecular weight chain fragments that are produced from hydrolysis of the polyester backbone.

Fig. 8 depicts the normalized dry weight of the two 5000 g/mol polymers as a function of immersion time. An analysis of these curves provides additional insight into the relative contribution of mass loss and moisture uptake. The 5000 g/mol diacid lost more than 40% of its mass during the first 22 days of immersion, whereas the hydroxyl-terminated polymer lost essentially no mass during the same period. In fact, the 5000 g/mol hydroxyl-terminated sample did not display significant mass loss until 60–80 days of immersion.

Analogous uptake behavior for the 20,000 g/mol diol and diacid samples is depicted in Fig. 9. The higher molecular weight and lower endgroup concentration diacid material showed a change in mass of around 80% after the first 22 days of immersion. The lower total change in mass during the first 22 days for this sample, when compared to the 5000 g/mol material, could be attributed to a higher T_g and/or a lower concentration of carboxylic acid endgroups. Also, instead of displaying a post 22-day mass loss, the 20,000 g/mol diacid continued to gain mass in an interval between 33 and 150 days of immersion, to more than 300% of its original weight. The higher molecular weight acid-terminated sample displayed a large change in mass, but did not show significant mass loss until after 150 days immersion. The difference in mass loss behavior between the 20,000 and 5000 g/mol diacid samples can be attributed to the reduction in free carboxylic acid concentration since free acid is known to catalyze polyester hydrolysis. The hydroxyl-terminated 20,000 g/mol sample in Fig. 9 displayed rapid weight loss in the time interval between 100 and 150 days, while the acid-terminated sample underwent rapid weight loss between 150 and 180 days.

Dry weight vs. time graphs for the 20,000 g/mol poly(D,L-lactide) diol and diacid depicted in Fig. 10 provide direct information with regard to actual polymer mass loss. Although the acid-terminated sample displayed a significant difference in mass change behavior associated with water absorption, increasing to more than 300% of the original weight vs. around 20% increase for the analogous diol, the actual mass loss kinetics were essentially unchanged between these two materials. This result is significant since both the

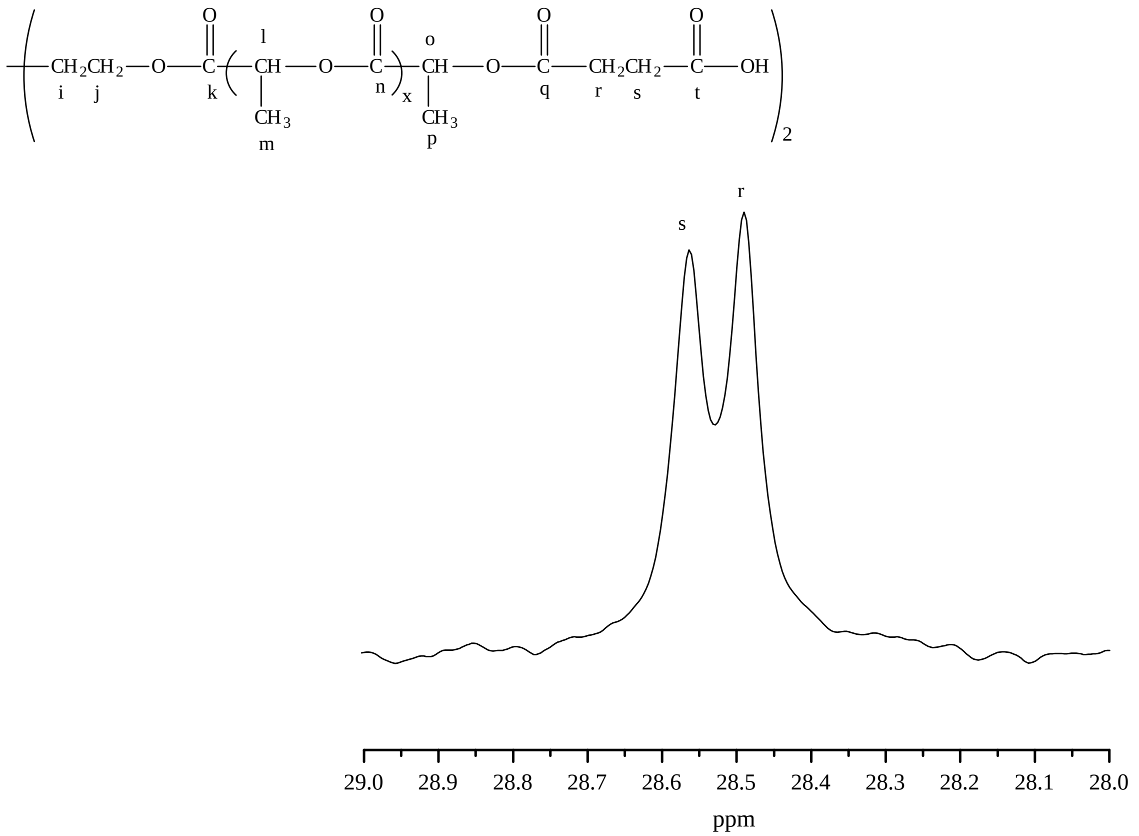

Fig. 6. Five hundred megahertz ^{13}C NMR spectra (28–29 ppm) for poly(D,L-lactide) diacid.

hydroxyl and acid-terminated materials began to show dry weight loss after around 80 days of immersion, and the acid-terminated sample actually degraded at a slightly slower rate than the hydroxyl-terminated material. This dry weight result for the 20,000 g/mol material was actually quite surprising when considering the dramatic difference in moisture uptake behavior between the materials. This result suggests that the degradation kinetics for higher molecular weight samples are independent of water uptake and water concentration inside the sample is not rate limiting. Schmitt et al. concluded that the hydrolysis rate of degradable polyesters was independent of the total water content of the polymers [9] and our data supports this conclusion.

Polymer morphology and acid group aggregation play a critical role in moisture uptake. At the initial time of immersion, only carboxylic acid groups on the surface of the sample will be exposed to moisture. The material may also undergo a morphological change in the form of water cluster formation during this period and the chains will acquire more segmental mobility due to plasticization by water. This will cause an increase in free volume and, therefore, a reduction of the glass transition temperature. These observations suggest an overall increase in hydrophilicity as the concentration of effective carboxylic endgroups increases, and the result is a second phase of moisture absorption for the higher molecular weight sample prior to significant hydrolysis.

A semi-logarithmic plot of the data in Fig. 8 is shown in Fig. 11. There is exponential mass decay of the acid sample along the linear curve section that suggests pseudo-first-order degradation kinetics. Two kinetic parameters are apparently sufficient to quantify an erosion profile of this sort: the onset time (t_{on}) over which there is insignificant mass loss, and the slope of the line after $t=t_{\mathrm{on}}$, k_{obs}, which is a degradation rate constant. These parameters are contained in the following first-order rate equation [10]:

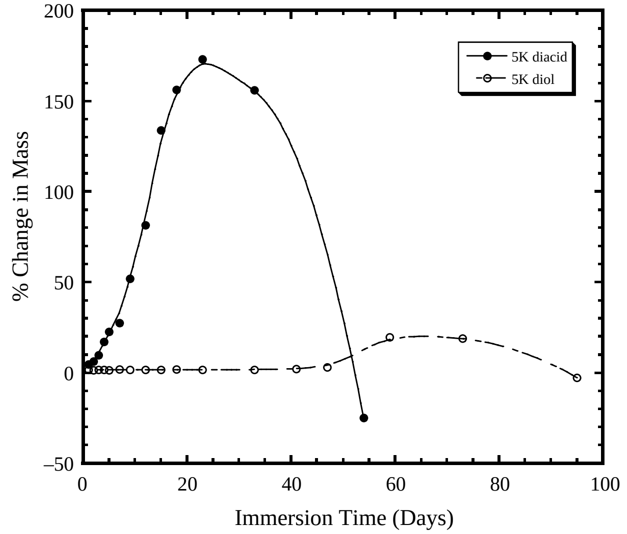

Fig. 7. %Change in mass vs. immersion time for 5000 g/mol poly(D,L-lactide) diol and diacid.

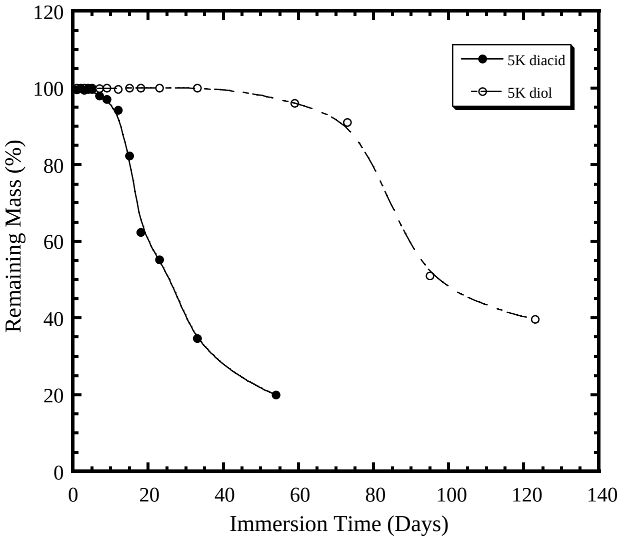

Fig. 8. Dry weight loss vs. immersion time for 5000 g/mol poly(D,L-lactide) diol and diacid.

$$\ln(\text{remaining mass percent}) = A - k_{\text{obs}} t \tag{3}$$

A is the vertical intercept of the linear curve section. t_{on} can be derived from the intersection of the regression line with the initial constant mass line using the expression based on Eq. (3):

$$t_{\text{on}} = \frac{[A - \ln(100)]}{k_{\text{obs}}} \tag{4}$$

The values for k_{obs} and t_{on} for all samples are given in Table 1. Most significant is the t_{on} values for the 20,000 g/mol acid and hydroxyl terminated samples. Although we observed a dramatic difference in moisture uptake and water content behavior between these samples (300% for the diacid vs. 20% for the diol), the onset of mass loss was essentially unchanged at around 85 days. This data further confirms the important fact that hydrolytic degradation is independent of moisture content for higher molecular weight poly(D,L-lactide).

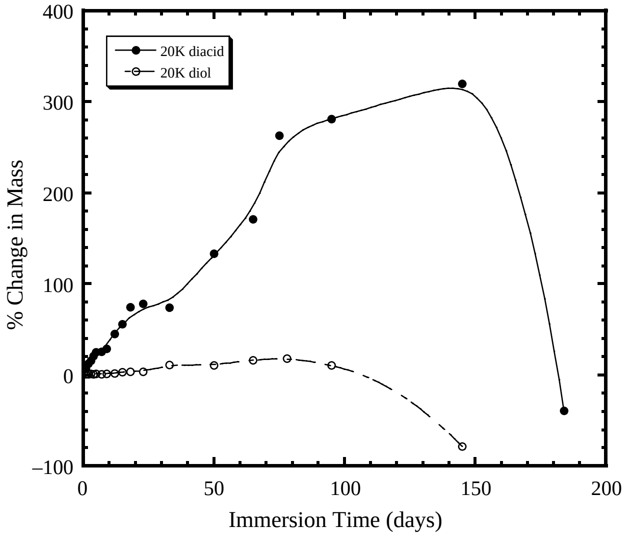

Fig. 9. % Change in mass vs. immersion time for 20,000 g/mol poly(D,L-lactide) diol and diacid.

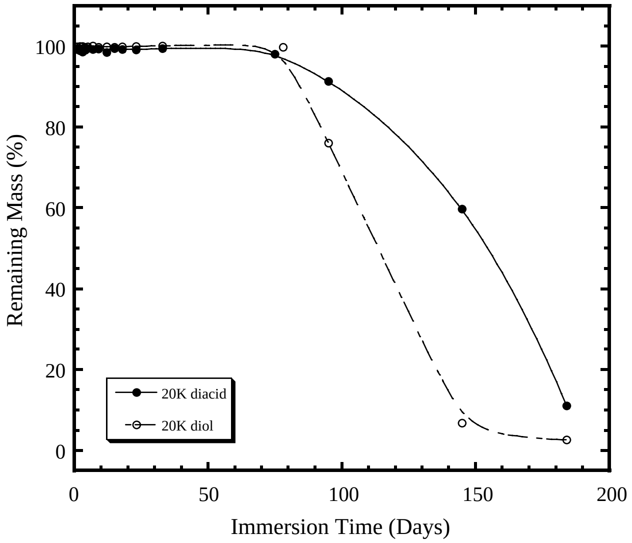

Fig. 10. Dry weight loss vs. immersion time for 20,000 g/mol poly(D,L-lactide) diol and diacid.

Fig. 12 displays the change in buffer solution pH with time for the immersed 5000 and 20,000 g/mol diol and diacid materials. The reduction in buffer solution pH with time is associated with the extent of fragmentation and mass loss for the hydrolyzed polyesters. A study of D,L-lactide oligomers showed that, typically, in a solution of pH 7.4, the local pH inside the material is lower due to the formation of carboxylic groups which are unable to rapidly leach out of the bulk polymer [11–13]. In contrast, the pH at the surface remains unchanged because of the buffer capacity and the exchange of buffer. The mass loss onset times (t_{on}) given in Table 1 correlate with the changes in pH shown in Fig. 12.

According to accepted views of bulk degradation, hydrolysis will be faster in the bulk than at the surface due to higher concentrations of ester and carboxylic acid groups, and this can be considered as an autocatalytic effect [9,14]. As free acid catalyzes the degradation process, lowering of the pH of the

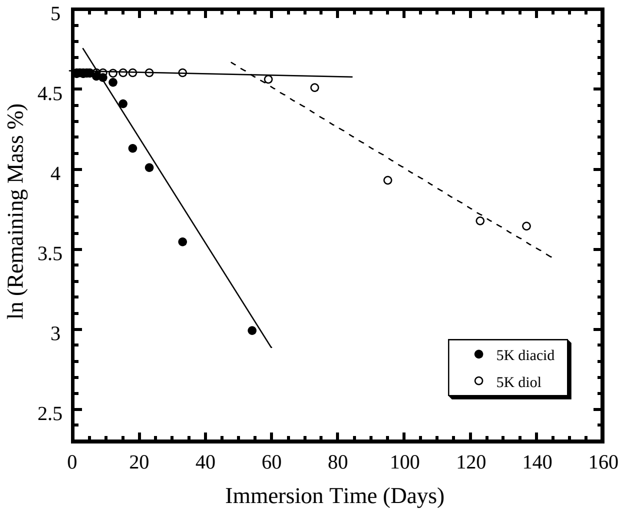

Fig. 11. Change in solution pH vs. immersion time for 5000 and 20,000 g/mol poly(D,L-lactide) diol and diacid.

Table 1
Summary of kinetic data for 5000 and 20,000 g/mol poly(D,L-lactide) diol and diacid

Sample	M_n[a]	Glass transition temperature (°C)	k_{obs}[b] (day^{-1})	t_{on}[c] (days)
5K diacid	6418	30	0.0365	7.7
5K diol	5275	34	0.0131	56
20K diacid	20,770	48	0.0188	87
20K diol	19,170	51	0.0344	84

[a] Number average molecular weight from GPC.
[b] Pseudo first order rate constant calculated from Eq. (3).
[c] The onset time for mass loss calculated from Eq. (4).

medium should enhance material degradation, which was observed for the 5K g/mol sample after 15 days of immersion as depicted in Fig. 8. Hydrolysis then slowed down when the pH decreased to approximately 4.5. The reduction in hydrolysis at this point might be attributed to a decrease in the dielectric constant of the buffer solution as discussed by Schliecker et al. [11]. Rationale for this phenomenon is based on an observed reduction in solubility of the hydrolyzed oligomer fragments in the buffer solution. After approximately 1 month of immersion for the 5K diacid sample, the buffer solution became noticeably turbid suggesting oligomeric insolubility. de Jonga et al. suggest that a decrease in dielectric constant of the buffer solution would stabilize the hydrolysis reaction ground state more than the transition state, and result in lower reactivity [13].

A general, hypothetical, mass (m) vs. time (t) curve for hydrolysable polyesters, plotted in a slightly different way, is displayed in Fig. 13. The vertical axis is the quantity $(m-m_i)/m$, expressed as a percent, where m_i is the initial mass. The horizontal axis is plotted as $\log_{10}t$ so that data can be displayed over a broad range of times. There are three distinct chronological regimes on this gravimetric profile: (1) simple water in-diffusion, (2) faster diffusion as accelerated by polymer plasticization by water with the onset of hydrolysis reactions, and (3) high water swelling with rapid hydrolysis and considerable molecular weight degradation such that low molecular weight products are leached out of the material and $(m-m_i)/m$ eventually becomes negative. Regime 1 is characterized by a somewhat constant diffusion coefficient that is influenced by polymer composition, additives, morphology, and surface chemistry. However, in regime 2, the water content reaches a level such that the polymer chains acquire more segmental mobility as they become solvent-separated; at this point the material volume increases more dramatically, the glass transition is lowered, and water uptake is commensurately accelerated. Regime 3 begins at a characteristic time t_{do} at maximum mass. At this time, local osmotic pressure within water clusters will drive chain separation to produce the optimum conditions for hydrolysis and catastrophic loss of mass.

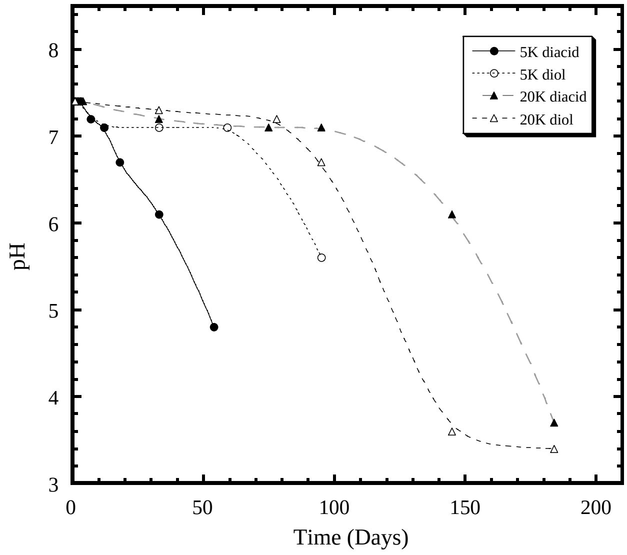

Fig. 12. Natural logarithm of dry weight loss vs. immersion time for 5000 g/mol poly(D,L-lactide) diol and diacid.

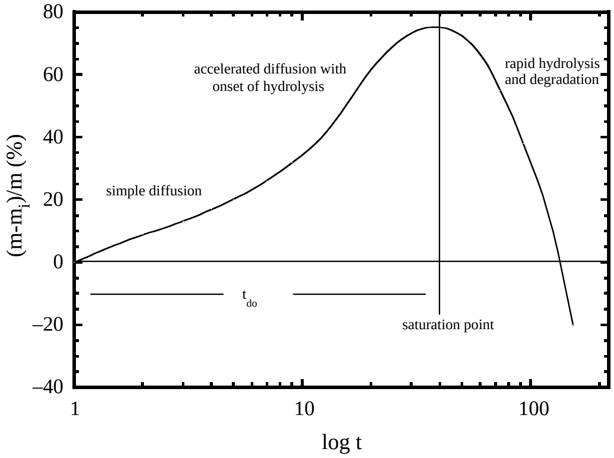

Fig. 13. Hypothetical percent mass vs. time profile for a hydrolysable polyester illustrating degradation regimes.

There is an advantage in re-plotting the gravimetric data in this way. First, a logarithmic time axis expands the curve at short times so as to reveal transitional behavior, related to T_g evolution, during this critical period. These transitions are in the form of inflection points and significant changes in instantaneous slope. Also, as the vertical axis values $(m-m_i)/m$ are scaled relative to the instantaneous weight, changes in mass are exaggerated.

The above-described three regimes are in fact observed for the poly(D,L-lactide) diacid and diol materials at 20,000 g/mol as shown in Fig. 14, where t_{do}, which might be considered as a time to failure, is ≅95 days for the acid-terminated material and ≅78 days for the hydroxyl-terminated material. The period of diffusion and preliminary hydrolysis in regime 1 for the poly(D,L-lactide) diacid sample occurred between 1 and 10 days over which there was a gradual and steady increase in mass to about 20%.

As the acid-terminated sample progressed through regime 2, it underwent an interesting transition as the measured T_g value approached, and then passed beneath, the experimental temperature of 37 °C after 12 days of immersion. Representative DSC traces for the wet samples are shown in Fig. 15. The mass uptake then displayed a temporary plateau between days

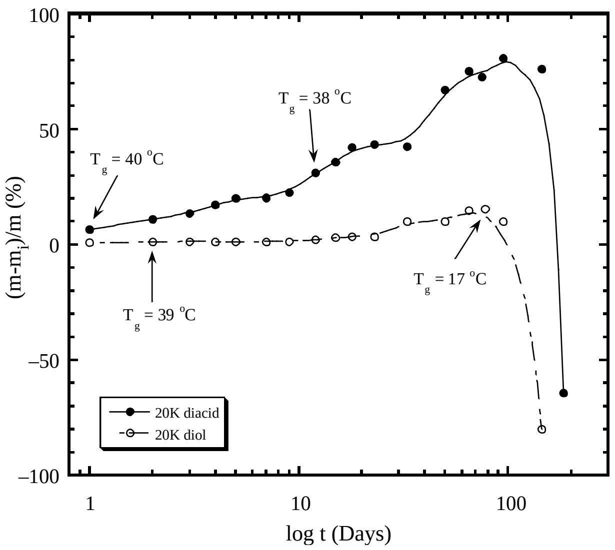

Fig. 14. Degradation profile for 20,000 g/mol poly(D,L-lactide) diol and diacid samples.

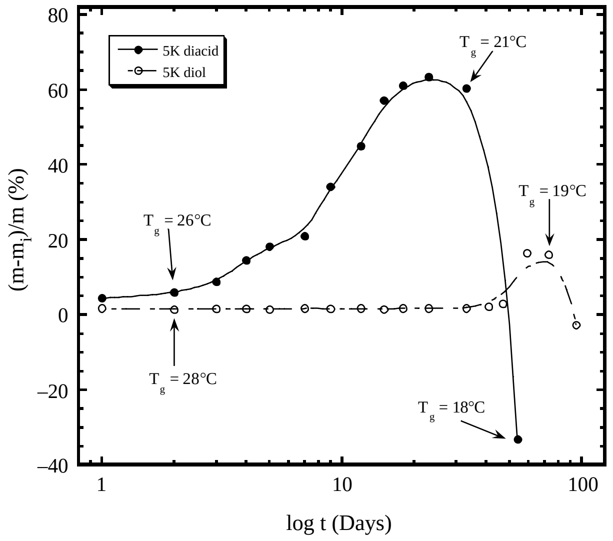

Fig. 16. Degradation profile for 5000 g/mol poly(D,L-lactide) diol and diacid samples.

20 and 30, after which it underwent another increase between days 30 and 100; it reached regime 3 at around an 80% change and then underwent a rapid fragmentation and loss in mass. The 20,000 g/mol poly(D,L-lactide) diol sample displayed a relatively slower mass change over the first 30 days of immersion in regime 1, and then a moderate increase in mass to around 15% between days 30 and 100 in regime 2. The polymer then underwent rapid fragmentation and loss during the next 50-day period during regime 3.

The three theoretical regimes were also observed for the poly(D,L-lactide) diacid and diol materials at 5000 g/mol, as shown in Fig. 16, where t_{do} is $\cong$23 days for the acid-terminated material and $\cong$73 days for the hydroxyl-terminated material. The initial period dominated by simple diffusion and onset of hydrolysis that leads to the condition influenced by water plasticization occurred between days 1 and 5 for the acid-terminated sample. There was a decrease in T_g between that of the dry original sample prior to immersion from 30 to 26 °C for the wet sample after only 2 days of immersion. The entire T_g range for the acid-terminated material was well below the experimental degradation temperature of 37 °C. The moisture absorption of this material led to a 20% increase in $(m-m_i)/m$ mass over the initial 5 days of immersion leading to the onset of regime 2, when the material rapidly increased in mass between 5 and 22 days. During this period, an increase in the hydrolysis of ester linkages and a gradual loss of low molecular weight fragments began to occur. Hydrolysis itself progressed at a greater rate than that depicted on the weight loss curve during this period, since some hydrolyzed chain fragments must have escaped from the polymer into the aqueous medium. Once the hydrolyzed chains fragmented enough to form lower molecular weight and more soluble products, rapid erosion and weight loss began and the profile entered regime 3 when rapid mass loss was observed. In contrast to the acid-terminated sample, the hydroxyl-terminated material demonstrated a longer period (45 days) of regime 1 diffusion with less than 10% $(m-m_i/m)$ increase, and a shorter regime 2 (between 45 and 75 days), at which point the catastrophic mass loss associated with regime 3 occurred.

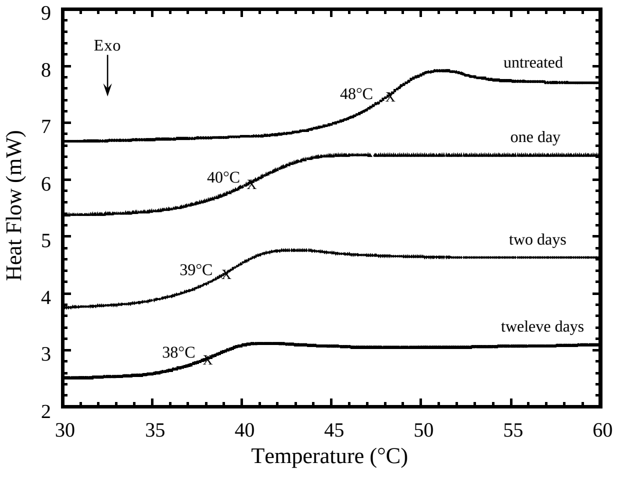

Fig. 15. DSC traces of wet 20,000 g/mol poly(D,L-lactide) diacid samples. Curves were shifted vertically for clarification.

4. Conclusions

Carboxylic acid-terminated poly(D,L-lactide)s were synthesized in relatively high yield and directly compared to their hydroxyl-terminated analogs with respect to moisture uptake and hydrolytic degradation behavior. Carboxylic acid end group functionality was shown to have a dramatic effect on the rate and extent of moisture absorption of both polymers, and on the hydrolytic degradation rate of the 5000 g/mol polymer. Although the 20,000 g/mol carboxylic acid-terminated poly(D,L-lactide) swelled to more than 300% of its original weight, compared to around 20% for the hydroxyl-terminated analog, both materials displayed rapid hydrolysis and degradation at around the same period of immersion. This result suggests that hydrolysis rate is independent of interior water concentration for higher molecular weight poly(D,L-lactide) materials.

A hypothetical mass vs. time curve for hydrolysable polyesters that contains three distinct regimes was presented. In chronological order, the regimes are: (1) simple water in-diffusion with the onset of hydrolysis reactions, (2) accelerated diffusion and increased hydrolysis as accelerated by polymer plasticization by water, and (3) high water swelling with rapid hydrolysis and considerable molecular weight degradation. These three regimes were observed for the 5000 and 20,000 g/mol poly(D,L-lactide) diacid and diol materials, and these concepts should be useful for describing other biodegradable polyesters.

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