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Evaluation of Kinetics Parameters for Poly(L-lactic acid) Hydrolysis under High-Pressure Steam

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Abstract

In order to evaluate more precise kinetics parameters: rate constant k and E_a values for poly(L-lactic acid) hydrolysis, the reaction was carried out under high-pressure steam in a temperature range of 100~130 °C. Molecular weights of hydrolyzates were calculated by the universal calibration method without being influenced by any weight loss. The changes in molecular weight could be successfully explained according to the auto-catalytic hydrolysis mechanism, clearly indicating the critical point. Resulting k and E_a values were estimated as $8.4 \times 10^{-5} \sim 7.2 \times 10^{-4} \text{ s}^{-1}$ and $87.2 \text{ kJ}\cdot\text{mol}^{-1}$ with high R^2 values, respectively. Moreover, to determine the deviation of the parameter values, influences of four factors on the measurements and calculation: 1) use of number average molecular weight value alone, 2) use of relative molecular weight based on polystyrene standards, 3) weight loss during the hydrolysis, and 4) selection of reaction mechanism were evaluated quantitatively.

Keywords: Activation energy; Hydrolysis; Kinetics; Molecular weight; Polylactic acid

Running head line: Kinetics Parameters for PLLA Hydrolysis under Steam

1. Introduction

Poly(L-lactic acid) (PLLA) is a bioabsorbable polymer, well known for its applications in the biomedical and pharmaceutical fields as a material used in surgical operations, tissue regeneration, and drug delivery systems [1]. PLLA has also been attracting much interest from researchers and engineers as an alternative to commercial polymers such as polyethylene, polypropylene, poly(ethylene terephthalate), and polystyrene, because it originates from renewable resources [2]. PLLA is also a superior material for feedstock recycling into L-lactic acid by hydrolysis [3,4] and into L,L-lactide by pyrolysis [5,6].

Many studies, in looking to control the hydrolysis of polymeric implant devices *in vivo*, have reported on the hydrolytic degradation of aliphatic polyesters including PLLA. Generally, it has been recognized that the polyesters undergo an auto-catalytic random chain scission during hydrolysis as a result of acceleration by their carboxyl end groups [7-11]. For example, Huffman et al. [7] have reported that the hydrolysis of poly(glycolic acid) in deionized water at 37 °C shows a linear relationship for $\log[\text{COOH}]$ against reaction time, suggesting that the hydrolysis is catalyzed by carboxyl end groups. Pitt et al. [9] have observed a kinetic relationship described by $M_{nt}/M_{n0}=\exp(-kt)$ on the hydrolysis of poly(μ -caprolactone), PLLA, and poly(glycolic acid-co-L-lactic acid) in a phosphate buffer solution (PBS) (pH 7.4), where M_{nt} and M_{n0} refer to the number-average molecular weight values at time t and $t=0$, respectively.

In most reports, the reaction rate constant, k , and the activation energy, E_a , of PLLA hydrolysis have been evaluated based on changes in M_n alone. This evaluation is based on the kinetics for the auto-catalytic random hydrolysis being considered as the main reaction mechanism, which occurs preferentially in an amorphous region [12-14]. The reported k values are in a range of $2.1\sim 9.7 \times 10^{-8} \text{ s}^{-1}$ at $37 \text{ }^\circ\text{C}$ in PBS (pH 7.4) [9,12,14-20] and the E_a values are in a range of $51.4\sim 100.5 \text{ kJ}\cdot\text{mol}^{-1}$ [3,19,21-23]. This large variation in the value of E_a suggests that there are some factors influencing the evaluation of the parameters, for example, crystallinity, optical purity, etc. The effect of crystallinity has been discussed in terms of its influence on the reaction rate [14], reaction mechanism [23], and critical value [13,24]. The critical value was defined by Gilbert et al. as the point at which molecular weight began deviating from the linear relationship of $\ln M_n$ against time. Beyond the critical point, the onset of fragmentation and significant weight loss occurs [12,25].

However, in these previous studies, there are some particular difficulties that should be re-evaluated, for example, 1) the influence of weight loss by dissolution of low molecular weight hydrolysates, 2) the effect of using relative molecular weight values based on polystyrene standards, and 3) the risk of relying on the use of M_n alone. Actually, the influence of the weight loss on the estimation of molecular weight has already been pointed out by Kotliar et al. [26] in their treatment of radiation-induced degradation of polymers. Vert et al. [27] also suggested that the heterogeneous degradation of P(LA-co-glycolic acid) was

based on the diffusion of hydrolyzates into the surrounding aqueous medium through the well-known auto-catalytic hydrolysis. The influence of weight loss on the number-average degree of polymerization was calculated by Yoon et al. [28]. They showed that the higher the degree of polymerization of the soluble oligomers in hydrolysis, the slower the rate of reduction in the number-average degree of polymerization calculated for the remaining portion. This suggests that the apparent hydrolysis rate will be estimated to be less than the true value. Unfortunately, Yoon et al. used a model based on the non-auto-catalytic hydrolysis mechanism to calculate the theoretical M_n after weight loss without employing a quantitative value or properly considering the auto-catalytic reaction.

The influence of the relative molecular weight based on standard polystyrenes may be serious, because the universal calibration method (UCM) [29-31] predicts that the exact molecular weight of PLLA is in a range of 0.3~0.5 when expressed as a ratio of the relative molecular weight based on polystyrene standards. In a few papers, the k value has been evaluated using the exact molecular weight: Pitt et al. [9] and Cha et al. [15] estimated the k value as 2.1×10^{-8} and $7.7 \times 10^{-8} \text{ s}^{-1}$, respectively, at 37 °C in PBS (pH 7.4) by using UCM [29], and Lyu et al. [20] evaluated the k value as $8.0 \times 10^{-8} \text{ s}^{-1}$ at 37 °C in PBS (pH 7.4) using SEC and a light scattering detector. These results indicate that the k value is of the order of 10^{-8} s^{-1} unless there are other serious factors to account for the variation.

The wide range of E_a values reported indicates that the slope of $\ln k$ vs. $1/T$ plot is very

sensitive to various factors, suggesting that, when the kinetics parameters of hydrolysis have been evaluated, the values have included some perturbing contributions resulting in the wide variations. For example, the calculation using M_n is straight forward, but M_n , as experimental chemists are well aware, is very sensitive to the oligomer components on the analysis of size exclusion chromatography (SEC) profiles. Moreover, it is not an appropriate method of evaluating the mechanism of degradation, because it is impossible to distinguish the random chain scission and the chain-end scission by using the change in M_n alone. Also previously pointed out is the difficulty in finding the critical point at which the molecular weight plot begins to deviate from the theoretical curve for the homogeneous random hydrolysis [25]. To reduce the effect of these factors, it is advisable to use both the M_n and M_w collaboratively.

Hence, to calculate the exact parameter values of k and E_a , whole reactants should be taken into account, more accurate molecular weight values used, and not only M_n but also M_w employed. In this study, the hydrolysis of PLLA was conducted under high-pressure steam without any dissolution of reactants and/or hydrolyzates. The number and weight-average molecular weights of hydrolyzed products were calculated with UCM. Moreover, the k and E_a values were evaluated with analytical methods for both the non-auto-catalytic and the auto-catalytic random degradation as well as the unzipping degradation mechanisms, using both M_n and M_w .

2. Experimental methods

2.1. Materials

Polymer: PLLA pellet (LACEA H-100J; Sn content: 40 ppm; M_n 23,700, M_w 56,300; width: 3.92 ± 0.32 mm, depth: 3.48 ± 0.20 , height: 4.52 ± 0.16 mm) was obtained from Mitsui Chemicals, Inc. and used as received.

2.2. Hydrolysis of PLLA under high-pressure steam

The hydrolysis of PLLA under high-pressure steam was done using an autoclave (Tomy autoclave model SS-325, unobstructed capacity 55 L). The PLLA pellets were autoclaved for prescribed periods at 100 (0.102 MPa), 110 (0.145 MPa), 120 (0.202 MPa), and 130 °C (0.276 MPa). Internal temperature of the autoclave was thermostated to within ± 0.5 °C. After autoclaving, the PLLA sample was dried in vacuo at room temperature for 1 night and refrigerated at -30 °C until analysis. The hydrolysis was carried out in duplicate with good reproducibility.

2.3. Measurement

Molecular weight (MW) was measured by size exclusion chromatography (SEC) on a TOSOH HLC-8120 GPC system at 40°C using TOSOH TSKGel Super HM-M column (linearity range: $1 \times 10^3 \sim 8 \times 10^6$; molecular weight exclusion limit 4×10^8) and a chloroform

eluent (0.6 mL·min⁻¹). Low polydispersity polystyrene standards with M_n from 5.0×10^2 to 1.11×10^6 were used for calibration. The SEC traces were evaluated by UCM [32] using the published Mark-Houwink-Sakurada constants for PLLA and polystyrene as follows:

$$\text{PLLA [29]} \quad [\eta] = 5.45 \times 10^{-4} \cdot M^{0.73}$$

$$\text{Polystyrene [33]} \quad [\eta] = 0.49 \times 10^{-4} \cdot M^{0.794}$$

3. Results and Discussion

3.1. Theoretical estimation of influences of weight loss during hydrolysis

It is well known that randomly degraded polymer converges to show the most probable distribution (MPD), which is defined by Eqs (1) and (2).

$$N_i = N_0 \alpha^{i-1} (1 - \alpha)^2 \quad (1)$$

$$W_i = i \alpha^{i-1} (1 - \alpha)^2 \quad (2)$$

where i , N_i , N_0 , α , and W_i are degree of polymerization, number fraction of i -mer, initial number of monomer, conversion of monomer, and weight fraction of i -mer, respectively. If a hydrolyzed polymer has a typical MPD and during hydrolysis a fraction of the hydrolyzates with lower molecular weights dissolves out into the surrounding media, then the apparent number and weight average molecular weights: M_n' and M_w' of the residual part of the polymer can be calculated using Eqs (3) and (4), respectively.

$$M_n' = M \frac{\sum_{i=x}^{\infty} i \cdot N_i}{\sum_{i=x}^{\infty} N_i} \quad (3)$$

$$M'_w = \mathbf{M} \frac{\sum_{i=x}^{\infty} i^2 \cdot N_i}{\sum_{i=x}^{\infty} i \cdot N_i} \quad (4)$$

where \mathbf{M} is the molecular weight of monomer. Based on Eqs (3) and (4), it is clear that the apparent values, M_n' and M_w' , are larger than the true values: M_n and M_w calculated using the totality of hydrolyzates. The percentage increase in the apparent average values are given by $(M_w'/M_w - 1) \cdot 100$. In Figure 1, the apparent percentage increases in M_n and M_w are plotted. Surprisingly, a loss of only 1 wt.-% in the lower molecular weight fractions results in about a 15% increase in M_n , whereas it only produces an increase of 0.95% in M_w . These results indicate that on hydrolysis accompanying a few weight losses the uncertainty in the kinetics values based on the M_n value alone is much greater than the uncertainty associated with M_w and therefore the M_w values are likely to be much more reliable.

[Figure 1]

In this study, the hydrolysis of PLLA was achieved under high-pressure steam, which prevents the dissolution of low molecular weight hydrolyzates from the sample into the surrounding gaseous phase. Taking into account the whole of the hydrolyzates, we can estimate average molecular weights and kinetic parameters more accurately than for those in a liquid phase.

3.2. Qualitative determination of critical point on hydrolysis

[Figure 2]

Illustrated in Figure 2 are the changes in M_w of PLLA, which were calculated by UCM, during the hydrolysis under high-pressure steam in a temperature range of 100~130 °C (0.102~0.276 MPa). Each M_w steadily decreased with time at a rate dependent on the reaction temperature. Figure 3 shows typical changes in SEC profiles of PLLA treated at 110 °C. The SEC profile gradually shifted from a uni-modal to a multi-modal profile, passing through the critical point, recognized by the appearance of shoulders in the profile. After 180 min of the hydrolysis, the intensity of the shoulders starts to increase with time eventually forming two sharp peaks at $\log MW$ 3.15~3.2 (MW 1400~1600) and at 3.5~3.6 (MW 3000~4000). These specific peaks were stationary at the values of $\log MW$ s during the hydrolysis, being assigned to chains of one of the single or several folds in the crystalline [13,24]. Molecular weights of these specific peaks decreased with increase in hydrolysis temperature as follows: MW 1700~1800 and 3800~4400 at 100 °C, 1300~1600 and 3000~3600 at 120 °C, and 1100~1600 and 2700~3300 at 130 °C as shown in Figure SI-1, SI-2, and SI-3, respectively, in Supplementary data. This shift in the peaks with increase in temperature is assumed to occur due to the temperature-dependent changes in diffusion efficiency of water vapor and the mobility of polymer chains neighboring the crystalline. Although these molecular weights are lower than previously reported values: MW 12000~6000 based on the polystyrene standards [13], the differences can be attributed to the calculation methods based on polystyrene standards and UCM.

In the figures, the critical point was qualitatively determined at times of around 300, 180, 90, and 45 min to be at 100, 110, 120, and 130 °C, respectively. After the critical points are passed, the homogeneous random degradation process is assumed to change into a heterogeneous degradation process, with the reaction tending to by-pass the crystalline phase.

[Figure 3]

3.3. Estimation of rate constant k and activation energy E_a values

As above mentioned, to estimate an accurate k value, the hydrolysis was carried out under high-pressure steam without any weight loss and the molecular weight was calculated using UCM. Moreover, data obtained during the period when the homogeneous random hydrolysis was continuing, i.e. before the critical point, were employed in the estimation. In order to find the critical point accurately, the theoretical changes in M_n , M_w , and polydispersity index (PD) were calculated according to Eqs (5), (6), and (7) for the auto-catalytic random degradation kinetics [25], and compared with the actual plots measured.

$$\ln M_n = \ln M_{n0} - kt \quad (5)$$

$$\ln M_w = \ln M_{w0} - kt \quad (6)$$

$$\frac{dPD}{dt} = \frac{2k}{3} PD(2 - PD) \quad (7)$$

where M_{n0} , M_{w0} , and k are initial number and weight average molecular weights, and rate

constant of reaction, respectively. One important point is that both the theoretical plots of M_n and M_w have the same slope as the rate constant k value. In Figure 4, the theoretical lines and measured plots of M_n and M_w on hydrolysis at 110 °C are illustrated. The theoretical lines successfully fitted the measured plots in the first half period. Deviation from the theoretical M_{n0} plot at $t = 0$ is due to an initial correction for MPD according to Eq 7 [25]. After 180 min of the hydrolysis, the measured plots gradually departed from the theoretical lines. Thus, this departing point is the critical point, precisely matching the change in SEC profile found in Figure 3. Further data obtained at 100, 120, and 130 °C also showed a good match with the theoretical lines during the first half period, giving individual slopes as k values (Figure SI-4, SI-5, and SI-6 in Supplementary data). Each point of departure from the theoretical line also coincided with the change into the multi-modal stage in the corresponding SEC profile. These results clearly indicate that the hydrolysis of PLLA under the high-pressure steam proceeded in the manner of the auto-catalytic degradation mechanism.

[Figure 4]

The rate constants based on the changes in M_w , k_{Mw} , and the coefficient of determination, R^2 , values were calculated from the first linear part of the M_w plots and listed in Table 1. Obtained k_{Mw} values were in a range of 8.4×10^{-5} (100 °C) $\sim 7.2 \times 10^{-4}$ s⁻¹ (130 °C) with excellent R^2 values at higher than 0.998. The activation energy, E_a , value was estimated from the Arrhenius plot (Figure 5) of the obtained k values, resulting in $E_a = 87.2$ kJ·mol⁻¹.

Estimated parameters: k_{M_w} and E_a values allowed us to predict a k value at a different temperature, found to be $2.7 \times 10^{-7} \text{ s}^{-1}$ (37 °C), which is higher than the previously reported values $2.1\sim 9.7 \times 10^{-8} \text{ s}^{-1}$ in PBS (pH 7.4). This suggests that PLLA hydrolysis effectively progressed under high-pressure steam without being inhibited by the action of PBS.

[Table 1]

[Figure 5]

3.4. Deviation of k and E_a values estimated in several manners

The estimated E_a value $87.2 \text{ kJ}\cdot\text{mol}^{-1}$ is close to the previously reported $83.7 \text{ kJ}\cdot\text{mol}^{-1}$ on the hydrolysis of PLLA micro-capsules dispersed in PBS (pH=7.4) without any weight loss [21]. However, the E_a value ($83.7 \text{ kJ}\cdot\text{mol}^{-1}$) was calculated from the Arrhenius plot of $1/T$ vs. dM_w/dt assuming the unzipping degradation mechanism, rather than assuming random hydrolysis. The estimated E_a value is higher than the $51.4 \text{ kJ}\cdot\text{mol}^{-1}$ obtained on hydrolysis using high-temperature and high-pressure water in a range of $180\sim 350 \text{ °C}$ [3], under which conditions dissolution of hydrolyzates in the medium also occurred. Moreover, the estimated E_a value is lower than $100.5 \text{ kJ}\cdot\text{mol}^{-1}$ calculated from the changes in exact M_n values on the hydrolysis of PLLA in PBS (pH=7.4) in a temperature range of $37\sim 70 \text{ °C}$ [19]. However, the high value was evaluated from the changes in M_n alone, with low R^2 values of $0.85\sim 0.96$.

The wide range of E_a values previously reported may be induced by differences in the

manner in which estimations were made, such as under conditions accompanying weight loss by dissolution of low molecular weight hydrolysates, use of the relative molecular weight value based on polystyrene standards, and use of only M_n values with low R^2 values. These conditions and risk factors may affect the k and E_a values independently and/or cooperatively.

In order to determine the deviation of k and E_a values due to differences in the manner of estimation, various approaches were employed to calculate the parameter values.

3.4.1. Use of M_n value alone

Generally only M_n values have been employed as a variable for the evaluation of k and E_a values in previous reports. In Figure 6, the relationships of $\ln M_n$ vs. t are illustrated. The k_{Mn} values based on the changes in M_n were calculated from the approximation of linear parts of the plots. From the approximation of $\ln M_n$ plots k_{Mn} values were found to be lower by 0.66 ~ 12.54 % and R^2 values lower by 0.975 ~ 0.997 than the k_{Mw} and its associated R^2 values as listed in Table 2. This is the influence of additional plots round the critical points. As a result, a tentative E_a value was calculated as 84.1 $\text{kJ}\cdot\text{mol}^{-1}$, a decrease of 3.1 $\text{kJ}\cdot\text{mol}^{-1}$ when compared with the 87.2 $\text{kJ}\cdot\text{mol}^{-1}$ estimated using the k_{Mw} values.

[Figure 6]

[Table 2]

3.4.2. Influences of relative $M_{w,r}$ value based on polystyrene standards

In many previous reports, relative $M_{n,r}$ and $M_{w,r}$ based on polystyrene standards have been employed for the evaluation of k and E_a values. However, the ratio of the molecular weights of PLLA calculated by UCM to the relative ones calculated from polystyrene standards is in a range of about 0.3:1 to 0.5:1. In order to estimate the influence of the difference between the molecular weights calculated by both methods, tentative rate constant, $k_{M_{w,r}}$, values were estimated by using relative $M_{w,r}$ values. In Figure SI-7 in Supplementary data, relationships of $\ln M_{w,r}$ vs. time for PLLA during the hydrolysis are plotted. The tentative rate constant, $k_{M_{w,r}}$, values were calculated from the slopes of plots in Figure SI-7 and listed in Table 3. As seen in the table, the influence on k value of the relative molecular weight was in a small range of -3.44 ~ -3.53 %. The $E_{a,r}$ value was also estimated using these $k_{M_{w,r}}$ values, resulting in the same value of $87.2 \text{ kJ}\cdot\text{mol}^{-1}$ as was estimated by using UCM.

Above results indicate that, in the case of random degradation, the use of the relative molecular weight slightly affects the k value estimated, but not the E_a value. However, in cases of chain reactions, such as unzipping degradation, the influence of the relative molecular weight must not be insignificant, because the rate constant is calculated based on an exact molar quantity of hydrolyzates.

[Table 3]

3.4.3. Influences of weight loss

As abovementioned, when quantitative parameter values for polymer degradation are required, the influences of weight loss may be serious. In Figure SI-8 in Supplementary data, simulation plots of the influences of weight loss on the E_a value were illustrated by the Arrhenius plot of apparent constant rate k' values in a temperature range of 100~130 °C. In the simulations, the weight loss value was assumed to be in parallel to the reaction time until the molecular weight reached from 100,000 to 10,000 calculated with parameter values of $E_a = 87.2 \text{ kJ}\cdot\text{mol}^{-1}$ and $\ln A = 18.679$. Obtained apparent E_a' values are listed in Table 4. The deviation of E_a value due to the weight loss was evaluated as having increased by $2.9 \text{ kJ}\cdot\text{mol}^{-1}$ at 3 wt.-% weight loss at 100 °C.

[Table 4]

3.4.4. Influences of the assumption of other hydrolysis mechanisms

In many previous reports, the hydrolysis of PLLA in PBS (pH 7.4) has been treated as progressing according to the auto-catalytic random degradation mechanism as found in this study. Recently, Lyu et al. [20] suggested that there was a beginning period when the chain ends did not significantly promote the hydrolysis, resulting in the reaction proceeding in a manner of the non-auto-catalytic mechanism. Makino et al. [21] reported an E_a value of $83.7 \text{ kJ}\cdot\text{mol}^{-1}$ for the unzipping hydrolytic degradation of PLLA micro-capsules dispersed in PBS

(pH=7.4). Shih [34] also suggested that the chain-end scission contributed the hydrolysis poly(D,L-lactic acid), indicating that the hydrolysis of chain-ends was approximately 10 times faster than the hydrolysis of internal PLA bonds. Similarly, Tsuji and Ikarashi [23] reported that the hydrolysis of the PLLA crystalline residues at 50~97 °C proceeded from their surface composed of very short chains with a free end along the chain direction, showing a low E_a value of 75.2 kJ·mol⁻¹. If a proper kinetics was employed for each reaction mechanism, the wide range of E_a values as reported previously may converge to some more precise values which correspond to the particular reaction mechanism that proceeded.

In order to determine the influences of hydrolysis mechanisms, the analytical equations for a non-auto-catalytic hydrolysis and an unzipping degradation mechanism were applied to analyze the PLLA hydrolysis data under high-pressure steam in a temperature range of 100~130 °C. Eqs (8), (9), and (10) were employed for the analysis, where Eq (9) was derived by Yoon et al. [28]

$$\frac{1}{M_n} = \frac{1}{M_{n0}} + kt \quad (8)$$

$$\frac{t^{1/3}}{M_w} = \frac{1}{2}(kt)^{4/3} + \left(\frac{1}{M_{n0}}\right)^{1/3} \left(\frac{1}{M_{w0}} - \frac{1}{2M_{n0}}\right) \quad (9)$$

$$M_n = M_{n0} - kt \quad (10)$$

In Figures SI-9 and SI-10 in Supplementary data, relationships of $1/M_n$ vs. time (t) and $t^{1/3}/M_w$ vs. $t^{4/3}$ according to Eqs (8) and (9), respectively, are illustrated. In spite of showing the best fitness (R^2 value > 0.998) to the simulation lines of the auto-catalytic hydrolysis

mechanism, the measured data plots also showed relatively high fitness ($0.990 > R^2 \text{ value} > 0.929$) to the simulation lines of the non-auto-catalytic mechanism, allowing us to calculate the kinetics parameter values. The relationship of $1/M_n$ vs. t was approximated by two approaches using a) all points and b) linear parts of data, to obtain constant rate k_{noc} values for the non-auto-catalytic hydrolysis. The approximation lines showed relatively high R^2 values of 0.929~0.986, 0.985~0.990, and 0.962~0.990 for the relationships of a) and b) of $1/M_n$ vs. t , and $t^{1/3}/M_w$ vs. $t^{4/3}$, respectively. Resulting $E_{a,noc}$ values were estimated as 95.6, 125.1 (Figure SI-11 in Supplementary data), and 99.3 $\text{kJ}\cdot\text{mol}^{-1}$ (Figure SI-12 in Supplementary data) for the relationships, respectively.

In Figure SI-13 in Supplementary data, relationships of M_n vs. t for the hydrolysis data according to Eq (10) are plotted. The plots in the initial region were approximated by simulation lines of the unzipping degradation mechanism with low R^2 values of 0.885~0.973 to give the constant rate k_{unzip} values. The $E_{a,unzip}$ value was calculated from the k_{unzip} values, giving a result of 65.0 $\text{kJ}\cdot\text{mol}^{-1}$ (Figure SI-14 in Supplementary data).

The E_a values of 95.6, 125.1, and 99.3 $\text{kJ}\cdot\text{mol}^{-1}$ for the non-auto-catalytic hydrolysis mechanism are considerably higher than the 87.2 $\text{kJ}\cdot\text{mol}^{-1}$ estimated for the auto-catalytic hydrolysis mechanism, but close to 102.7 $\text{kJ}\cdot\text{mol}^{-1}$ obtained with R^2 values of 0.63~0.99 reported by Weir et al. [19] for the non-auto-catalytic hydrolysis mechanism. On the other hand, The E_a value of 65.0 $\text{kJ}\cdot\text{mol}^{-1}$ for the unzipping degradation mechanism is significantly

lower than $87.2 \text{ kJ}\cdot\text{mol}^{-1}$, but close to the $75.2 \text{ kJ}\cdot\text{mol}^{-1}$ estimated for the unzipping degradation from chain-ends of the crystalline [23].

The above results represent an important caveat: that the employment of unsuitable reaction mechanisms to analyze kinetics results can produce large deviations in E_a value.

4. Conclusions

In order to confirm the precise kinetics parameters: k and E_a values, PLLA hydrolysis was carried out under high-pressure steam in a temperature range of 100~130 °C. Molecular weights of hydrolyzates were calculated by the universal calibration method without any influence of weight loss. The changes in molecular weight could be successfully fitted with the simulation plots generated according to the auto-catalytic hydrolysis mechanism, clearly indicating the critical point. Resulting k and E_a values were estimated as $8.4 \times 10^{-5} \text{ (100 °C) } \sim 7.2 \times 10^{-4} \text{ s}^{-1} \text{ (130 °C)}$ and $87.2 \text{ kJ}\cdot\text{mol}^{-1}$, respectively, with extremely high R^2 values.

To determine the deviation of the parameter values induced by several factors on measurements and analyses, the influences of four different conditions on the calculation: 1) use of M_n value only, 2) use of the relative molecular weight based on polystyrene standards, 3) weight loss during the hydrolysis, and 4) selection of various reaction mechanisms were estimated. Results showed the use of M_n value alone considerably increased the uncertainty in the determination of the rate constant k value. The use of the relative molecular weight had a

slight effect on the k value estimated, but did not significantly influence E_a value in the case of random degradation. The weight loss of 3 wt.-% induced an increase in E_a value of 2.9 kJ·mol⁻¹. Finally, it was found that the employment of unsuitable reaction mechanisms to analyze the kinetics results produced a large deviation in E_a value.

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Figure Captions

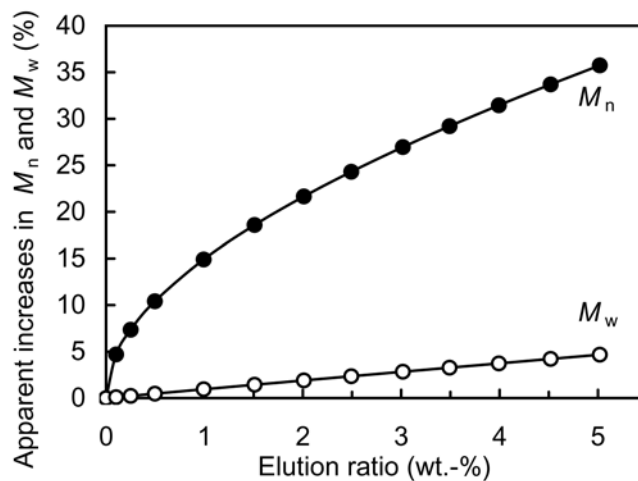


Figure 1. Apparent increases in M_n and M_w due to loss of the low molecular weight fraction.

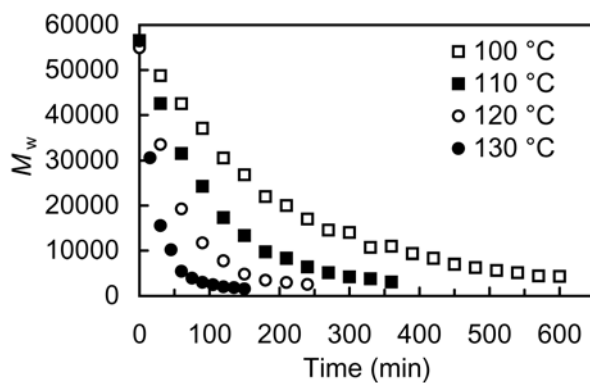


Figure 2. Changes in M_w of PLLA calculated by UCM during hydrolysis under high-pressure steam. Conditions: 100 (0.102), 110 (0.145), 120 (0.202), and 130 °C (0.276 MPa)

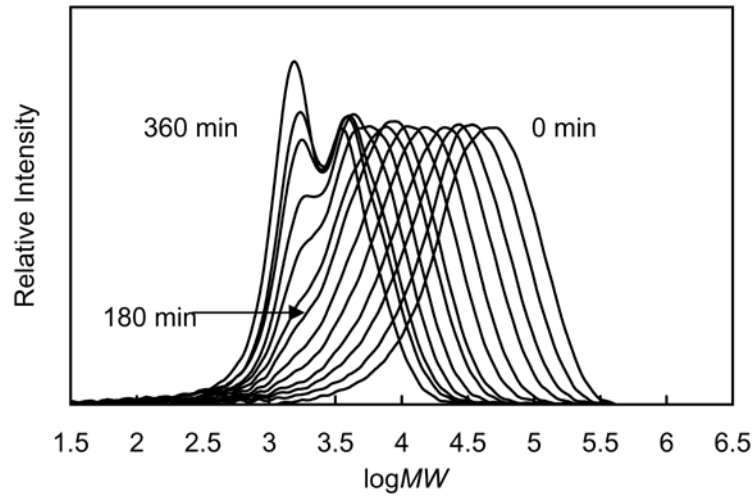


Figure 3. Changes in SEC profile of PLLA during hydrolysis for 360 min under high pressure steam at 110 °C.

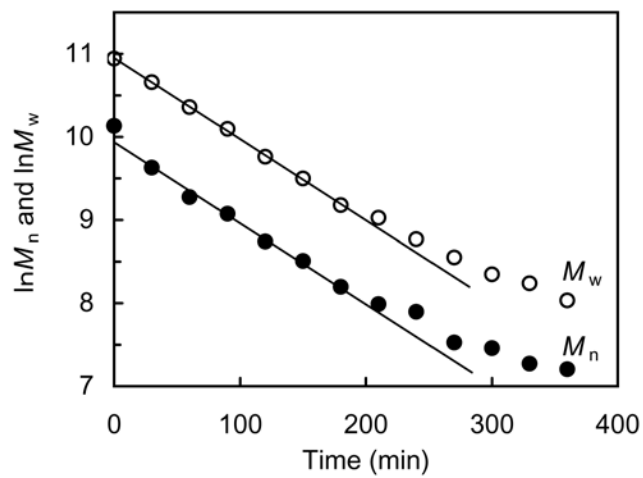


Figure 4. Plots of $\ln M_n$ vs. $\ln M_w$ vs. time for PLLA during hydrolysis under high pressure steam at 110 °C. Solid lines indicate the predictions of Eqs 5 and 6.

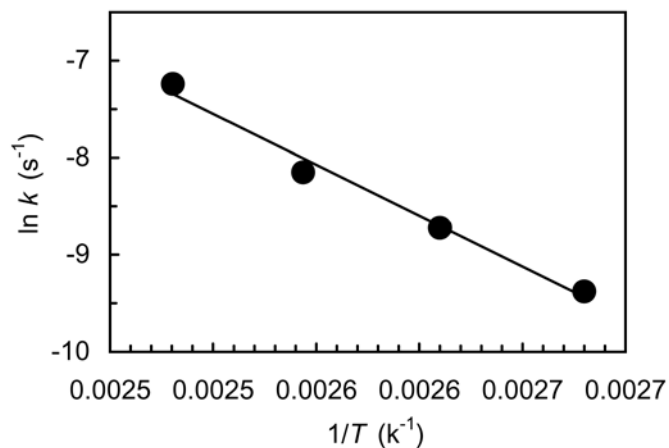


Figure 5. Arrhenius plot of the rate constant k_{M_w} of PLLA hydrolysis under high-pressure steam in a temperature range of 100~130 °C.

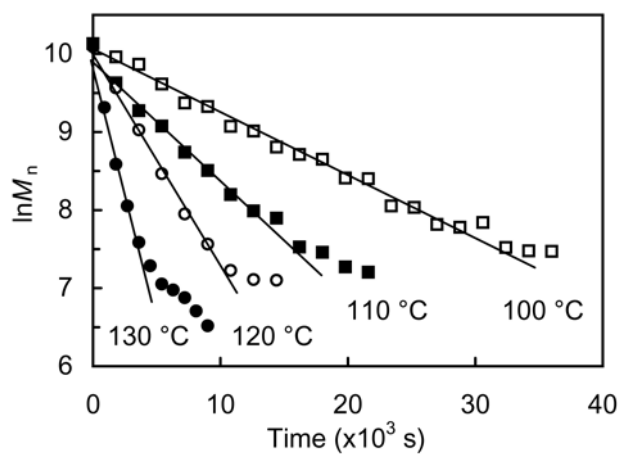


Figure 6. Plots of $\ln M_n$ vs. time for PLLA during hydrolysis under high-pressure steam in a temperature range of 100~130 °C. M_n values were calculated based on UCM.

Table 1. Rate constant, k_{M_w} , values for PLLA hydrolysis under high-pressure steam.

Temperature (°C)	100	110	120	130
$k_{M_n} \times 10^6$ (s ⁻¹)	84.4	162.9	288.6	716.9
R^2	0.998	0.999	1.000	0.999

* based on the changes in M_w calculated using UCM.

Table 2. Tentative rate constant, k_{Mn} , values for PLLA hydrolysis under high-pressure steam.

Temperature (°C)	100	110	120	130
$k_{Mn} \times 10^6$ (s ⁻¹)	82.3	151.1	286.7	627.0
R^2	0.991	0.983	0.997	0.975
$(k_{Mn}/k_{Mw}-1) \times 100$ (%)	-2.49	-7.24	-0.66	-12.54

* based on the changes in M_n calculated using UCM.

Table 3. Tentative rate constant, $k_{M_{w,r}}$, values for PLLA hydrolysis under high-pressure steam.

Temperature (°C)	100	110	120	130
$k_{M_{w,r}} \times 10^6$ (s ⁻¹)	81.5	157.2	278.4	691.8
R^2	0.998	0.999	1.000	0.999
$(k_{M_{w,r}}/k_{M_w}-1) \times 100$ (%)	-3.44	-3.50	-3.53	-3.50

* based on the changes in $M_{w,r}$ calculated based on polystyrene standards.

Table 4. Simulated apparent activation energy, E_a' , values for PLLA hydrolysis accompanying weight loss.

Weight loss at 100 °C	0	1	2	3
E_a' (kJ·mol ⁻¹)	87.2	88.9	89.6	90.1

* Conditions: parameters: $E_a = 87.2$ kJ·mol⁻¹; temperature range: 100~130 °C; set values of molecular weight: 100,000 (initial) to 10,000 (final).

* Weight loss value is assumed to occur in parallel with the reaction time at each temperature.

Supplementary Data

Evaluation of Kinetics Parameters for Poly(L-lactic acid) Hydrolysis under High-Pressure Steam

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3.2. Qualitative determination of critical point on hydrolysis

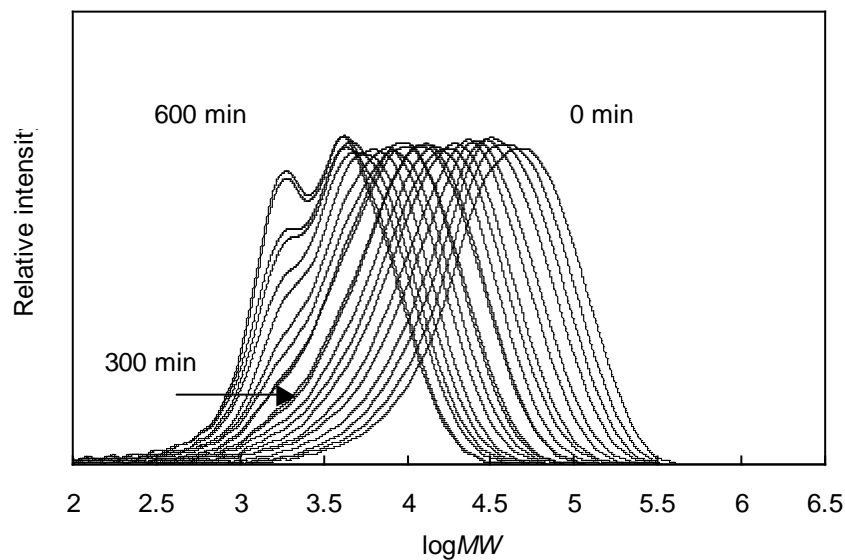


Figure SI-1. Changes in SEC profile of PLLA during hydrolysis for 600 min under high pressure steam at 100 °C.

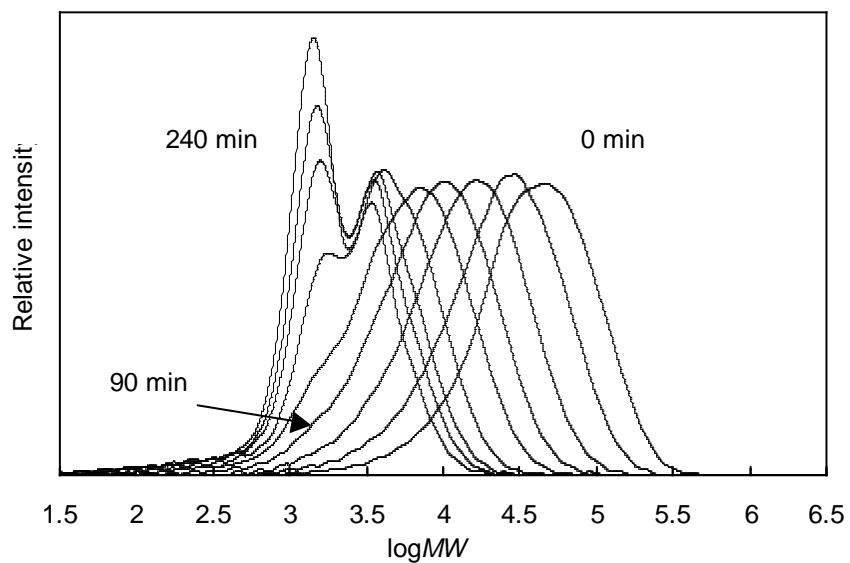


Figure SI-2. Changes in SEC profile of PLLA during hydrolysis for 240 min under high pressure steam at 120 °C.

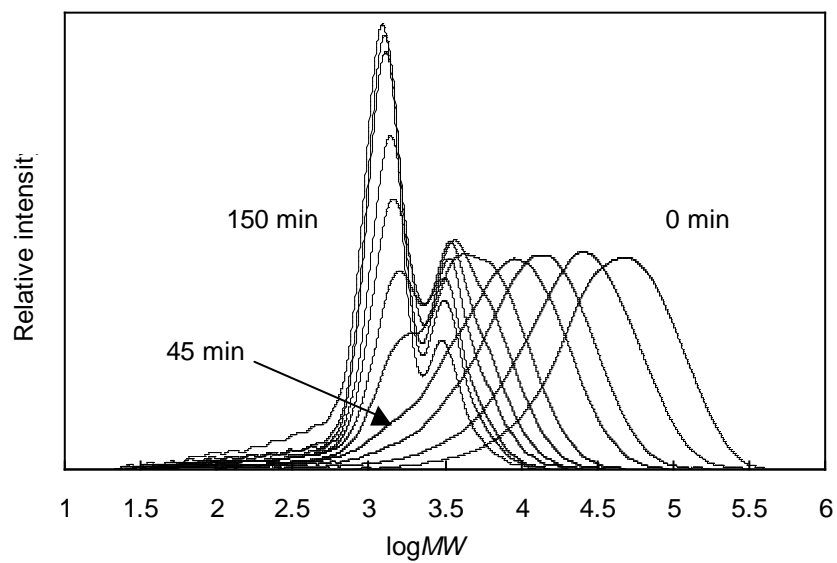


Figure SI-3. Changes in SEC profile of PLLA during hydrolysis for 150 min under high pressure steam at 130 °C.

3.3. Estimation of rate constant k and activation energy E_a values

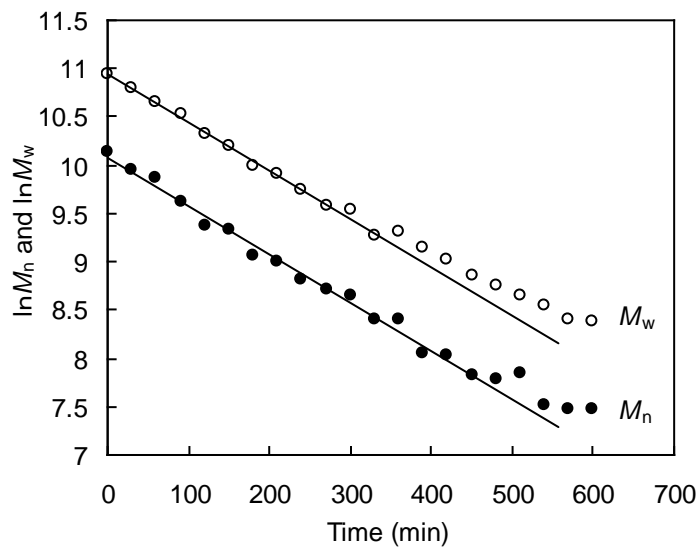


Figure SI-4. Plots of $\ln M_n$ vs. $\ln M_w$ vs. time for PLLA during hydrolysis under high pressure steam at 100 °C. Solid lines indicate the predictions of Eqs 5 and 6.

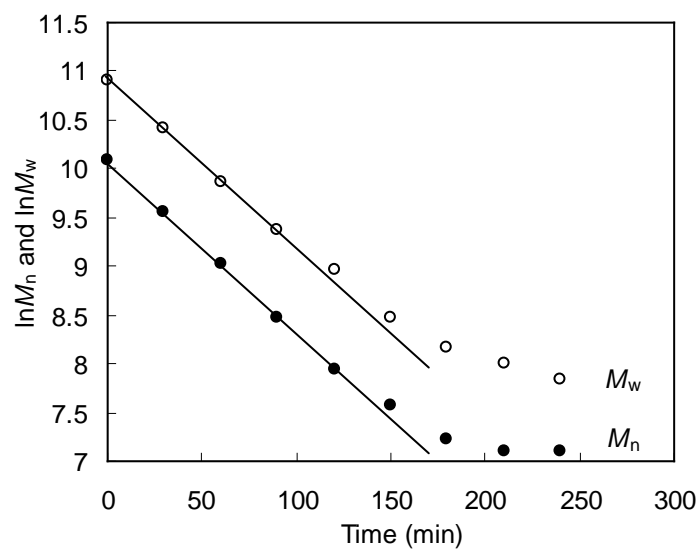


Figure SI-5. Plots of $\ln M_n$ vs. $\ln M_w$ vs. time for PLLA during hydrolysis under high-pressure steam at 120 °C. Solid lines indicate the predictions of Eqs 5 and 6.

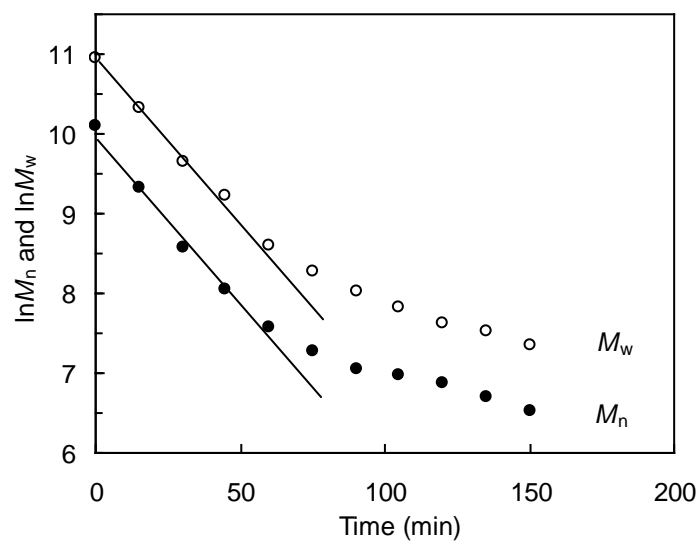


Figure SI-6. Plots of $\ln M_n$ vs. $\ln M_w$ vs. time for PLLA during hydrolysis under high pressure steam at 130 °C. Solid lines indicate the predictions of Eqs 5 and 6.

3.4. Deviation of k and E_a values estimated in several manners

3.4.2. Influences of relative $M_{w,r}$ value based on polystyrene standards

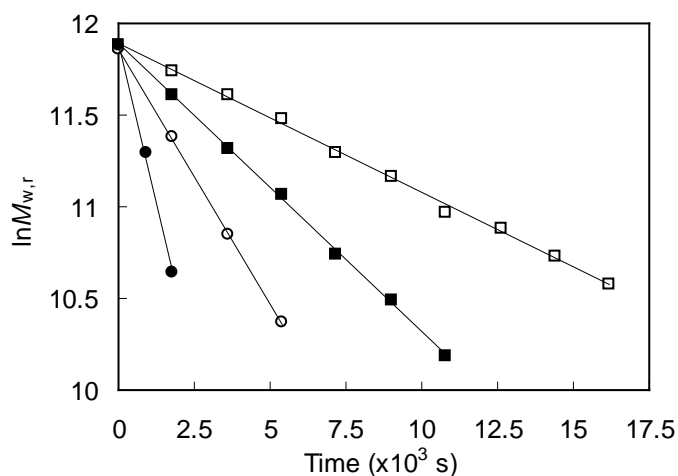


Figure SI-7. Plots of $\ln M_{w,r}$ vs. time for PLLA during hydrolysis under high pressure steam in a temperature range of 100-130 °C. Relative values: $M_{w,r}$ were calculated based on polystyrene standards.

3.4.3. Influences of weight loss

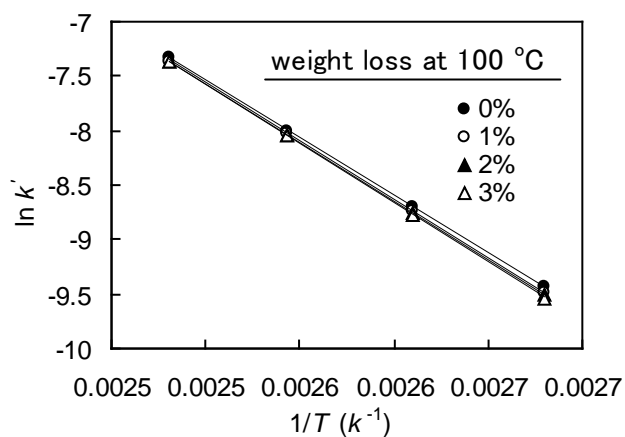


Figure SI-8. Simulation plots of influences of weight loss on the Arrhenius plot of the rate constant k' for PLLA hydrolysis in a temperature range of 100-130 °C. Conditions: weight loss is assumed to occur in parallel with the reaction time until molecular weight reaches from 100,000 to 10,000.

3.4.4. Influences of assumption of other hydrolysis mechanisms

(i) Non-auto-catalytic hydrolysis mechanism

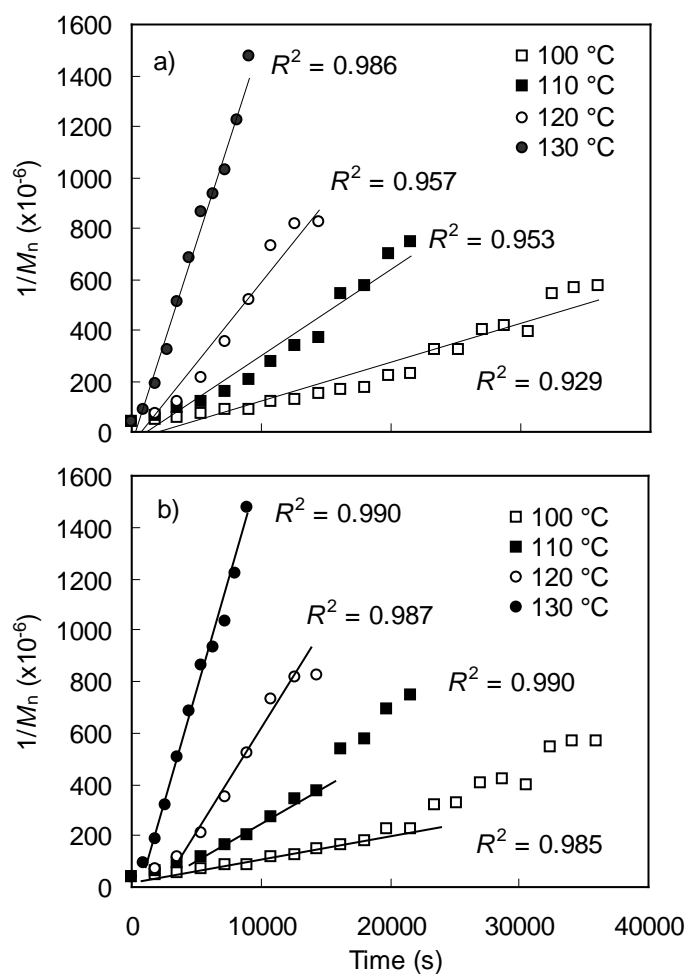


Figure SI-9. Plots of $1/M_n$ vs. time for PLLA during hydrolysis under high pressure steam in a temperature range of 100-130 °C. Approximation area: a) all points, b) linear part. Solid lines indicate the predictions of Eq 8. M_n values were calculated by UCM.

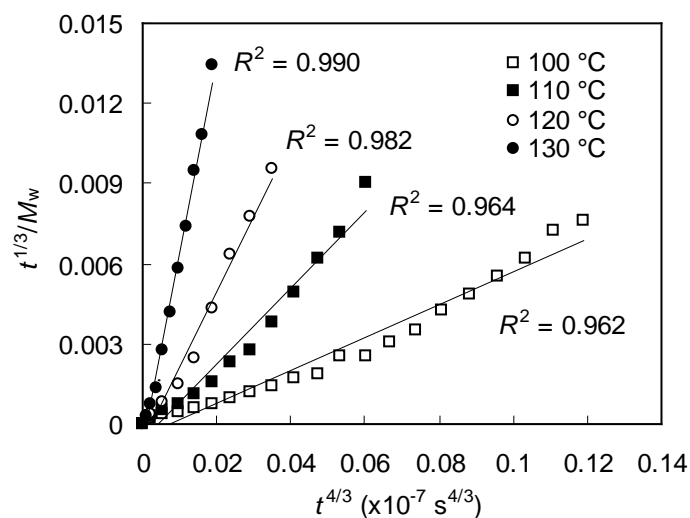


Figure SI-10. Plots of $t^{1/3}/M_w$ vs. $t^{4/3}$ for PLLA during hydrolysis under high pressure steam in a temperature range of 100-130 °C. Solid lines indicate the predictions of Eq 9. M_w values were calculated by UCM.

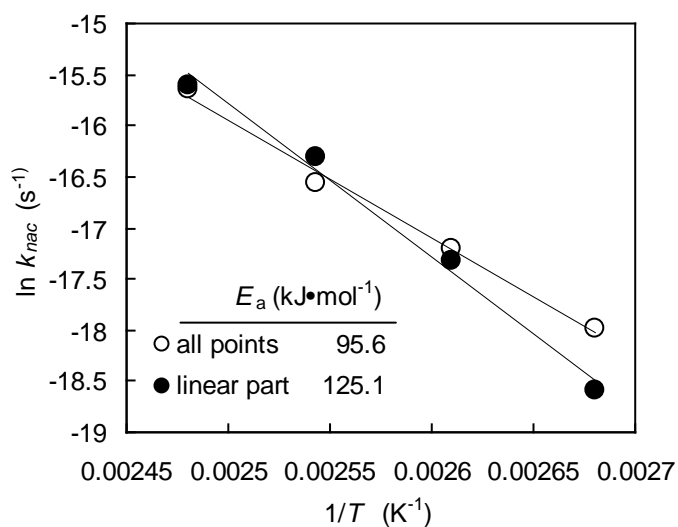


Figure SI-11. Arrhenius plot of the rate constant k_{nac} calculated from changes in M_n values for non-auto-catalytic hydrolysis of PLLA under high-pressure steam in a temperature range of 100-130 °C.

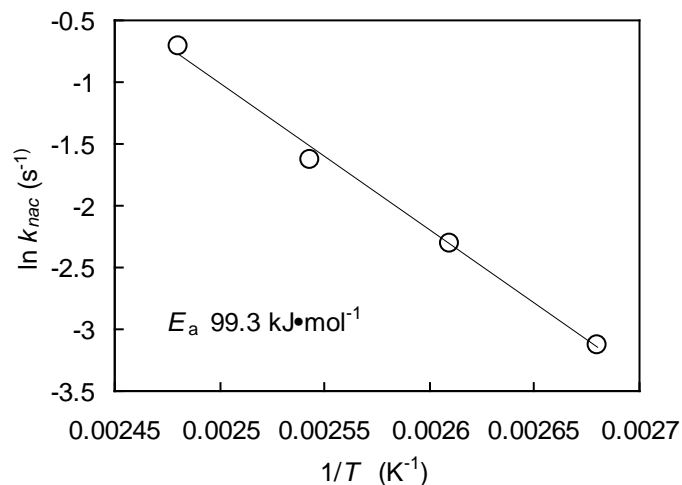


Figure SI-12. Arrhenius plot of the rate constant k_{nac} calculated from changes in M_w values for non-auto-catalytic hydrolysis of PLLA under high-pressure steam in a temperature range of 100-130 °C.

(ii) Unzipping degradation mechanism

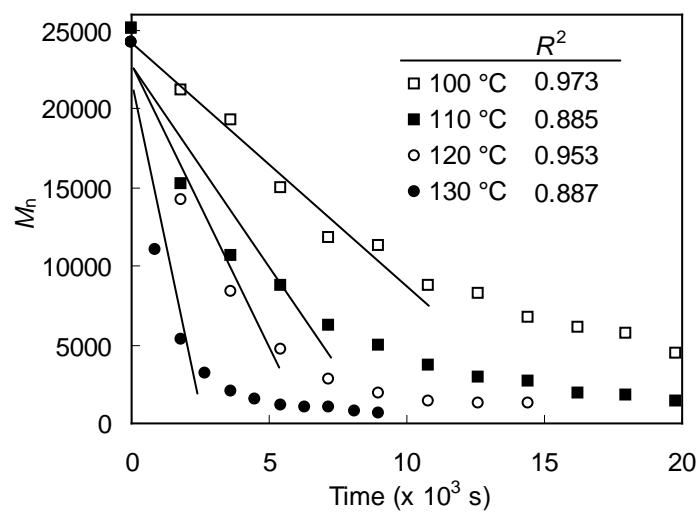


Figure SI-13. Plots of M_n vs. time for PLLA during hydrolysis under high pressure steam in a temperature range of 100-130 °C. Solid lines indicate the predictions of Eq 10. M_n values were calculated by UCM.

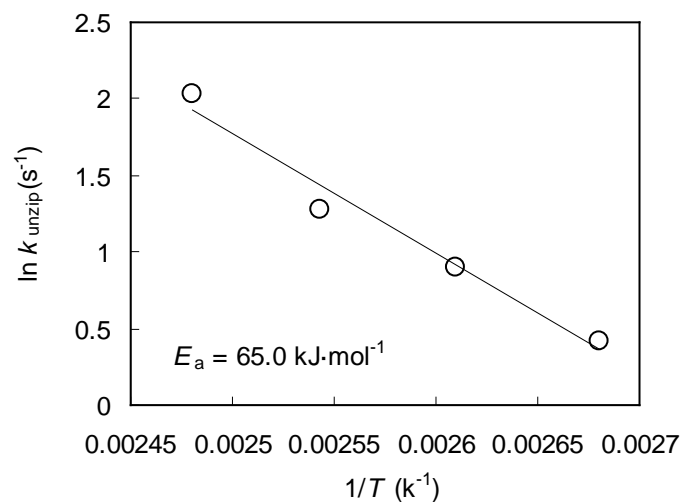


Figure SI-14. Arrhenius plot of the rate constant k_{unzip} calculated from changes in M_n values for non-auto-catalytic hydrolysis of PLLA under high-pressure steam in a temperature range of 100-130 °C. M_w values were calculated by UCM.