

# Synthesis of PDLLA Homopolymers with Different Molecular Weights

## INTRODUCTION

Poly( $\alpha$ -hydroxy acids), especially, poly(lactic acids) (or polylactides) and poly(glycolic acids) (or polyglycolides), and their copolymers make up the most widely known synthetic polymer family used for the production of biodegradable biomaterials.<sup>1-3</sup> Low molecular weight polymers (usually no greater than about 10,000) can be prepared by the direct polyesterification of lactic and/or glycolic acids.<sup>4</sup> These polymers have not found a practical use because of the very poor mechanical properties of the materials produced. However, it should be noted that they are used for the synthesis of cyclic dimers (i.e., lactides and/or glycolides) which are the starting materials for production of high molecular weight polymers. The most important method for synthesis of high molecular weight poly( $\alpha$ -hydroxy acids) is the ring-opening polymerization of the corresponding cyclic mono- or diesters.<sup>5</sup>

Recently, we also attempted to synthesize homopolymers of lactides and or glycolides and their copolymers with poly(ethylene glycol) and to process these polymers into particle or fiber forms for diverse biomedical applications.<sup>6-9</sup> Here, we briefly present the synthesis of poly(D,L-lactic acid) [or poly(D,L-lactide)] (PDLLA) homopolymers with different molecular weights and discuss the effects of some important parameters on the average molecular weights.

## MATERIALS AND METHODS

### Materials

The monomer, i.e., D,L-lactic acid, was purchased from BDH Chemicals Ltd. (UK) as an 88% aqueous solution (density: 1.2 g/mL) and was kept in a refrigerator until use. The dimer, i.e., D,L-lactide, and the catalyst, i.e., stannous chloride ( $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ ), were purchased from Polyscience (USA) and BDH (UK), respectively. All other solvents and reagents were obtained from Merck (Germany) and were used without any further purification.

## Synthesis

Low molecular weight PDLLAs were synthesized as follows: Polymerizations were conducted in ampule bottles under a nitrogen atmosphere. D,L-Lactic acid (6.0 g) was charged into the bottle which was placed in an oven equipped with a temperature-controlling system. To synthesize PDLLAs with different molecular weights, polymerizations were conducted at three different temperatures (i.e., 160, 180, or 200°C), and the polymerization time ranged from 4 to 24 h.

For synthesis of high molecular weight PDLLs, the ring-opening polymerization of D,L-lactide in bulk was carried out as follows: Polymerizations were conducted in pretreated (with aqueous solutions of potassium dichromate/sulfuric acid) ampule bottles. D,L-Lactide (3.6 g) was transferred to the bottle under a dry nitrogen atmosphere, and 0.5 mL of a freshly prepared stannous chloride solution in ethyl ether was added. The bottle was connected via an adaptor to a purge valve system with access to vacuum or dry nitrogen. It was evacuated for about 5 min to remove the nitrogen and then was refilled with dry nitrogen, heat-sealed, and placed in an oven with a temperature-controlling system. The dimer was melted by preheating up to the desired temperature and polymerization was started. After the desired polymerization period, the ampule bottle was transferred to a refrigerator to terminate the reaction. For purification, the product was dissolved in chloroform and precipitated in a solution of acetone/heptane (1/2, v/v). To synthesize PDLLAs with different molecular weights, the polymerization time and temperature and the molar ratio of the dimer to the initiator ( $D/I$ ) were changed in the range of 40–360 min, 160–200°C, and 1000–25,000, respectively.<sup>9</sup>

## Determination of Average Molecular Weights

The number-average molecular weights of the PDLLAs with low molecular weights were obtained by end-group analysis. PDLLA solutions in benzyl alcohol containing an indicator (i.e., phenolphthalein) were titrated with 0.03N potassium hydroxide (KOH) (in benzyl alcohol). The number-average molecular weights ( $MW_n$ ) of PDLLAs were calculated from the following equation<sup>9,10</sup>:

$$MW_n = \frac{1000 w}{0.03 f(V - V_0)}$$

where  $w$  is the weight of the polymer (g);  $f$ , the titer of KOH solution, and  $V$  and  $V_0$ , the volumes (mL) of the KOH solutions consumed for the polymer and the blank solutions, respectively.

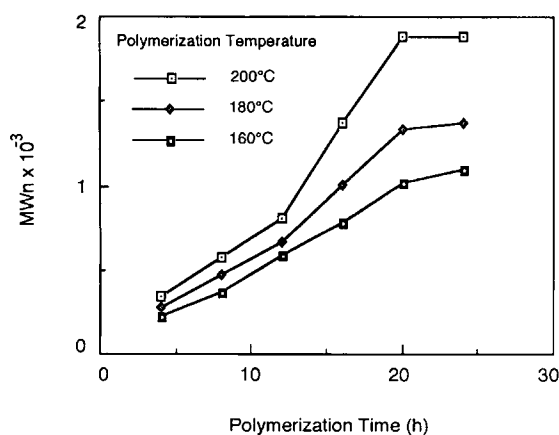
Viscosity measurements were used to obtain average molecular weights of the PDLLAs with high molecular weights. Viscosities of the PDLLA solutions with different concentrations (0.1–2.0 g/100 mL) were measured with a capillary viscosimeter (i.e., Ubbelohde viscosimeter) at  $25.0 \pm 0.1^\circ\text{C}$ . Ethyl acetate was used as the solvent. The Mark-Houwink equations given below were used to calculate the number ( $MW_n$ ) and weight ( $MW_w$ ) average molecular weights from the intrinsic viscosities, i.e.,  $[\eta]$ , evaluated from the experimental data<sup>9,11,12</sup>:

$$[\eta] = 1.58 e^{-4} \cdot MW_n^{0.78} \quad [\eta] = 1.63 e^{-4} \cdot MW_w^{0.73}$$

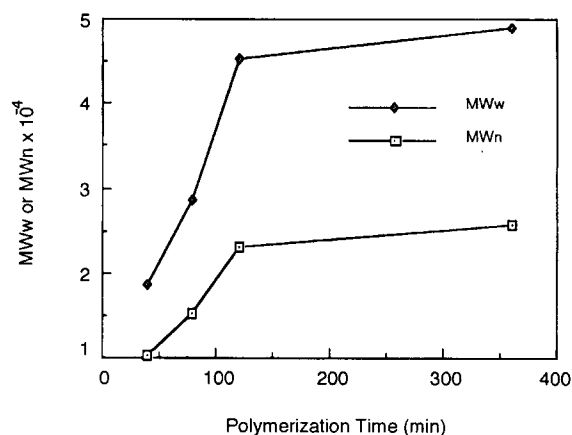
## RESULTS AND DISCUSSION

### Low Molecular Weight PDLLAs

Figure 1 gives the number-average molecular weights ( $MW_n$ ) of the PDLLAs obtained by the end-group analysis, which were synthesized at different polymerization temperatures and with different polymerization times. As seen here, the  $MW_n$  of the PDLLA increased significantly with the polymerization time, almost linearly up to about 20 h; little or no benefit was gained by further extension of the polymerization time. This is a general behavior in all condensation polymerizations.<sup>13</sup> Theoretically, polycondensation reactions are equilibrium reactions. These reactions usually take place by the elimination of a low molecular weight component, which is water in our case. An equilibrium is achieved depending on the degree of dehydration. Higher molecular weights require higher de-



**Figure 1** Effects of polymerization time and temperature on  $MW_n$  of PDLLAs (obtained by end-group analysis).

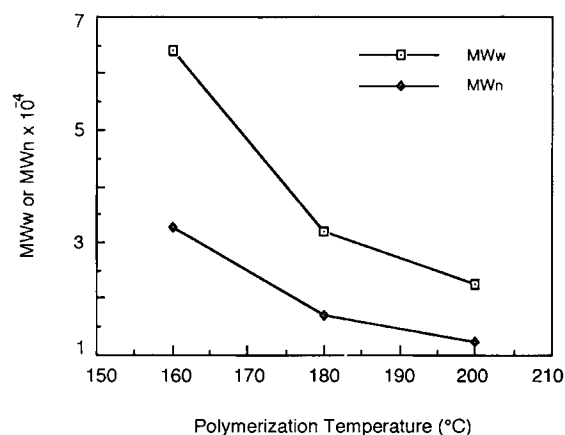


**Figure 2** Effects of polymerization time on average molecular weights of PDLLAs (polymerization temperature and  $D/I$  ratio,  $160^\circ\text{C}$  and 1000, respectively).

grees of dehydration. It is difficult to remove water in the bulk (melt) polymerization, which results in lower molecular weights, as also observed in our case.

The  $MW_n$  of the PDLLA increased also with temperature. PDLLAs with different molecular weights in the range of 500–2300 were synthesized by changing the polymerization temperature. Note that in this direct polycondensation procedure it was not possible to utilize temperatures higher than  $200^\circ\text{C}$  because a severe oxidation occurred, which was observed by the formation of the dark brown color. The condensation equilibrium constant usually increases with temperature; therefore, one might expect to achieve higher molecular weights at higher temperatures, as observed here.

It should be noted that the yields of homopolymers, which were defined as “(the amount of monomer/the amount of polymer)  $\times 100$ ,” obtained by direct polymerization of D,L-lactic acid were around 96–98% in all cases described above.



**Figure 3** Effect of polymerization temperature on average molecular weights of PDLLAs (polymerization time and  $D/I$  ratio, 360 min and 10,000, respectively).

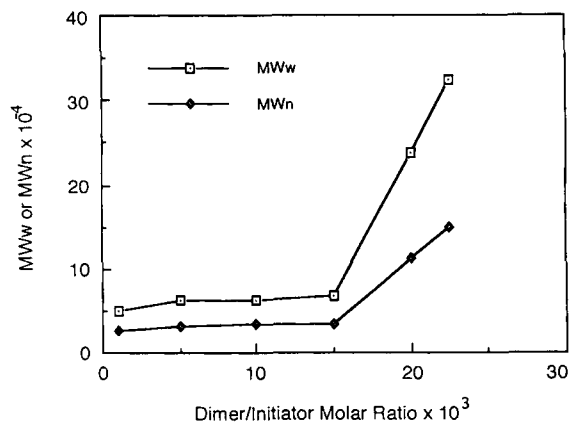
## High Molecular Weight PDLAs

Figures 2–4 show the number- and weight-average molecular weights of the PDLAs obtained by viscosimetric measurements, which were synthesized with different polymerization times, at different temperatures, and by changing the initial molar ratio of the dimer and the initiator ( $D/I$ ), respectively.

The average molecular weights increased with increase in the polymerization time almost linearly up to certain values. Then, plateau values were reached in 120 min. Note that the yields of homopolymers produced with different polymerization times, namely, 40, 80, 120, and 360 min, were 45, 78, 94, and 96%, respectively. Here, the yield was defined as “(the amount of dimer/the amount of polymer after purification)  $\times$  100.” This may be considered as an indication that polymerization reactions were completed in around 2 h. Note also that the heterogeneity indices (the ratio of  $MW_w$  to  $MW_n$ ) increased with time (which means that the molecular weight distribution became wider). These effects may be due to transesterification between the homopolymer molecules which may occur for longer polymerization times.<sup>14</sup>

The average molecular weights decreased very significantly with temperature (Fig. 3). Higher heterogeneity indices (which means wider molecular weight distributions) were obtained at low temperatures. This effect is different from what we observed in the direct polymerization of D,L-lactic acid. Here, polymerization is a catalytic reaction. Therefore, as expected, at high temperatures, more initiator molecules can be activated, which means that the polymerization reactions are initiated from more points, which, in turn, leads to polymer chains with lower molecular weights. Note that the yields of homopolymers produced by ring-opening reactions in the temperature range studied here were above 95%.

Effects of the  $D/I$  ratio on the average molecular weights up to about a value of 15,000 were insignificant (Fig. 4). However, above this value, there were steep increases in the average molecular weights and also in the heterogeneity indices. It seems that the change in the concentration of the initiator did not affect the polymerization kinetics



**Figure 4** Effect of  $D/I$  molar ratio on average molecular weights of PDLAs (polymerization time and temperature, 360 min and 160°C, respectively).

at constant temperature at higher initiator concentrations (i.e., lower  $D/I$  ratios). However, as proposed in the related literature, at low initiator concentrations ( $D/I > 15,000$ ), some unknown reactions may occur.<sup>15</sup> These side reactions may terminate some of the growing polymer chains. This gives a chance for the other chains to become longer. This means that the average molecular weights may increase and, at the same time, molecular weight distribution becomes wider. Note that the yields of homopolymers produced by ring-opening reactions in the temperature range studied here were above 95%.

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