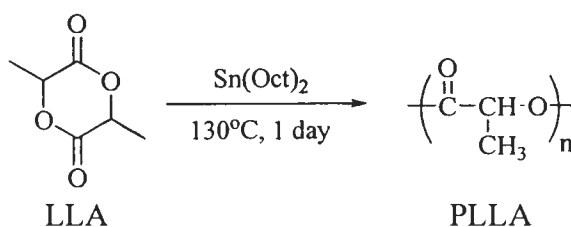


CHAPTER IV

RESULTS AND DISCUSSION

4.1 Homopolymerization

4.1.1 Polymerization of LLA



Scheme 4.1 Polymerization of LLA

Homopolymerization of either LLA was carried out in order to verify the reaction condition reported earlier by Sunsaneeyametha [20]. The ring-opening polymerization of LLA was carried out at 130°C for 1 day. The amounts of Sn(Oct)₂ of 0.3 and 0.5 mol % of LLA were used. PLLA yields were above 85% (Table 4.1) of a white powder.

Table 4.1 \overline{M}_n and yield of PLLA

Entry	% Sn(Oct) ₂	\overline{M}_n ¹ (Da)	PDI	% Yield
1	0.3	14,500	1.40	88
2	0.5	3,600	1.93	86

¹The molecular weight was obtained by GPC.

A typical ¹H NMR spectrum of L-lactide monomer in CDCl₃ is shown in Fig. 4.1. The signals at 5.07 and 1.71 ppm belong to -CH-, and -CH₃, respectively. For PLLA (Fig. 4.2) in CDCl₃, the signals of -CH- and -CH₃ shifted slightly to 5.16, and 1.57 ppm, respectively.

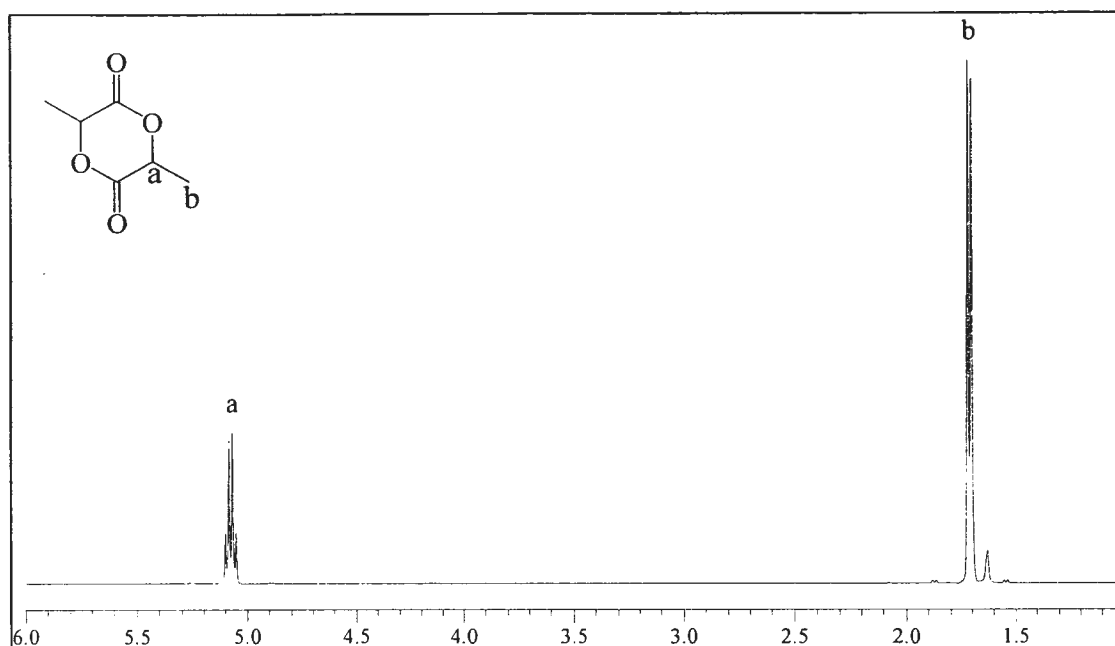


Figure 4.1 ^1H NMR spectrum of LLA

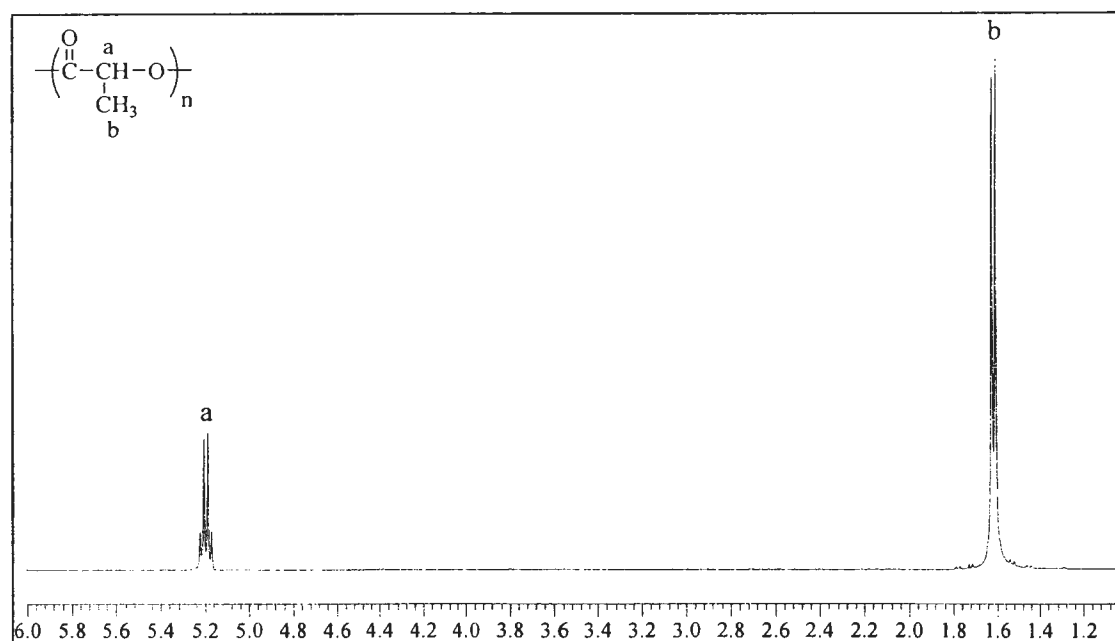


Figure 4.2 ^1H NMR spectrum of PLLA

The molecular weight of PLLA was determined by GPC (Fig. 4.3). The molecular weight of PLLA exhibited multimodal distribution, indicating uncontrollable polymerization of LLA. It was possible that polymerization of PLLA

was not living, also resulting in the molecular weight that was lower than it should be. It was first suspected that the monomer, L-lactide, was somewhat impure due to the formation of lactic acid. Recrystallization of the monomer in ethyl acetate was therefore carried out following the methods reported by other researchers [19]. Nevertheless the GPC chromatogram of the polymer from recrystallized L-lactide remained unchanged. From the results, it was found that the $\text{Sn}(\text{Oct})_2$ amount affected the molecular weight. Higher initiator content led to polymer with lower molecular weight.

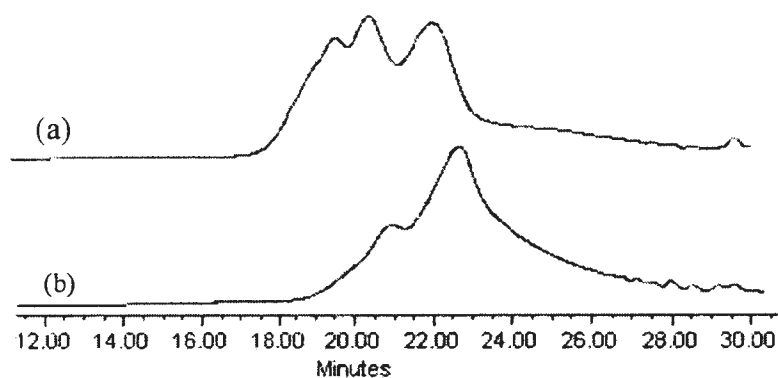
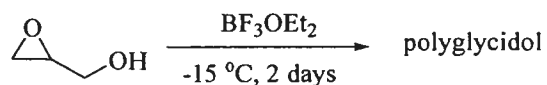


Figure 4.3 GPC chromatograms of PLLA using $\text{Sn}(\text{Oct})_2$ 0.3 (a) and 0.5 (b) mol% of LLA

4.1.2 Polymerization of Glycidol



Scheme 4.2 Polymerization of glycidol

Polyglycidol was synthesized in order to be used as macro-initiator for the preparation of PLLA-*b*-PG. The obtained PG was pale yellow and highly viscous

liquid with the yield of above 80%. A typical ^1H NMR spectrum of glycidol (G) monomer in D_2O is shown in Fig. 4.4: 3.78 ppm ($\text{HOCH}\underline{\text{H}}\text{H}'$), 3.66 ($-\text{OH}$), 3.42 ($\text{HOCH}\underline{\text{H}}\text{H}'$), 3.04 (m, CH), 2.70 ($\text{CHCH}\underline{\text{H}}\text{H}'$), and 2.60 ($\text{CHCH}\underline{\text{H}}\text{H}'$).

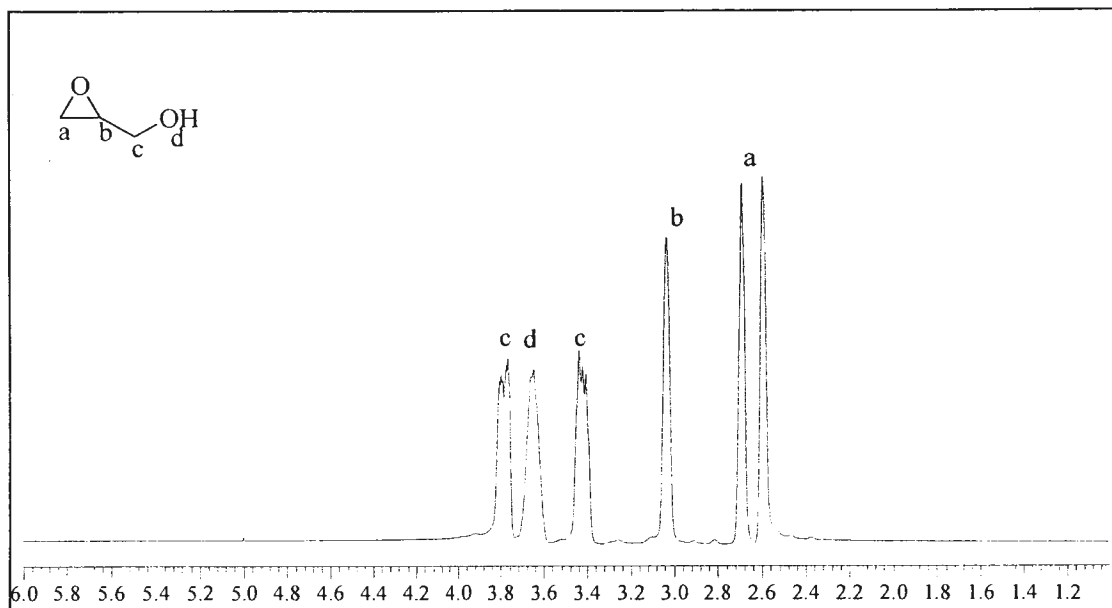


Figure 4.4 ^1H NMR spectrum of glycidol monomer

After polymerization, the methine proton signal at 3.04 ppm and methylene protons at 2.70 and 2.60 ppm of the epoxide ring disappeared. The signals for those protons shifted to the region between 3.3-3.9 ppm together with all other protons (Fig. 4.5).

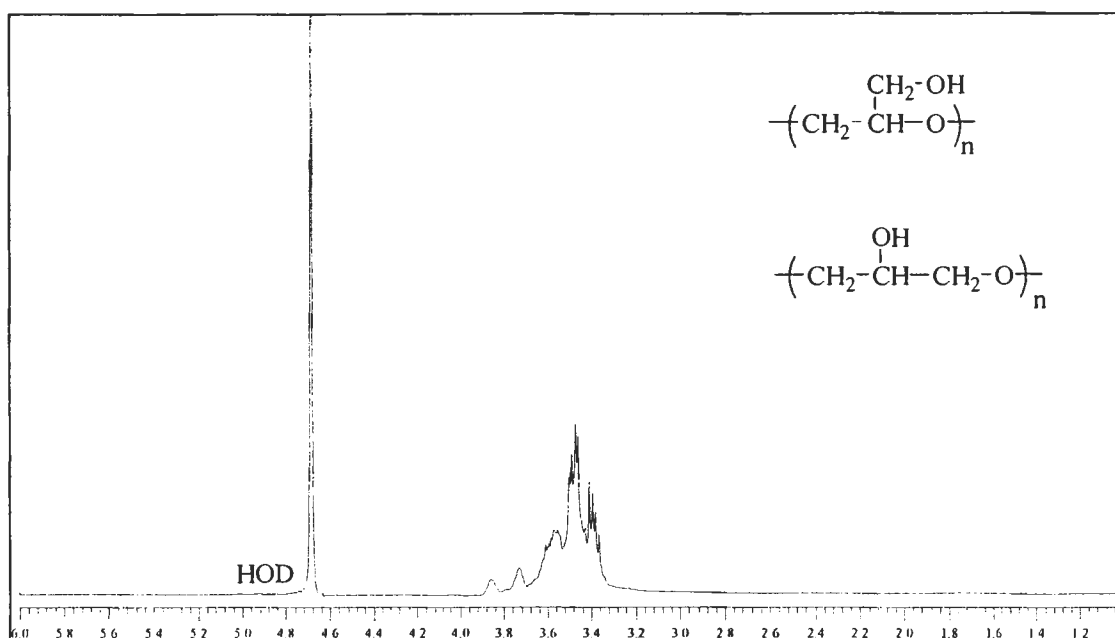


Figure 4.5 ^1H NMR spectrum of PG

In order to fully characterize the structure of PG, ^{13}C NMR and DEPT analysis were performed (Fig. 4.6 and 4.7). Signal assignments for ^{13}C NMR spectrum of PG were first reported by Dworak [24] and Frey [22]. Dworak *et al.* used a number of model compounds in order to assign most of the signals for the linear and terminal units. Invert gated (IG) NMR was used for a reliable signal assignment by Frey *et al.* The ^{13}C NMR spectrum of PG possesses seven well-resolved peak regions between 60 and 82 ppm. The DEPT spectrum can be employed to distinguish CH and CH_2 groups. All signals correspond to the value reported previously [22,24] as follows- (i) linear 1,3-unit ($\text{L}_{1,3}$): $\underline{\text{C}}\text{H}_2\text{OH}$ at 60.6, $\underline{\text{C}}\text{H}_2$ at 68.9, and $\underline{\text{C}}\text{H}$ at 79.2; (ii) linear 1,4-unit ($\text{L}_{1,4}$): both $\underline{\text{C}}\text{H}$ at 72.0, $\underline{\text{C}}\text{HOH}$ at 68.7; (iii) terminal unit (T): $\underline{\text{C}}\text{H}_2\text{OH}$ at 62.5, $\underline{\text{C}}\text{HOH}$ at 70.3, and the $\underline{\text{C}}\text{H}_2$ at about 70.4; (iv) dendritic unit: $\underline{\text{C}}\text{H}$ at 78.1, one $\underline{\text{C}}\text{H}_2$ 70.8, and the other at about 70.4 ppm overlapping with a $\underline{\text{C}}\text{H}_2$ of a terminal unit.

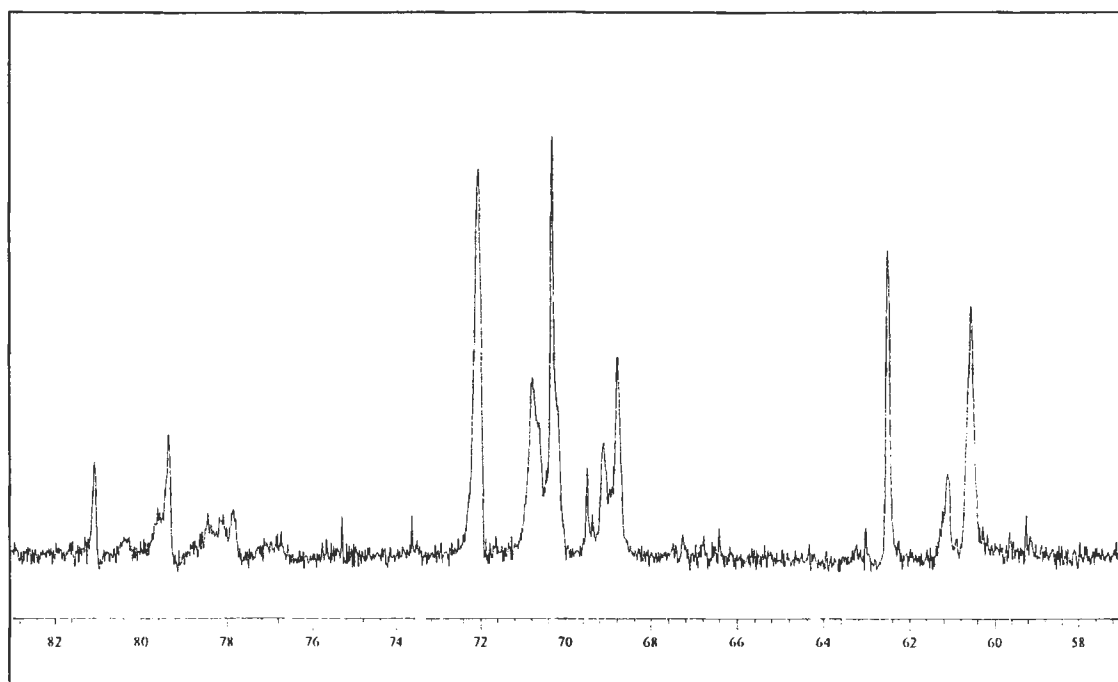


Figure 4.6 ^{13}C NMR spectrum of PG.

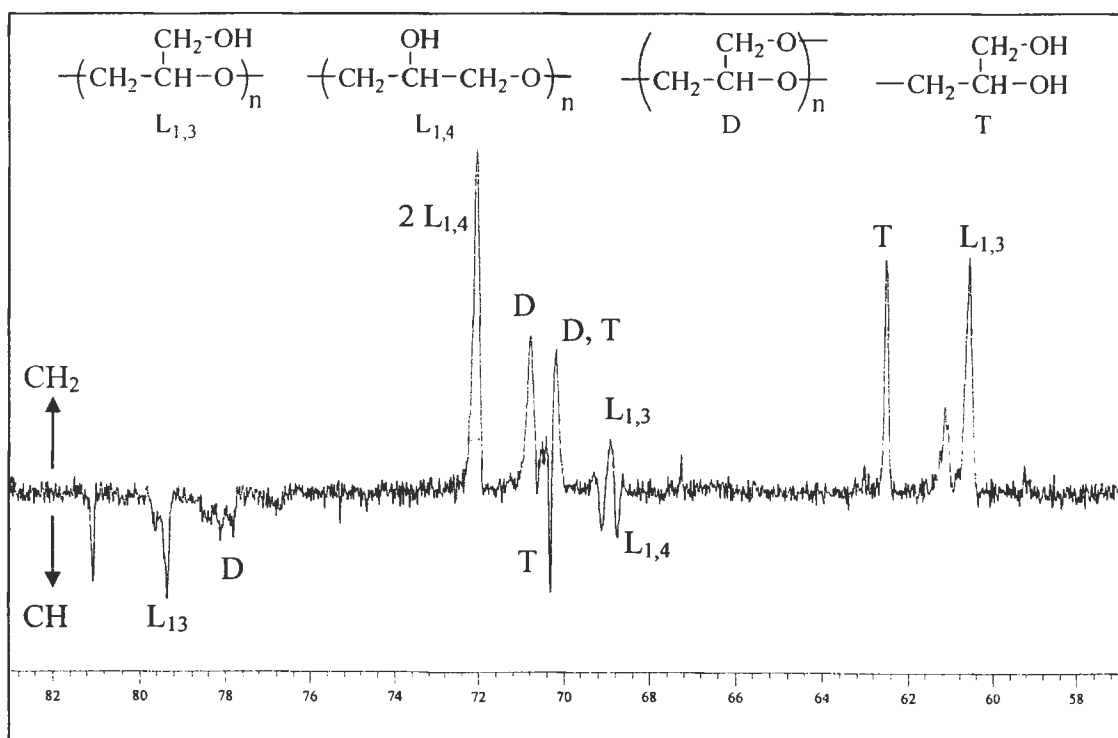


Figure 4.7 DEPT ^{13}C -NMR spectrum of PG.

It was therefore proven that the structure of PG was branched (Fig. 4.8), occurring by two pathways; active chain end and activated monomer mechanism, explained earlier in Chapter II.

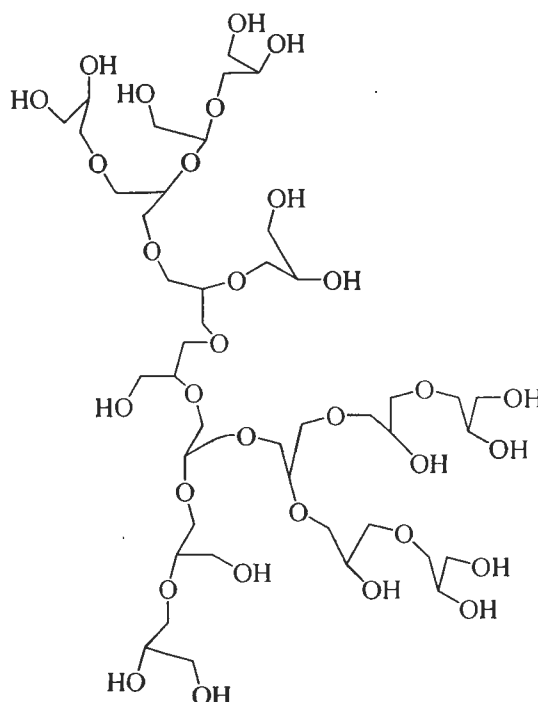


Figure 4.8 A possible structure of hyperbranched polyglycidol

The molecular weight of PG could not be obtained by using GPC because the polymer did not dissolve in THF, a mobile phase used in the GPC. The molecular weight of PG was instead obtained from MALDI-TOF-MS. The mass spectrum of PG is shown in Fig. 4.9. This spectrum appears as groups of doublet peaks, appearing at mass numbers of m and $m+16$. The mass difference between peaks in each series is 74, which indicates the difference of one repeat unit in PG. In one series, each peak corresponds to a polymer species that has x number of G units (MW = 74.08) plus the mass of the end groups (H, OH MW = 18.02) and a potassium (K) ion (MW = 39.10). The other peak series can be assigned to the polymer species with sodium (Na) ion (MW = 22.99) instead of K^+ . The number of G units can be uniquely determined as follows.

$$\begin{aligned}
 x(74.08) + 18.02 + 39.10 &= 860.01; & x = 11 \\
 &1007.10; & x = 13 \\
 &1153.66; & x = 15, \text{ etc.} \\
 x(74.08) + 18.02 + 22.99 &= 842.80; & x = 11 \\
 &989.93; & x = 13 \\
 &1136.83; & x = 15, \text{ etc.}
 \end{aligned}$$

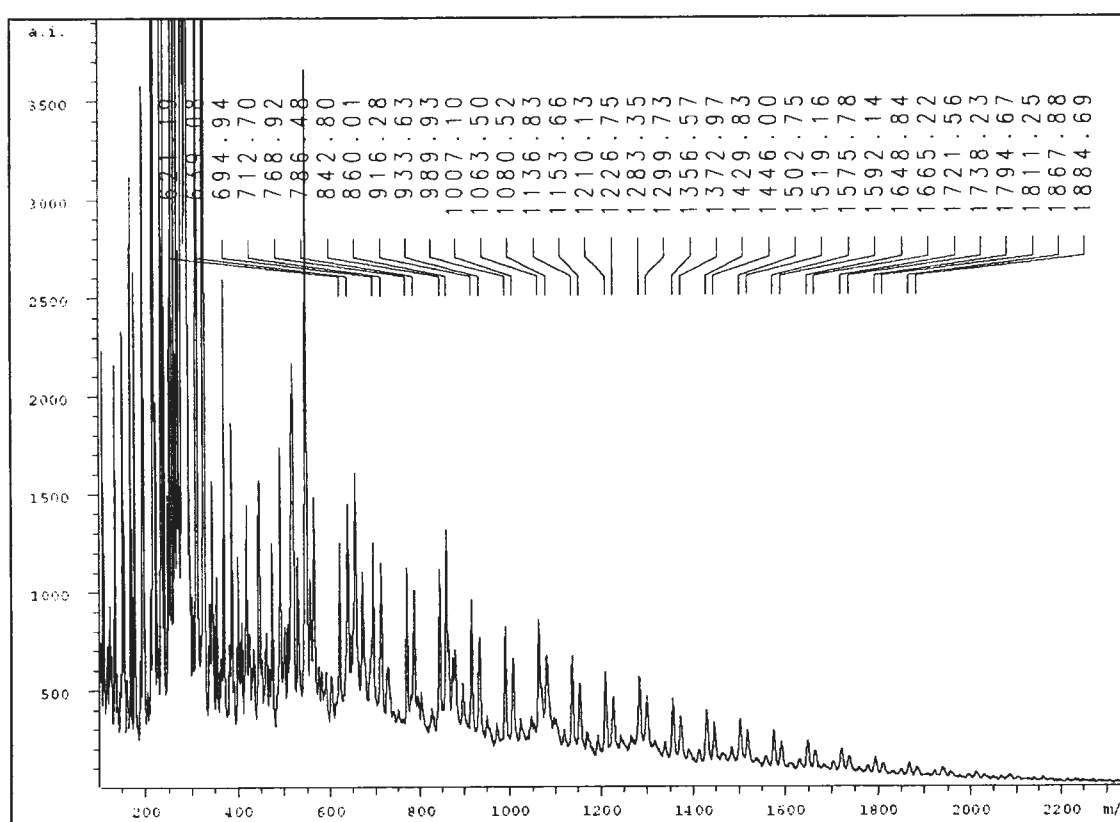


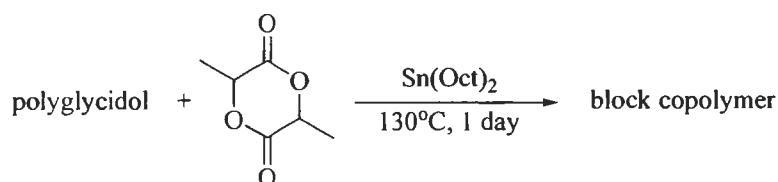
Figure 4.9 MALDI-TOF-MS spectrum of PG.

The number-average molecular weight (\overline{M}_n) of PG calculated from the MS was 1,100 Da, close to the value of 1,300 that obtained earlier by Sunsaneeyametha [20]. The average number of repeat unit was 15. The average amount of hydroxyl groups in the synthesized PG was 17 (including two hydroxyl end groups). A general equation for calculating of the $-OH$ groups in PG is shown in Eq. 4.1.

$$\text{OH content} = \frac{W}{\overline{M}_n} \times \left(\frac{\overline{M}_n}{74.08} + 2 \right) \quad (\text{Eq. 4.1})$$

where W : weight of PG (g)
 \overline{M}_n : molecular weight of PG was calculated by MALDI-TOF-MS
 74.08 : molecular weight of the repeating unit of PG ($\text{C}_3\text{H}_6\text{O}_2$)
 2 : number of hydroxyl group at the PG chain ends

4.2 Block Copolymerization of Poly(L-lactide-*block*-glycidol)



Scheme 4.3 Copolymerization of LLA and PG using $\text{Sn}(\text{Oct})_2$ as an initiator.

To synthesize the block copolymer, PG was used as a macroinitiator for the polymerization of LLA. Polymerization was carried out in bulk at 130°C , using 5 mol% of $\text{Sn}(\text{Oct})_2$ [compared to the total content of hydroxyl group in PG (calculated from (Eq. 4.1))] as a catalyst. Since no solvent was used in the polymerization heating the reaction mixture at 130°C was necessary in order to melt and activate the ring-opening polymerization (ROP) of the LLA monomer. The mole ratio between LLA monomer and hydroxyl groups of PG (LLA:G) was 10:1.

At the feed ratio for LLA:G of 10:1, two types of white solid product having different solubilities in MeOH were obtained. The yields of the MeOH-soluble and insoluble residues were 25 and 66 %, respectively (Table 4.2).

Table 4.2 Molecular weight and yield of PLLA-*b*-PG

Temperature	:	130 °C
Time	:	1 day
Sn(Oct) ₂	:	5 mol% of the total content of hydroxyl group in PG
LLA:G	:	10:1

Entry	Solubility in MeOH	\overline{M}_n^1 (Da)	PDI	% Yield
1	soluble	2,100	1.98	25
2	insoluble	13,700	1.83	66

¹The molecular weight was obtained by GPC.

GPC chromatograms of MeOH-soluble and MeOH-insoluble products are shown in Fig. 4.10. The MeOH-soluble residue has unimodal distribution, but the MeOH-insoluble residue exhibits multimodal distribution, indicating different polymerized species were formed.

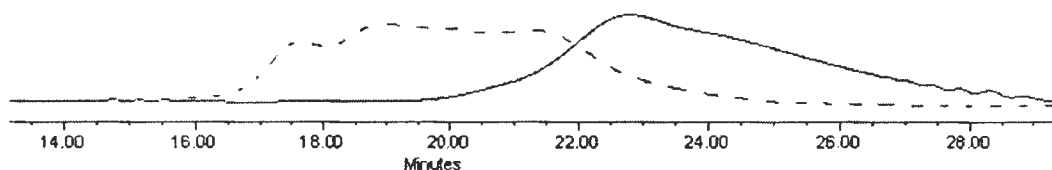


Figure 4.10 Chromatograms from GPC analysis of MeOH-soluble (—) and MeOH-insoluble (--) PLLA-*b*-PG.

The ¹H NMR spectrum of PLLA-*b*-PG from MeOH-soluble and insoluble residues in CDCl₃ were shown in Fig 4.11 (a) and (b): 5.21 ppm (-CH₂CH₃ of PLLA), 5.16 (-CHO(COCH(CH₃)O)_n-), 4.39 (-COCH₂(CH₃)OH of PLLA), 4.24 (-CH₂O(COCH(CH₃)O)_n-), 4.00-3.40 (-(CH₂CH(CH₂OH)O)_n- and (-(CH₂CHOHCH₂O)_n-) of PG), 1.58 (-CHCH₃ of PLLA), 1.49 (-COCH₂(CH₃)OH of PLLA.

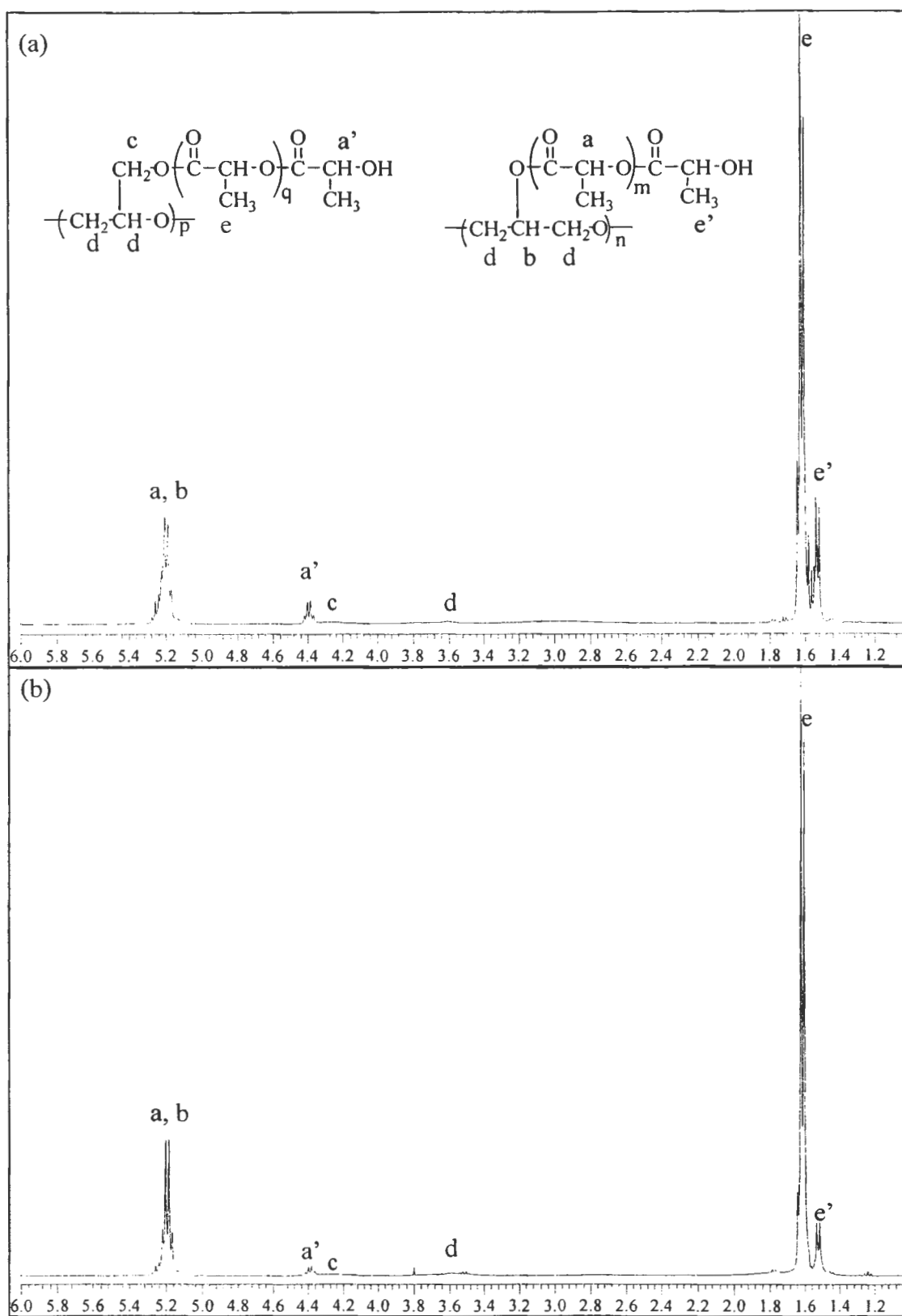


Figure 4.11 ^1H NMR spectrum of PLLA-*b*-PG from MeOH-soluble (a) and insoluble products (b)

Since the copolymer synthesized here is a block copolymer, major structures of each block and also their ^1H NMR signals should remain unchanged from each homopolymer (Fig. 4.11). New signals in fact were observed at 4.24 ppm, and a small shoulder at 5.16 ppm. Additional data from COSY experiment (Fig. 4.12) revealed that both signals coupled with the proton signals at the ether segment of PG. These protons were therefore the $-\underline{\text{CH}}-$ and $-\underline{\text{CH}}_2-$ of PG unit that linked to the LLA by ester bonds. These two signals are major evidences for the ester linkage between PG block and LLA. This finding is in agreement with the work reported by Sunsaneeyametha [20].

COSY-NMR of copolymer; 5.21 coupling with 1.58 ($-\underline{\text{CH}}\text{CH}_3$ of PLLA coupling with $-\underline{\text{CH}}\underline{\text{CH}}_3$ of PLLA), 5.16 coupling with 3.73 ($-\underline{\text{CH}}\text{O}(\text{COCH}(\text{CH}_3)\text{O})_n-$ coupling with $-\underline{\text{CH}}$ or $-\underline{\text{CH}}_2$ of PG unit), 4.39 coupling with 1.49 ($-\underline{\text{CH}}(\text{CH}_3)$ and $-\text{CH}\underline{\text{CH}}_3$ of LLA terminal unit), and 4.39 coupling with 3.73 ($-\underline{\text{CH}}_2\text{O}(\text{COCHCH}_3)_n-$ of PG coupling with $-\underline{\text{CH}}$ or $-\underline{\text{CH}}_2$ of PG unit).

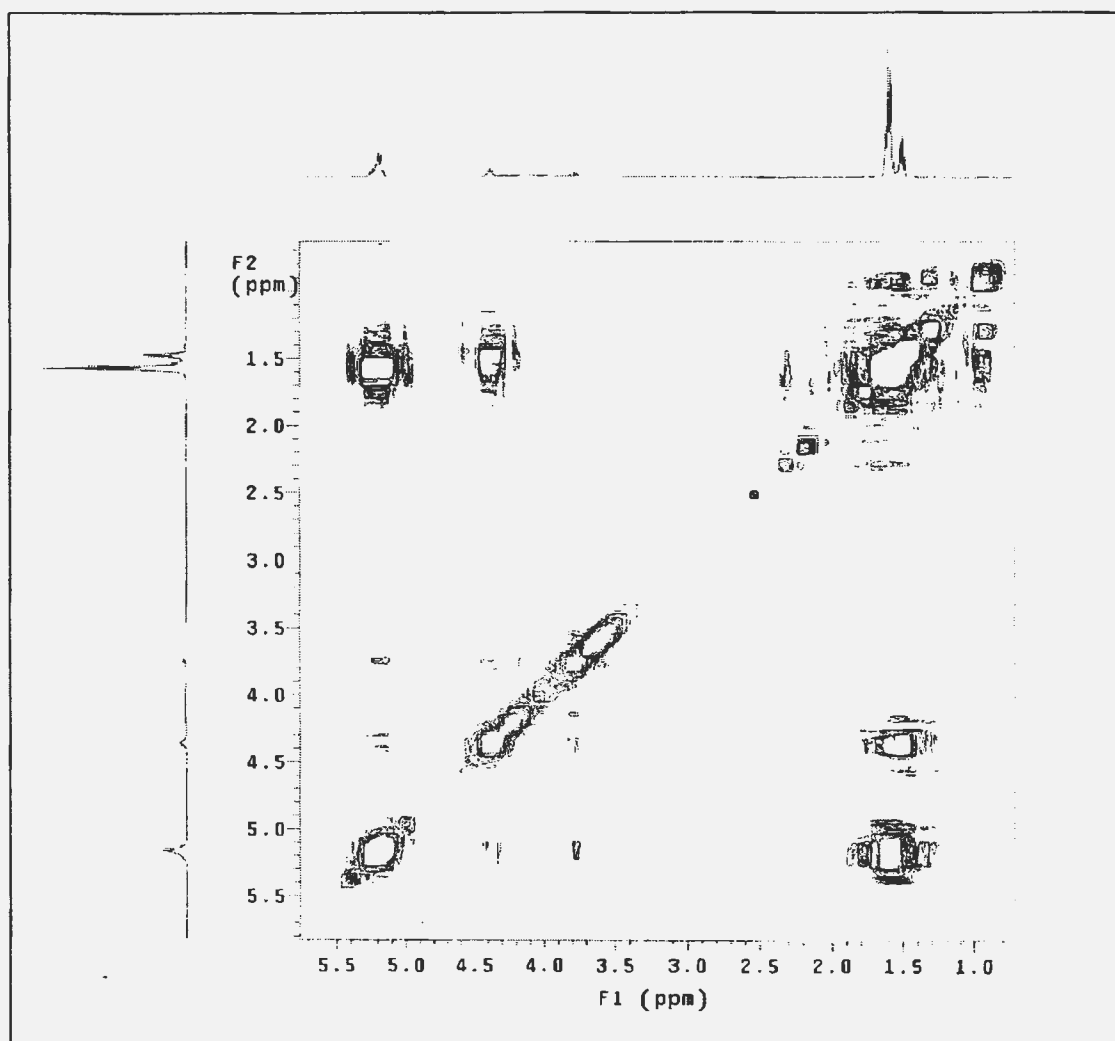


Figure 4.12 COSY-NMR spectrum of PLLA-*b*-PG.

The average PLLA chain length in the block copolymer was determined from ^1H NMR by correlating the peak area of the methyl protons of all LLA units (1.60 ppm) and the terminal methine protons (4.40 ppm) as shown in Eq. 4.2.

$$\text{average PLLA chain length} = \frac{I_{1.60} / 3_{\text{H}}}{I_{4.40 \text{ ppm}}} \quad (\text{Eq. 4.2})$$

where $I_{x \text{ ppm}}$ represents signal intensity at x ppm.

The total LLA content relative to G units in the block copolymer was also determined by ^1H NMR. The peak at 1.50-1.70 ppm corresponds to the methyl group of PLLA. Signals from 3.40-5.40 ppm belong to all protons associated with both PG and PLLA segment. In order to tally the peak area of PG segment, the peak areas belonging to PLLA at 1.60 ppm must be subtracted from the total peak areas from 3.40-5.40 ppm. Thus LLA:G was calculated using Eq. 4.3.

$$\text{LLA:G} = \frac{I_{1.50-1.70} / 3_{\text{H}}}{\frac{1}{5} [I_{3.40-5.40} - (I_{1.60 \text{ ppm}} / 3_{\text{H}})]} \quad (\text{Eq. 4.3})$$

where $I_{x \text{ ppm}}$ represents signal intensity at x ppm. 1.50-1.70

As mentioned earlier, at the feed ratio for LLA:G of 10:1, two types of products having different solubilities in methanol were obtained. The calculated LLA:G ratio and the average PLLA chain length obtained from NMR are shown in Table 4.3.

Table 4.3 LLA:G and the average PLLA chain length of PLLA-*b*-PG

Temperature: 130 °C

Time: 1 day

Sn(Oct)₂: 5 mol% of the total content of hydroxyl group in PG

LLA:G: 10:1

Entry	Solubility in MeOH	LLA:G ¹	Average PLLA chain length (units) ¹	\bar{M}_n (Da)	PDI	% Yield
1	soluble	22:1	9	2,100	1.98	25
2	insoluble	20:1	17	13,700	1.83	66

¹determined from ^1H NMR

²molecular weight was obtained by GPC

Calculation of LLA:G ratios from the obtained products revealed that PG contents found in those copolymers were less than the amount fed into the polymerization reaction. This suggested that there was some unreacted PG that was lost from the product during material transfer.

The average PLLA chain length or repeat units were 9 and 17 (entry 1 and 2), indicates that 9 and 17 units of L-lactic acid are connected to one hydroxyl group of the PG. One lactide monomer gives two lactic acid units. At the feed ratio for LLA:G of 10:1, theoretical PLLA chain length should be 20 units for each hydroxyl groups of PG. The MeOH-soluble portion has the average PLLA chain length much lower than the feed ratio, meanwhile the MeOH-insoluble product has the average PLLA chain length rather close to the feed amount.

The average molecular weight of PLLA chain can be calculated from the average PLLA chain length. The MeOH-soluble portion has 9 units of L-lactic acid, meaning that the average molecular weight of PLLA chain was about 650 Da (MW of lactic acid unit = 72.07). The average molecular weight of the MeOH-soluble portion was 12,200 (\overline{M}_n of PG = 1,100). In case of MeOH-insoluble portion, the average molecular weight of PLLA chain was 1,230 Da from L-lactic acid 17 units and the average molecular weight of copolymer was about 22,000 Da. The average molecular weight of copolymer calculated from ^1H NMR was lower than that obtained from GPC. It was possible that not only one hydroxyl group of PG connected to PLLA chain but also some hydroxyl groups of PG were used to initiate PLLA chain. Another possible explanation was the present of PLLA homopolymer in the copolymer.

Since the structure of PG is branched, it is expected that the structure of this PLLA-*b*-PG copolymer may be in the form of 'core-shell' structure; the inner branched PG core and the outer PLLA shell (Fig. 4.13).

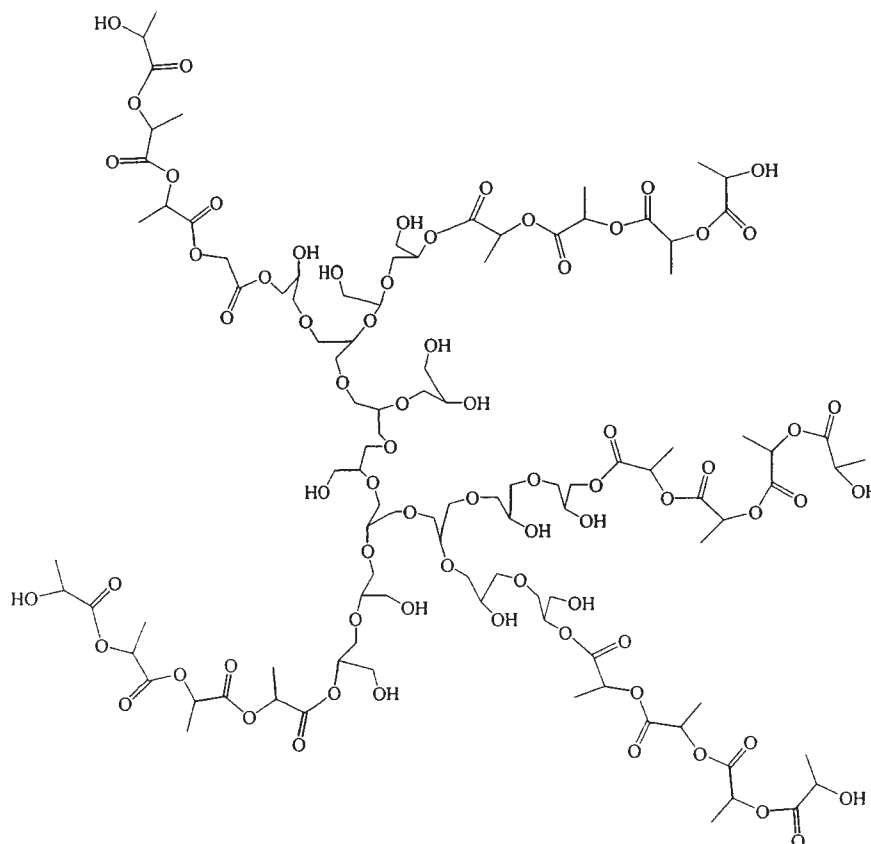


Figure 4.13 A possible structure of PLLA-*b*-PG.

4.2.1 Optimization of polymerization condition

- Drying of PG macroinitiator

For a typical block copolymer of PLLA and PG, the obtained product can be divided into 2 portions; MeOH-soluble and insoluble residues. The low MW (MeOH-soluble) residue has unimodal distribution from the GPC analysis (Fig. 4.10), but the high MW (MeOH-insoluble portion) exhibits multimodal distribution, indicating different polymerized species were formed. It was possible that water trace might initiate the formation of PLLA homopolymer. To overcome the problem, an additional drying step of the PG macroinitiator was introduced in order to completely remove any water.

Azeotropic distillation under low pressure was performed by using choices of drying agents, i.e. diethyl ether, toluene, and *n*-butanol. PG was stirred at room temperature with the mentioned agent as an azeotropic solvent. The drying agent was then removed by evaporation under heat and low vacuum using rotary evaporation apparatus. The effect of azeotropic distillation of PG before polymerization on the resulting copolymer is shown in Table 4.4. The GPC chromatograms of the copolymers are also shown in Fig. 4.14.

It was found that toluene and *n*-butanol, with high boiling point of 110.8 and 117.8°C, could not be completely removed from the viscous PG liquid, as observed in NMR analysis. The hydroxyl group rich environment of PG caused a difficulty in total removal of the *n*-butanol. Trace amount of *n*-butanol also initiated the ring-opening polymerization of LLA leading to the formation of undesired homo PLLA that was confirmed by ¹H NMR. Peaks of *n*-butyl group, -CH₃ at 0.91 and -CH₂- at 1.20 ppm were also found. Uses of *n*-butanol also led to an increase of low molecular weight portion and a decrease of high molecular weight block copolymer as depicted in Fig. 4.14(b). This corresponded to the lowest \overline{M}_n listed in Table 4.4. In case of toluene and diethyl ether (Fig. 4.14(c) and (d)), the peaks representing low molecular weight species were lower in height than the non-distilled monomer shown in Fig. 4.14(a). Therefore the average molecular weights of both cases were higher than that of the product prepared from non-distilled PG. The average PLLA chain lengths of the copolymer obtained from the pre-drying PG using toluene and diethyl ether were similar to the non-distilled case. In conclusion diethyl ether was the most suitable drying agent. Therefore, PG macroinitiator was dried by azeotropic distillation with diethyl ether before polymerization of L-lactide in the next step.

Table 4.4 Effect of drying agents on the polymerization results of PLLA-*b*-PG.

Temperature	:	130 °C
Time	:	1 day
Sn(Oct) ₂	:	5 mol% of the total content of hydroxyl group in PG
LLA:G	:	10:1

Drying agent	Solubility in MeOH	LLA:G ¹	Average PLLA chain length (units) ¹	\overline{M}_n ² (Da)	PDI	% Yield
-	soluble	22:1	9	2,100	1.98	25
-	insoluble	20:1	17	13,700	1.83	66
<i>n</i> -Butanol	soluble	5:1	8	1,500	1.56	43
<i>n</i> -Butanol	insoluble	19:1	17	7,800	2.16	51
Toluene	soluble	5:1	9	2,200	2.01	47
Toluene	insoluble	14:1	14	18,800	1.75	40
Diethyl ether	soluble	19:1	9	2,500	2.13	26
Diethyl ether	insoluble	15:1	17	16,900	1.75	69

¹determined from ¹H NMR

²molecular weight was obtained by GPC

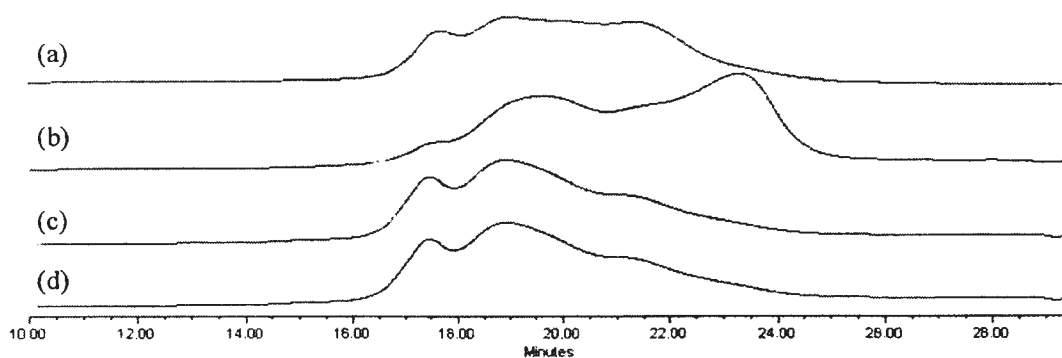


Figure 4.14 GPC chromatograms of PLLA-*b*-PG; without azeotropic distillation (a), with azeotropic distillation using *n*-BuOH (b), toluene (c), and diethyl ether (d).

- Polymerization temperature

Three temperatures (130, 140, and 150°C) were studied for the polymerization of LLA by PG and Sn(Oct)₂. Since there was no solvent used in the reaction, high temperature was required in order to melt the LLA to its liquid state. The amount of Sn(Oct)₂ was set at 5 mol% of the total content of hydroxyl group in PG and the polymerization time was 1 day. Two sets of monomer feed ratios were carried out; 2:1 and 10:1 for LLA:G. Results are presented in Table 4.5.

Table 4.5 Results of polymerization temperature for PLLA-*b*-PG.

Sn(Oct)₂: 5 mol% of the total content of hydroxyl group in PG

Time: 1 day

Entry	Temp (°C)	Solubility in MeOH	LLA:G		Average PLLA chain length (units) ¹	\overline{M}_n^2 (Da)	PDI	% Yield
			Feed	NMR ¹				
1	130	soluble	2:1	2:1	3	2,300	3.35	82
2	140	soluble	2:1	2:1	4	2,500	3.51	75
3	150	soluble	2:1	2:1	4	4,500	2.40	83
4	130	soluble	10:1	19:1	9	2,500	2.13	26
		insoluble		15:1	17	16,900	1.75	69
5	140	soluble	10:1	13:1	7	2,000	1.86	18
		insoluble		36:1	16	14,700	1.79	78
6	150	soluble	10:1	9:1	6	2,300	1.92	17
		insoluble		16:1	15	16,400	1.80	74

¹determined from ¹H NMR

²molecular weight was obtained by GPC

From Table 4.5, the %yield, average PLLA chain length, and molecular weight of each polymer are listed. The total yields of all polymers are above 75%. At the feed ratio of 2:1, the molecular weight tends to increase when increasing the polymerization temperature. The total LLA units in the copolymers are about the same as the feed ratios. It was however found that the average PLLA chain length was 3 to 4, meaning 3 or 4 L-lactic acid units were connected to each hydroxyl group of the PG. The average molecular weight of PLLA chain calculated from the average PLLA chain length was about 290 Da. The average molecular weight of copolymer calculated was about 6,000 Da, lower than the value obtained by GPC. It is possible that the present of PLLA homopolymer in the copolymer or the copolymer has many PLLA chains connected to PG. It could further imply, based on the monomer ratio in the copolymer and the average PLLA chain length, that there are some free hydroxyl groups of the PG remaining in the copolymer structure.

Analysis of the copolymer products by ^1H NMR revealed that the mole ratios of LLA:G in the products were not different from the feed ratio when the feed ratio was 2:1, whereas at the feed ratio of 10:1, the PG contents in the copolymers were less than the feed amount in both MeOH-soluble and insoluble portions. The reason for these results has not been clear. It was found that average PLLA chain lengths slightly increased when decreasing the polymerization temperature.

The GPC chromatograms of PLLA-*b*-PG obtained from low (2:1) and high LLA feed ratio (10:1) are shown in Fig. 4.15 and 4.16, respectively. In case of high LLA feed ratio, two types of products having different solubilities in methanol were obtained. Only the GPC results of methanol-insoluble portion are shown. At low LLA feed ratio (2:1), the intensity of high molecular weight (short retention time) peak was increased when increasing the reaction temperature. The suitable temperature for the polymerization was 130°C because at 150°C, samples appeared darkens, probably due to thermal decomposition.

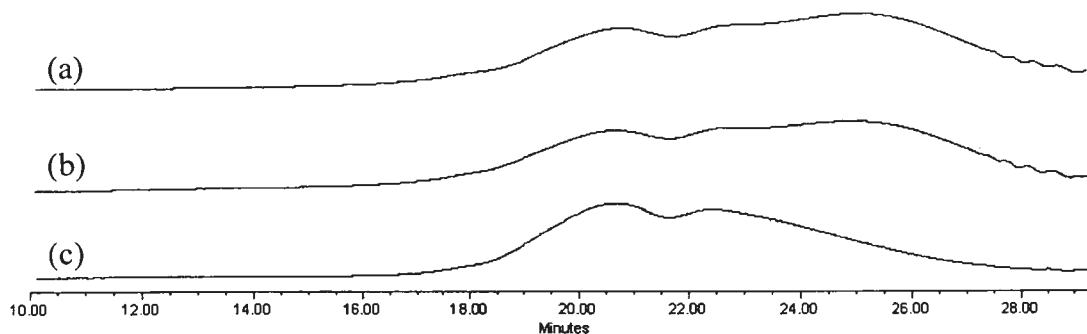


Figure 4.15 GPC chromatograms of PLLA-*b*-PG from the initial LLA:G feed ratio of 2:1 at the polymerization temperature of 130 °C (a), 140 °C (b), and 150 °C (c).

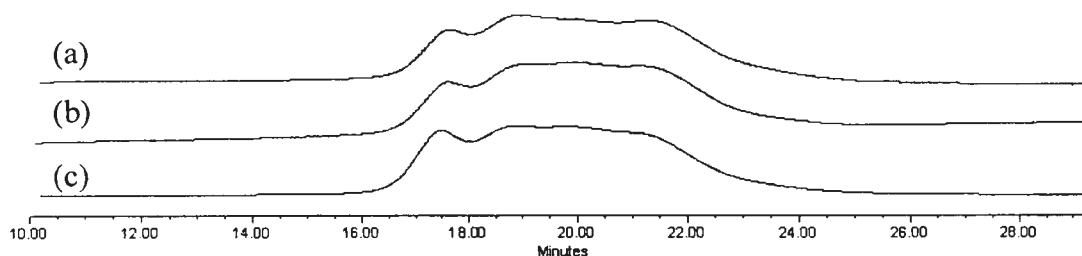


Figure 4.16 GPC chromatograms of MeOH-insoluble PLLA-*b*-PG from the initial LLA:G feed ratio of 10:1 at the polymerization temperature of 130 °C (a), 140 °C (b), and 150 °C (c).

- Polymerization time

The results of polymerization of LLA using PG initiator and Sn(Oct)₂ catalyst with different polymerization times are listed in Table 4.6. It was found that the molecular weight increased and molecular weight distribution decreased with the increasing polymerization time. It should be noted here that when the reaction was allowed to be more than 1 day the reaction products turned slightly yellow.

Table 4.6 Results of varying the polymerization time for PLLA-*b*-PG.Sn(Oct)₂: 5 mol% of the total content of hydroxyl group in PG

Temperature: 130°C

LLA:G: 10:1

Entry	Time (day)	LLA:G ¹	Average PLLA chain length (units) ¹	\overline{M}_n ² (Da)	PDI	% Yield
1	1	19:1 ³	9	2,500	2.13	26
		15:1 ⁴	17	16,900	1.75	69
2	4	24:1 ³	10	4,600	1.84	25
		15:1 ⁴	18	18,800	1.67	58
3	7	21:1 ³	12	4,600	1.96	18
		17:1 ⁴	19	21,000	1.55	70

¹determined from ¹H NMR²molecular weight was obtained by GPC³soluble in methanol⁴insoluble in methanol

Analysis of the copolymer products by ¹H NMR revealed that the mole ratios of LLA:G in the methanol insoluble products were less than the amount of PG fed into the polymerization. In case of MeOH-soluble portion, the average PLLA chain length increased at longer polymerization time but was still lower than the feed amount. The average PLLA chain length of MeOH-insoluble portion was quite similar to the feed amount. The GPC chromatograms of the polymer obtained after different reaction time (Fig. 4.17) are not significantly different from one another.

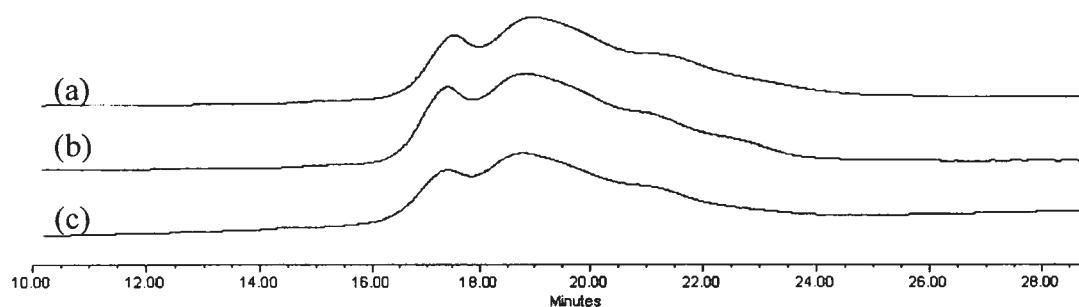


Figure 4.17 GPC chromatograms of MeOH-insoluble PLLA-*b*-PG from the initial LLA:G feed ratio of 10:1. The polymerization was carried out for 1 day (a), 4 days (b), and 7 days (c).

- Amount of Sn(Oct)₂

The amount of Sn(Oct)₂ was varied to 2, 5, 10 % of the total content of hydroxyl group in PG. The \overline{M}_n was highest when Sn(Oct)₂ was set at 5 mol% as listed in Table 4.7. For 2 and 10 mol%, the amount of Sn(Oct)₂ catalyst had no influence on the \overline{M}_n .

Table 4.7 Results of varying the amount of Sn(Oct)₂ for PLLA-*b*-PG.

Temperature : 130 °C
 Time : 1 day
 LLA:G : 5:1

Entry	Sn(Oct) ₂ (mol%) ¹	LLA:G ²	Average PLLA chain length (units) ¹	\overline{M}_n ³ (Da)	PDI	% Yield
1	2	6:1	8	4,800	3.10	90
2	5	6:1	8	9,500	2.02	90
3	10	4:1	7	5,000	3.06	94

¹mol% of the total content of hydroxyl group in PG

²determined from ¹H NMR

³molecular weight was obtained by GPC

The average PLLA chain lengths in all cases did not differ from one another but the values were lower than the feed amount that should be 12 units for each hydroxyl groups of PG. The LLA:G ratios of copolymer were similar to the feed ratio. The average molecular weight of PLLA chain calculated from the average PLLA chain length was about 580 Da and the average molecular weight of copolymer was about 11,000 Da that much lower than obtained by GPC. GPC chromatograms shown in Fig. 4.18 exhibited the same retention time but the intensity of each retention time was varied.

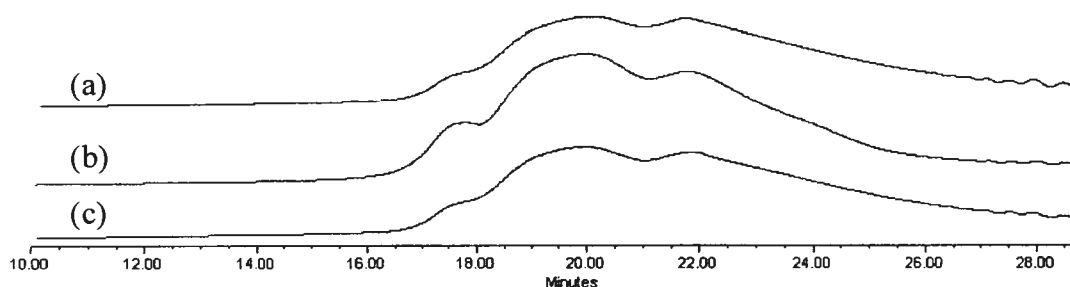


Figure 4.18 GPC chromatograms of PLLA-*b*-PG from the initial LLA:G feed ratio of 5:1. The amount of Sn(Oct)₂ used was 2 % (a), 5 % (b), and 10 % of the total content of hydroxyl group in PG (c).

- Monomer ratio

To investigate the effect of LLA ratio on polymerization, the ROP of LLA was carried out with branched PG macroinitiator and Sn(Oct)₂ catalyst in bulk at 130 °C. The molar ratios of LLA and G were varied as 2:1, 5:1, and 10:1. Results are shown in Table 4.8.

Table 4.8 Results of varying the mole ratio of LLA:G for PLLA-*b*-PG.Sn(Oct)₂: 5 mol% of the total content of hydroxyl group in PG

Temperature: 130 °C

Time: 1 day

Entry	LLA:G		Average PLLA chain length (units) ¹	\overline{M}_n ² (Da)	PDI	% Yield
	Feed	NMR ¹				
1	2:1	2:1	3	2,300	3.35	2
2	5:1	6:1	8	9,500	2.02	90
3	1:10	19:1 ³	9	2,500	2.13	26
		15:1 ⁴	17	16,900	1.75	69

¹determined from ¹H NMR²molecular weight was obtained by GPC³soluble in methanol⁴insoluble in methanol

The molecular weight of block copolymer was measured by GPC. Changing ratios of LLA to G monomer resulted in molecular weight change. When the LLA/G ratios increased, the molecular weight of PLLA-*b*-PG also increased. Analysis of the copolymer products by ¹H NMR revealed that the mole ratios of LLA:G in the products were not different from the feed ratio when the feed ratio was 2:1 and 5:1, whereas at the feed ratio of 10:1, the PG portions in the copolymers were less than the amount of PG fed into the polymerization.

In this study, all polymers were synthesized under rigorously anhydrous conditions in order to avoid an initiation by water, which will lead to PLLA homopolymer. Nevertheless, the GPC traces are multimodal (Fig. 4.19), suggesting there are different macromolecular species present. If the polymerization were to be living in behavior, a unimodal distribution would have been generally obtained.

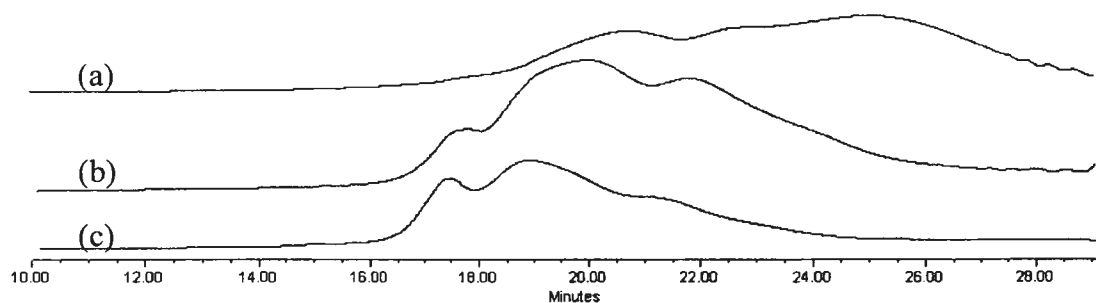


Figure 4.19 GPC chromatograms of PLLA-*b*-PG from the initial LLA:G feed ratio of 2:1 (a), 5:1 (b), and 10:1 (only the MeOH-insoluble portion) (c).

From the result of varying the polymerization temperature, polymerization time, and amount of Sn(Oct)₂, the suitable condition of ROP of LLA with PG macroinitiator was carried out at 130°C for 1 day in bulk, using Sn(Oct)₂ 5 mol% of the total content of hydroxyl group in PG.

4.3 Properties of PLLA-*b*-PG

4.3.1 Thermal properties of PLLA-*b*-PG

Table 4.9 and Fig. 4.20 show the results of glass transition temperature (T_g) and melting temperature (T_m) of branched PG, PLLA, and PLLA-*b*-PG. For the homopolymers, only T_g was present for PG at -51°C while PLLA shows T_g and T_m at 59 and 170°C, respectively. The T_g of block copolymers, increased with molecular weight and was found to be between the T_g 's of PG and PLLA homopolymers. The T_g of each homopolymer (-51 and 59°C) was not found in the copolymer. The low molecular weight (2.1 and 2.5 kDa) copolymers did not exhibit T_m probably because the lengths of LLA block were too short to crystallize. The T_m at 135°C was possibly caused by two events. One was due to the presence of PLLA homopolymer mixed with the copolymer. The other was due to the LLA block that was long enough to crystallize.

Table 4.9 Glass transition temperatures and melting temperature of PLLA-*b*-PG and the homopolymers. The molecular weights are listed in parenthesis.

Polymer	T_g (°C)	T_m (°C)
PG (1.1K)	~ -51	-
PLLA (14.5K)	59	170
PLLA- <i>b</i> -PG ¹ (2.1K)	14	-
PLLA- <i>b</i> -PG ² (2.5K)	27	-
PLLA- <i>b</i> -PG ³ (16.9K)	48	135

¹ LLA:G (2:1)
² LLA:G (19:1)
³ LLA:G (15:1)

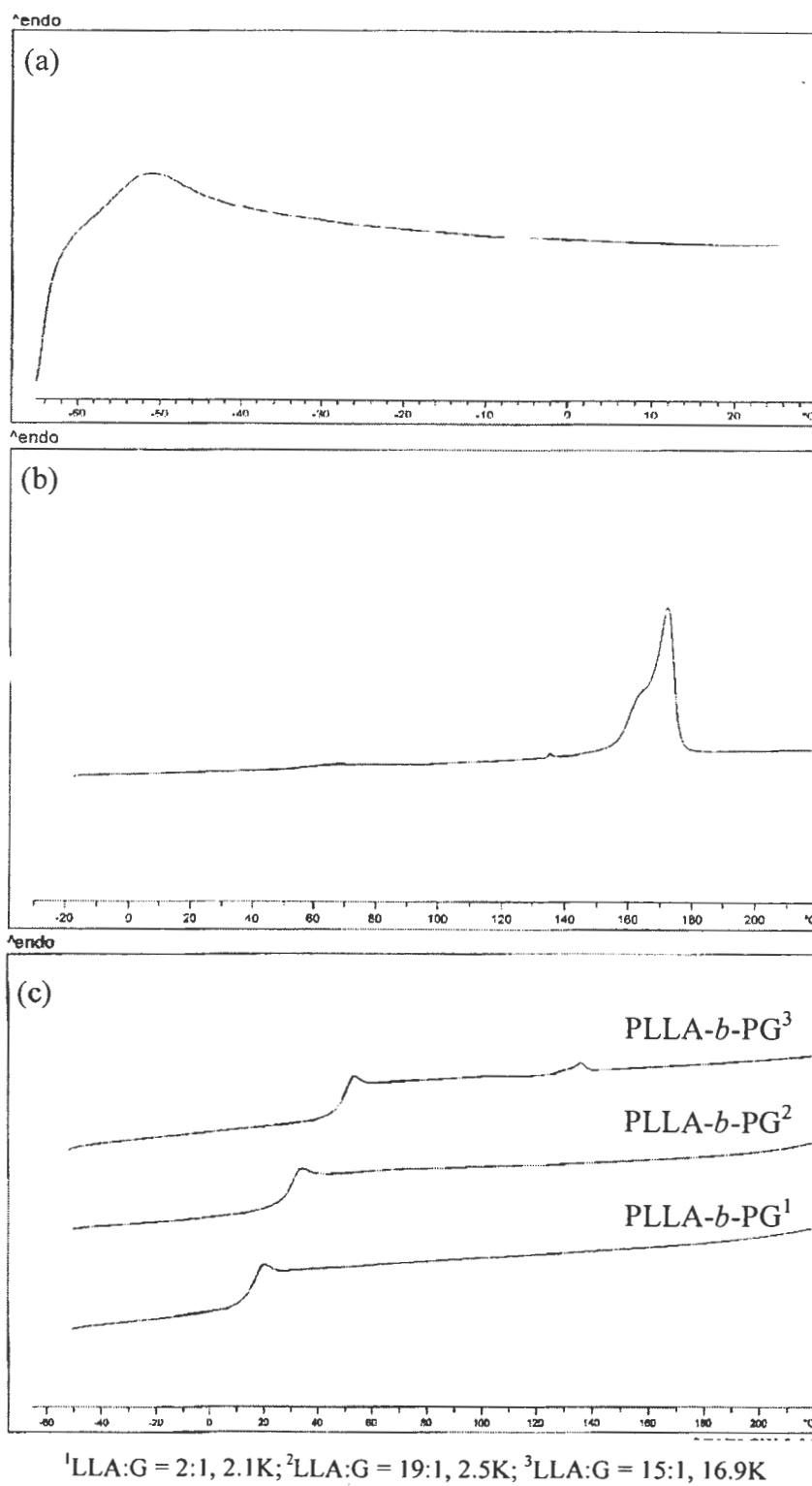


Figure 4.20 DSC thermograms of PG (a), PLLA (b), and PLLA-*b*-PG (c)

4.3.2 Solubility of PLLA-*b*-PG

The solubility profiles of PG, PLLA, and PLLA-*b*-PG are listed in Table 4.10. The solubility of polymer depends upon the polarity of its structure. PG has a number of hydroxyl groups, therefore, is soluble in polar solvents. PLLA with more hydrophobic structure can be dissolved in common organic solvents. For the high molecular weight block copolymer, the solubility was found to be quite similar to that of PLLA. This is due to the fact that the low polar PLLA chain is designed to be the outer layer of the hyperbranched PG core. Moreover, the relative amounts of LLA and G was found to affect its solubility in methanol. The low molecular weight (2,500 Da) copolymer with less LLA content is soluble in MeOH, while the high molecular weight (16,900 Da) one is not soluble.

Table 4.10 Solubility of PLLA-*b*-PG and the homopolymers.

Solvent	PG	PLLA	PLLA- <i>b</i> -PG ¹	PLLA- <i>b</i> -PG ²
CH ₂ Cl ₂	-	+	+	+
MeOH	+	-	+	-
H ₂ O	+	-	-	-
EtOAc	-	+	+	+
THF	-	+	+	+
acetone	-	-	+	-
diethyl ether	-	-	-	-

+ Soluble, - Insoluble

¹ $\overline{M}_n = 2,500$ Da

² $\overline{M}_n = 16,900$ Da

Hydrophobic/hydrophilic behavior of the copolymer was examined in the form of cast film by air-water contact angle measurement. Results of the contact angle are presented in Table 4.11. It was found that the contact angle decreased when PG block was present in the copolymer. The block copolymer obtained was therefore more hydrophilic than PLLA homopolomer. This confirmed the hypothesis

that the PG represented hydrophilic part while the PLLA represented hydrophobic part.

Table 4.11 Results of water-contact angle of polymer.

Polymer	\overline{M}_n	Contact angle
PLLA	14.5K	97 ± 2.3
PLLA- <i>b</i> -PG ¹	16.9K	90 ± 1.5

¹ LLA:G (15:1)

PLLA could be cast into film by using dichloromethane as solvent. PLLA-*b*-PG films were however so fragile that decent film pieces could not be obtained. It was possible due to the presence of PG block, which was more flexible than PLLA and also the low molecular weight nature of the copolymer.

4.4 *In vitro* degradation of poly(L-lactide-*b*-glycidol)

PLLA-*b*-PG was designed to contain ester and ether bonds in the structure. In the physiological condition, the ester can normally undergo decomposition or hydrolysis by water or esterase-typed enzymes. The ether bond is, however, not susceptible to hydrolyze under neutral or slightly basic condition. The high water solubility of the PG block would ensure the excretion of the molecules, thus leading to fast degradation or mass loss. In this study, the synthesized PLLA-*b*-PG was tested for degradation behavior in phosphate buffer saline solution (PBS) which has the pH of 7.4. The incubation was carried out at 37°C, the same temperature as human body. Changes in molecular weight and specimen mass were monitored throughout 84 days.

The weight loss is an index of the content of water-soluble oligomers and monomers formed by hydrolytic degradation and then released from the films into the surrounding media. The weight loss profiles of PLLA and PLLA-*b*-PG in PBS at 37°C was determined gravimetrically by Eq. 3.1. The results are shown in Fig. 4.21.

After 7 days in the phosphate buffer saline solution, losses of material were detected in all cases- 3% loss for PLLA and 6% loss for PLLA-*b*-PG. Thereafter, the percentage of weight loss increased steadily to attain 8, and 11% after 84 days for PLLA, and PLLA-*b*-PG, respectively. The copolymers lost their weight faster than homo PLLA because the block copolymer contained hydrophilic PG segments that were also water soluble. The observed weight loss was possibly due to the release of L-lactic acid monomer, short chain PLLA and PG segments.

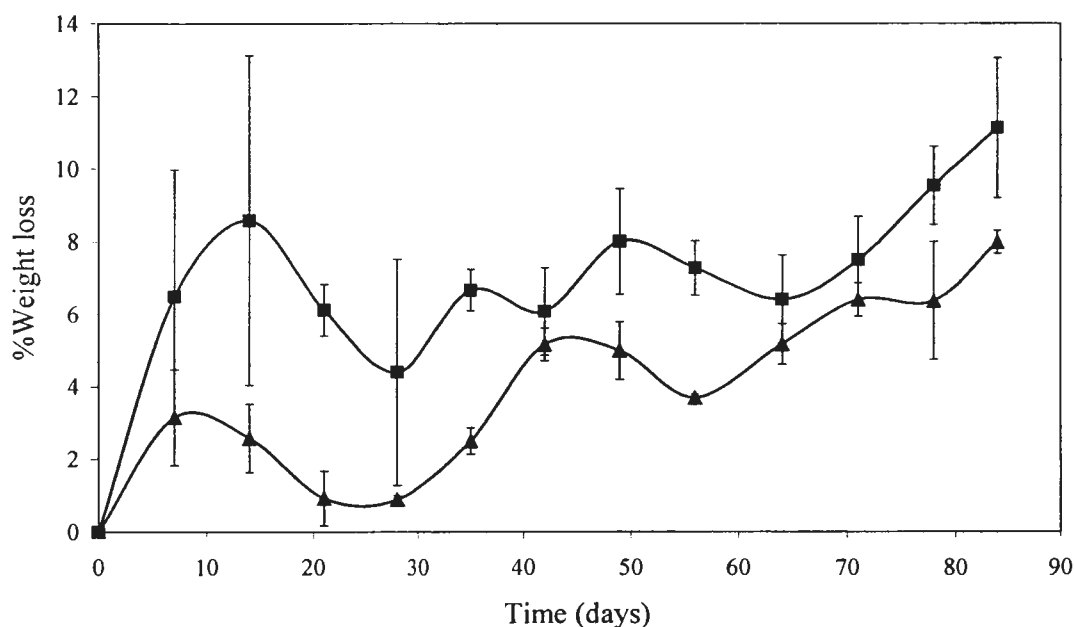


Figure 4.21 Weight loss profiles of PLLA (▲) and PLLA-*b*-PG (■) as a function of incubation time at 37°C in PBS pH 7.4

The starting \overline{M}_n 's of PLLA and PLLA-*b*-PG were 14,500 and 15,300 Da respectively. Changes of molecular weight during the incubation of polymer samples were plotted against time as shown in Fig. 4.22 and 4.23. It was found that the molecular weights of both polymers decreased with time. The \overline{M}_n value for PLLA decreased progressively from 14,500 to 5,600 after 84 days, whereas for PLLA-*b*-PG, it decreases from 15,300 to 8,100. The average molecular weight of PLLA decreased 17% for \overline{M}_w and 23% for \overline{M}_n in the first week, whereas the %change of molecular weight for the block copolymer decreased slowly at the same period.

After 84 days, the average molecular weight of PLLA decreased about 60% for both \overline{M}_w and \overline{M}_n whereas the average molecular weight of PLLA-*b*-PG decreased only 23% for \overline{M}_w and 47% for \overline{M}_n . These results were somewhat surprising since it was expected that the copolymer would have degraded faster than the homo PLLA. A possible explanation might relate to the geometry and size of the incubated specimens. PLLA sample was finer in size than the PLLA-*b*-PG. Therefore the surface area of PLLA sample was probably larger than that of PLLA-*b*-PG, leading to faster hydrolysis. Another possible explanation was the presence of homo PLLA in the copolymer which occurred during the polymerization.

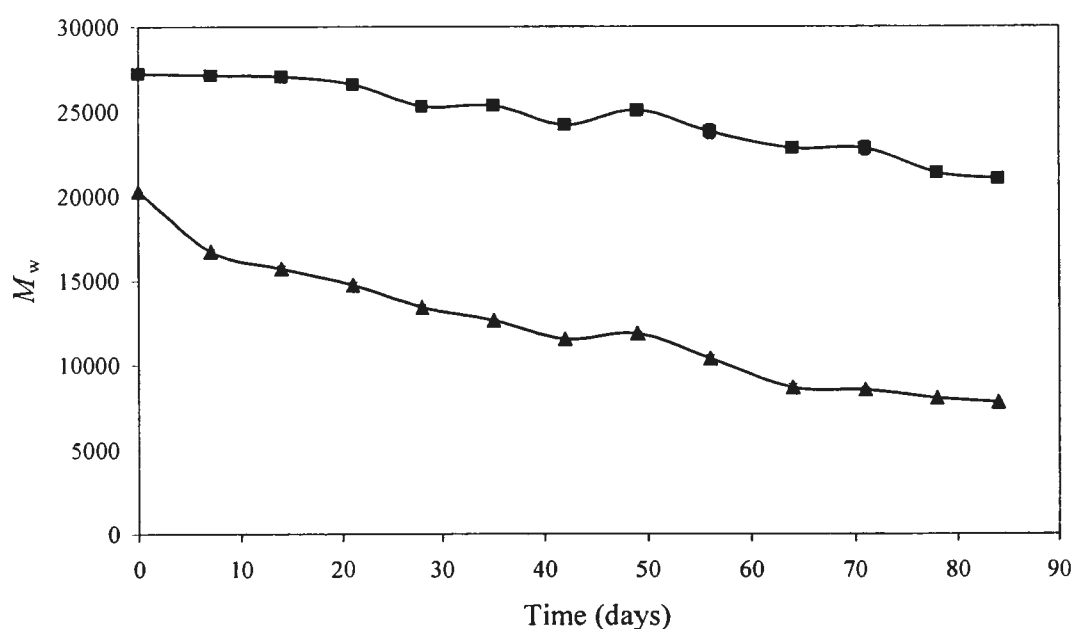


Figure 4.22 Changes of \overline{M}_w of PLLA (\blacktriangle) and PLLA-*b*-PG (\blacksquare) as a function of incubation time at 37°C in PBS pH 7.4

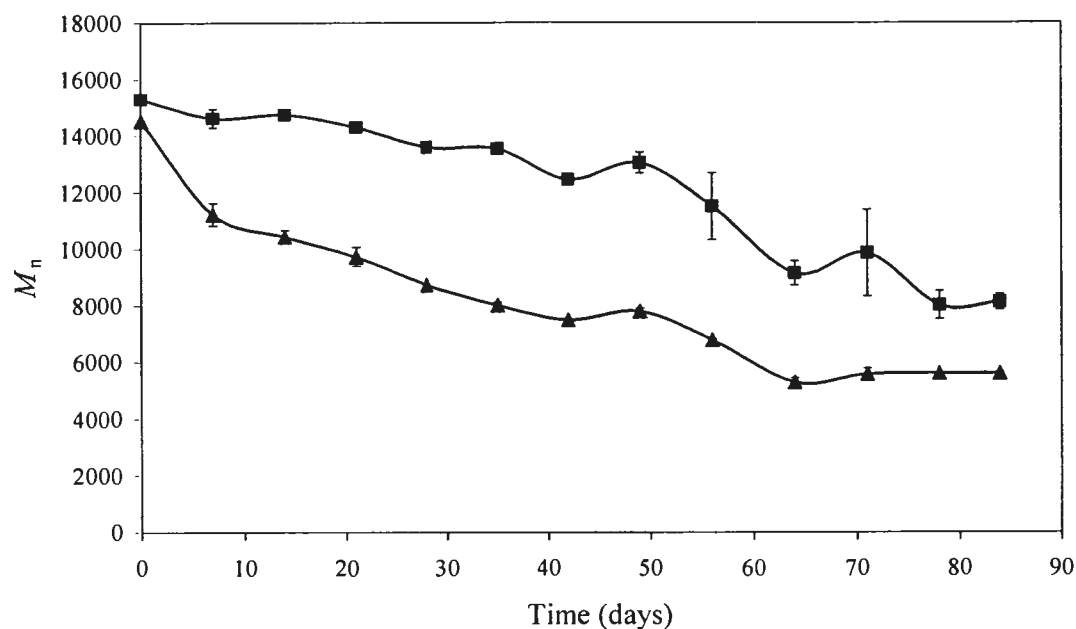


Figure 4.23 Changes of \bar{M}_n of PLLA (▲) and PLLA-*b*-PG (■) as a function of incubation time at 37°C in PBS pH 7.4

Changes in the GPC traces of the polymers with time (2, 4, 6, 8, 10, and 12 weeks of incubation) are given in Fig. 4.25. All polymers exhibited initially multimodal molar mass distribution. After incubation, the low molecular weight species appeared in the GPC chromatograms. The proportion of the low molecular weight species increased as the degradation proceeded. At week 12, the chromatograms remained multimodal with an increase of the relative intensity of the low molar mass peak.

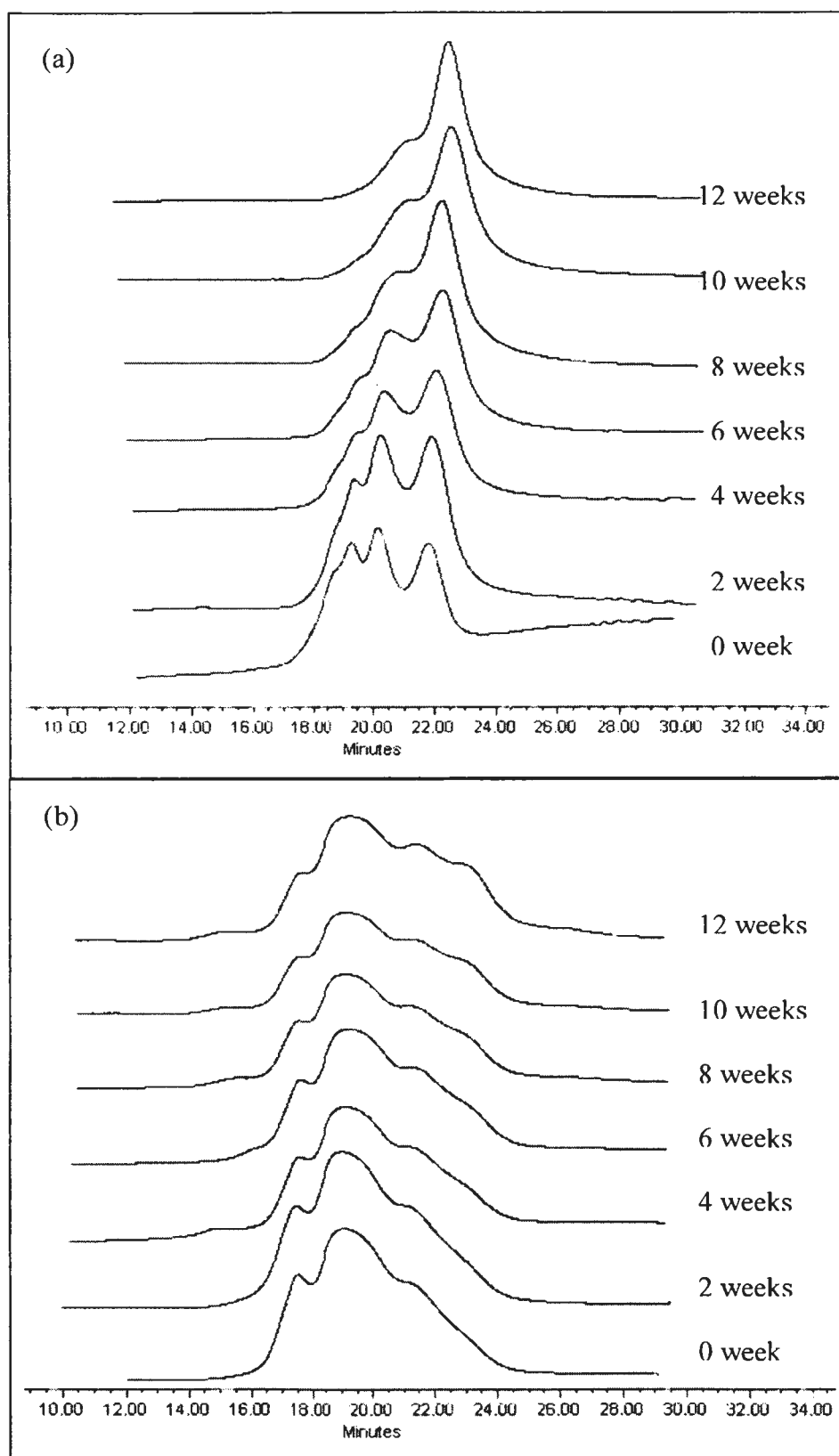


Figure 4.24 Changes of GPC chromatograms as a function of incubation time of PLLA (a) and PLLA-*b*-PG (b) at 37 °C in PBS pH 7.4

4.5 Fractionation of PLLA-*b*-PG

The methanol insoluble portion (\overline{M}_n 16,900 Da) has been fractionated into four fractions based on their solubility in four proportions of EtOAc-MeOH mixed solvent. The higher molecular weight PLLA-*b*-PG has poorer solubility in methanol and requires mixed methanol-ethyl acetate to be completely solubilized.

In Fig. 4.25 GPC chromatograms of the fractionated copolymer were compared with that of the bulk copolymer. If the amount of EtOAc in mixed solvent increased, the copolymer with higher molecular weight was extracted as shown in the result of \overline{M}_n in Table 4.12. This study in fact suggested that a mixture of polymers coexisted in the copolymer. Homo PLLA and copolymers with different LLA chain lengths were possibly formed together as a blend during the polymerization. A better polymerization method or better fractionation method is needed.

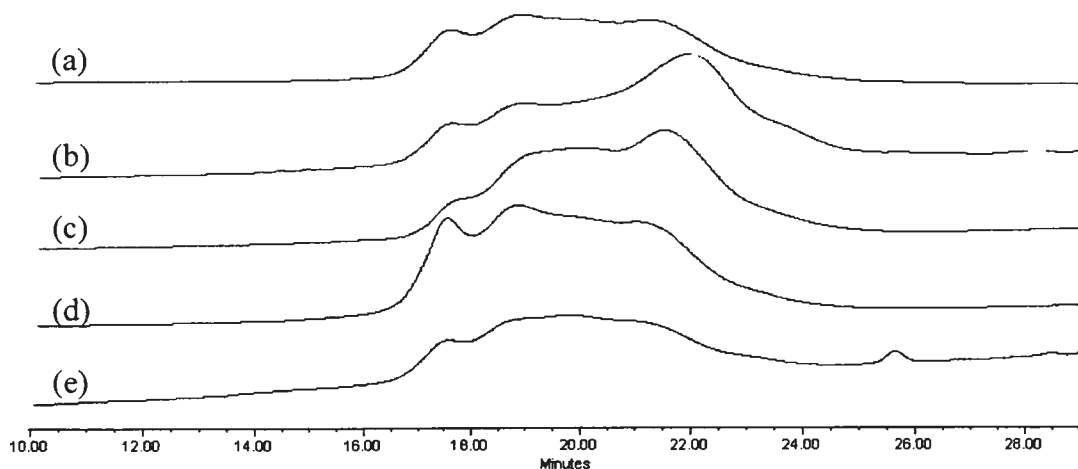


Figure 4.25 GPC chromatograms of PLLA-*b*-PG (a) and its fractions obtained from 20 % (b) 40 % (c), 60 % (d), and 80 % EtOAc in MeOH (e).

Table 4.12 Results of the fractionation of PLLA-*b*-PG from entry 2 Table 4.4.

EtOAc in MeOH (%v/v)	GPC		% Yield
	\overline{M}_n	PDI	
20	10,600	1.86	17
40	12,500	1.62	25
60	16,800	1.71	37
80	17,400	1.57	8