

## Effect of initiators on synthesis of poly(L-lactide) by ring opening polymerization

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**Abstract.** We studied the effect of several aliphatic alcohols, including 1-dodecanol, 1-octanol and methanol, as initiators on synthesis of poly(L-lactide) (PLLA) by ring opening polymerization. The reaction starts with L-lactide monomer and uses stannous octoate as catalyst. Fourier transform infrared spectroscopy and X-ray diffraction analysis verified that PLLAs were produced successfully. Weight, number average molecular weight and polydispersity index of PLLAs were measured by gel permeation chromatography. The PLLA initiated by methanol (PLLA-Meth) presented the highest molecular weight and yield percent. From differential scanning calorimetry, PLLA-Meth showed the highest melting temperature at ~167°C, crystallization temperature at 110°C and degree of crystallinity 80%. The thermal stability was assessed by thermogravimetric analysis: this confirmed that PLLA-Meth was superior with the highest degradation temperature compared to PLLA initiated by other initiators. We concluded that methanol was the most appropriate initiator for PLLA synthesis by ring opening polymerization.

### 1. Introduction

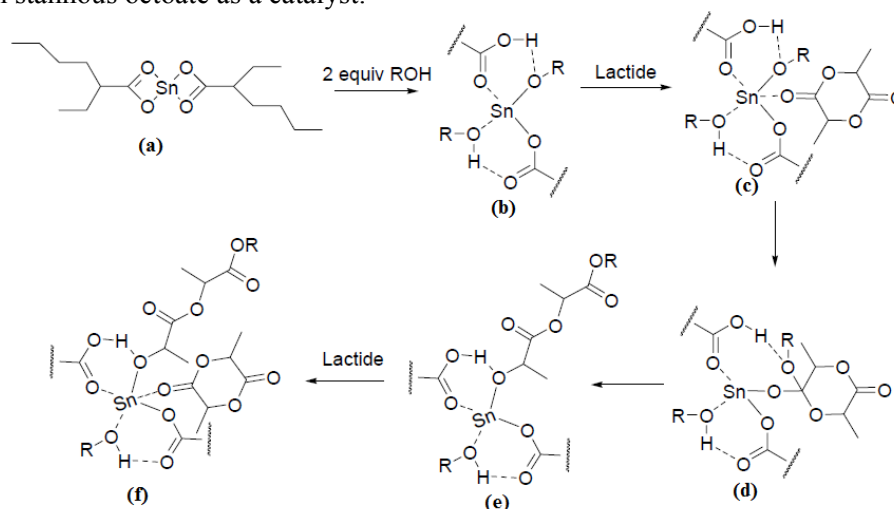
Poly(lactic acid) or polylactide (PLA) can be derived from natural sources such as cassava, corn and sugar beet. It is a sustainable development plastic which is biodegradable and biocompatible [1]. So it has extensive medical applications including sutures, bone fixation material and drug delivery by microspheres. PLA has stereoisomers: poly(L-lactide) (PLLA), poly(D-lactide) (PDLA) and poly(DL-lactide) (PDLLA). Readily available from natural sources, PLLA has been studied extensively because of its excellent biocompatibility and mechanical properties [2].

PLA can be synthesized in two ways: the first is direct polycondensation of lactic acid and the second is ring opening polymerization of lactide. In direct condensation, solvent is used and higher reaction times are required. The resulting polymer has low molecular weight and poor mechanical properties. Ring opening polymerization (ROP) of the lactide needs a catalyst and results in PLA with controlled molecular weight, depending on the monomer used and reactions conditions [2-3]. Several different types of metal catalysts, e.g. zinc (II) and titanium (IV) have been evaluated, but tin (II) 2-ethylhexanoate or stannous octoate ( $\text{Sn}(\text{Oct})_2$ ) has been widely used because of high reaction rates, solubility in the monomer melt and the ability to produce high molecular weights [4]. An initiator is important for ring opening polymerization. Duda and Penzek described a polymerization scheme based on the insertion-coordination mechanism as shown in Figure 1. In lactide polymerization



catalyzed by stannous octoate (a), a hydroxyl compound (alcohol) is required as an initiator. The alcohol first reacts with stannous octoate to form a tin alkoxide bond by ligand exchange (b). Then, an exocyclic carbonyl oxygen of the lactide temporarily coordinates with the catalyst tin atom in the alkoxide form (c), enhancing the nucleophilicity of the initiator's alkoxide group and also the lactide carbonyl group's electrophilicity. Then the acyl-oxygen bond (between the carbonyl group and the endocyclic oxygen) of the lactide breaks (d), opening the lactide chain allowing insertion into the tin-oxygen bond (alkoxide) of the catalyst (e). Repeated addition of additional lactide molecules into the tin-oxygen bond propagates forming the polymer (f) [5-6].

However, there are no reported studies of the effect of different alcohols used as initiator for ring opening polymerization. Therefore, we assessed the effect of initiator on yield percent, molecular weight, thermal properties and thermal stability of PLA (specifically PLLA) polymerized by ring opening with stannous octoate as a catalyst.



**Figure 1.** Coordination-insertion mechanism of  $\text{Sn}(\text{Oct})_2$  catalyzed polymerization of L-lactide (taken from [5]).

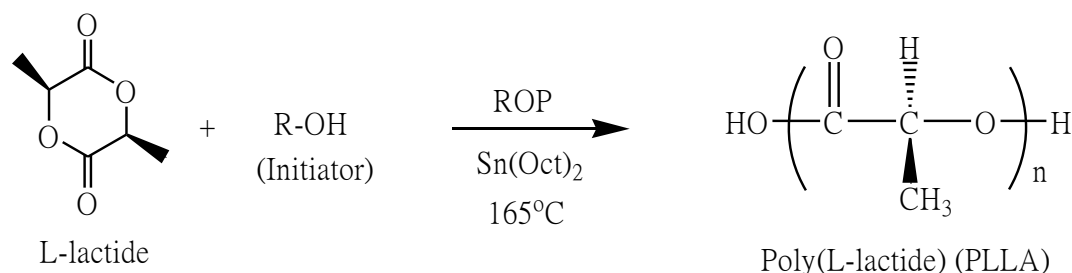
## 2. Experimentals

### 2.1. Materials

98% L-lactide was donated by Purac (Thailand) Ltd. For ring opening initiators, AR grade methanol 99% was purchased from Carlo Erba, 1-octanol 99% from Panreac Sintesis and 1-dodecanol 98% from Across Co. Ltd. Stannous octoate ( $\text{Sn}(\text{Oct})_2$ ) was supplied by Sigma Aldrich. Solvents, including toluene and chloroform, were obtained from RCI Lab scan.

### 2.2. Synthesis of Poly(L-Lactide) by ring opening polymerization

PLLA was prepared from L-lactide. Before using, it was dried in a vacuum oven at  $45^\circ\text{C}$  for 12h. Poly(L-lactides) (PLLA) were synthesized by bulk L-lactide ring opening polymerization in a nitrogen atmosphere at  $165^\circ\text{C}$  for 4 h, initiated with methanol, 1-octanol and 1-dodecanol.  $\text{Sn}(\text{Oct})_2$  0.1mol% was used as a catalyst. We varied temperature and synthesis time and found an optimum matching previous reports [1-3, 7]. After incubation, the product was dissolved in chloroform and removed to purify by precipitation in methanol. The precipitate was filtered under vacuum. Finally, PLLA was dried in a vacuum oven at  $50^\circ\text{C}$  for 24 h. The synthesis scheme of the PLLA by ring opening polymerization is shown in Figure 2. The samples were labelled PLLA-*initiator* where the *initiator* was Dodec, Oct and Meth, standing for 1-dodecanol, 1-octanol and methanol, respectively.



**Figure 2.** Synthesis of PLLA by ring opening polymerization.

### 2.3. Measurements and characterization

**2.3.1. Fourier transform infrared spectroscopy (FTIR).** The chemical structure of L-lactide and PLLAs were verified by FTIR spectra from 500 to 4,000  $\text{cm}^{-1}$  (2  $\text{cm}^{-1}$  resolution) recorded with OPUS 7.0 software on a Bruker Tensor 27 FTIR spectrometer, using the Attenuated Total Reflection (ATR) mode.

**2.3.2. X-ray diffraction analysis (XRD).** To confirm the crystal structure, X-ray diffraction (XRD) spectra were recorded on a Bruker/D8 Advance Bruker BioSpin AG (Karlsruhe, Germany). After synthesis, samples were ground and placed on the XRD platform. The range of  $2\theta$  from 2° to 40° in the reflection mode was scanned at 2°/min.

**2.3.3. Gel permeation chromatography (GPC).** The  $M_n$ ,  $M_w$  and PDI of PLLAs were measured by GPC. About 7 mg of samples were dissolved in 3 ml tetrahydrofuran (THF) via continuous stirring in a water bath at 60 °C for 1 h. GPC columns were packed with Styragel HR5E 7.8 × 300 mm column (molecular weight resolution range: 2,000-4,000,000). A Waters 2414 refractive index (RI) detector was used. The GPC columns were eluted using tetrahydrofuran at a flow rate of 1.0 mL/min at 40 °C and monodispersed polystyrenes were used for calibration.

**2.3.4. Differential scanning calorimetry (DSC).** Thermal histories of the samples were analyzed by DSC (Perkin-Elmer, model DSC 4000). Approximately 5 mg of samples were placed in aluminium pans and subjected to two heating scans from -10 to 200 °C at 10 degC/min.  $T_m$  was determined from the second scan peak at maximum value of the endotherm peak. After the first heating scan, the sample was kept at 200 °C for 3 min and then cooled to -10 °C at 10 degC/min, to determine the crystallization temperature ( $T_c$ ). Results from the initial heating cycle in DSC experiments were discarded because they included the previous thermal history. The melting temperature ( $T_m$ ) and apparent melting enthalpy ( $\Delta H_m$ ) were determined from the second heating scan. The degree of crystallinity  $\chi_c(\%)$  was estimated from the first heating cycle using

$$\chi_c(\%) = \frac{\Delta H_m}{\Delta H_m^0} \times 100 \quad (1)$$

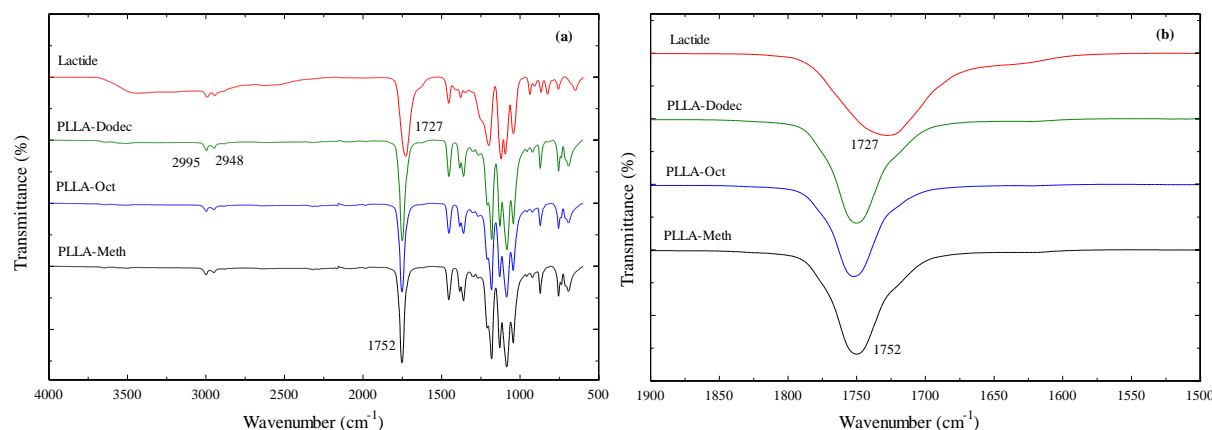
where  $\Delta H_m$  is the heat of fusion of PLA and  $\Delta H_m^0$  is theoretical melting enthalpy of perfect PLA crystal (93 J/g) [8]

**2.3.5. Thermogravimetric analysis (TGA).** Thermal stabilities of L-lactide and PLLAs were investigated using a TGA 4000 (Perkin-Elmer) under a constant nitrogen flow. About 10 mg of samples was heated from 25 to 800 °C at 20 degC/min. The weight loss was recorded and normalized against the initial weight.

## 3. Results and discussions

### 3.1. Chemical structure

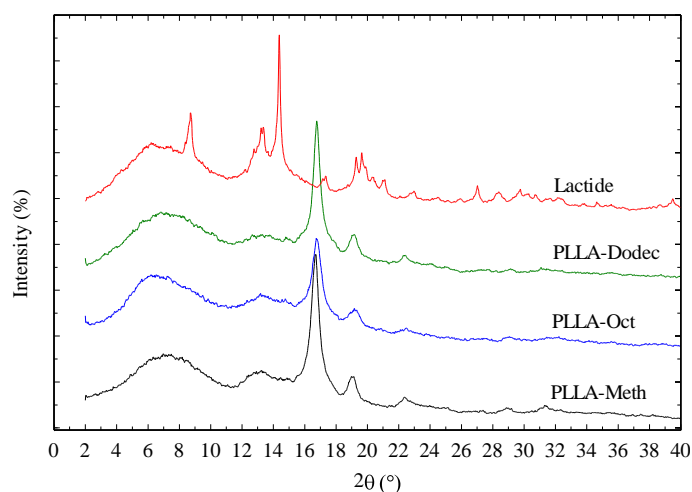
Figure 3(a) and (b) shows the FTIR spectra of lactide monomer and PLLAs. PLLAs were initiated with 1-dodecanol (PLLA-Dodec), 1-octanol (PLLA-Oct) and methanol (PLLA-Meth): their spectrum showed peaks corresponding to asymmetric ( $2,995\text{ cm}^{-1}$ ) and symmetric  $\text{-CH}$  stretching ( $2,948\text{ cm}^{-1}$ ). We also observed a band shift of the  $\text{C=O}$  stretch in the lactide at  $1,727$  to  $1,752\text{ cm}^{-1}$  in the PLLA as show in Figure 3(b). This, accompanied by a difference in the peak intensity caused by changing of the environment of molecules in the polymer chain, confirms polymerization [3, 9]. This confirms that the synthesis conditions and all initiators used were able to synthesize PLLA by ring opening.



**Figure 3.** FTIR spectra of lactide and PLLAs.

### 3.2. Crystallize analysis

X-ray scattering was used to probe the crystallinity of lactide and PLLA and to confirm PLLA formation when using different initiators. The diffraction traces of the lactide and PLLAs are shown in Figure 4. The lactide shows several important diffraction peaks at  $8.7^\circ$ ,  $13.3^\circ$  and  $14.3^\circ$ . After ring opening polymerization, the lactide polymerized to PLLA which presented three strong peaks at around  $16.7^\circ$ ,  $19.2^\circ$  and  $22.4^\circ$  [8]. For all PLLAs samples, we clearly see all the diffraction peaks corresponding to PLA without lactide diffraction peaks. This confirms that all initiators were effective at initiating the reaction of lactide because unreacted lactide monomer was not present. This agrees with the FTIR results. However, the difference effect of the initiators will be shown and discussed in other results.



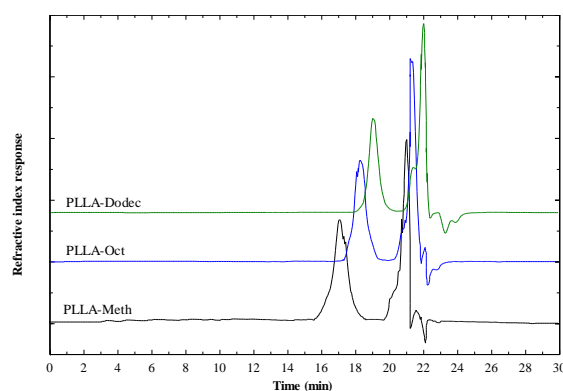
**Figure 4.** XRD patterns of lactide and PLLAs.

### 3.3. Molecular weight and yield percent

Number average molecular weights ( $M_n$ ), weight average molecular weights ( $M_w$ ) and polydispersity indices (PDI) of synthesized PLLAs were measured by gel permeation chromatography. The yield percent of PLLAs promoted with different initiators were calculated and shown in Table 1. It is notable that PLLA initiated by methanol (PLLA-Meth) displayed  $M_n$  (11,800 g/mol),  $M_w$  (14,400 g/mol) and yield percent (89%) higher than other PLLA samples and that the PLLA-Oct showed higher molecular weight and yield percent than PLLA-Dodec. The higher yield percent indicated a more complete reaction: we believe that it related to the effect of initiator on the polymerization initiation step because all factors (ratio of monomer/initiator, catalyst type and amount, temperature and reaction time) were similar except for initiator type. The highest molecular weight of PLLA-Meth was observed even when the reaction time was equal. We attribute this to higher initiation rate. Based on the insertion-coordination mechanism, the propagation continues by repeatedly adding additional lactide molecules into the tin-oxygen bond [5], so all propagation rates are expected to be similar because all factors governing this step are similar. Therefore, the higher initiation rate is the only variable affecting the molecular weight. However, all PLLA samples had PDI values nearly 1 and it was observed that the molecular weight distribution peak was quite sharp (Figure 5), indicating that the number of polymer chains remained constant, equal to the number of the original initiating species and the polymer chains approach uniform length [8]. These results indicate that methanol was the most efficient initiator for ring opening polymerization under our conditions.

**Table 1.** Molecular weight and yield percent of polylactide.

Sample	$M_n$ (g/mol)	$M_w$ (g/mol)	PDI	Yield (%)
PLLA-Dodec	5,460	6,200	1.14	65
PLLA-Oct	9,310	11,600	1.24	78
PLLA-Meth	11,800	14,400	1.22	89



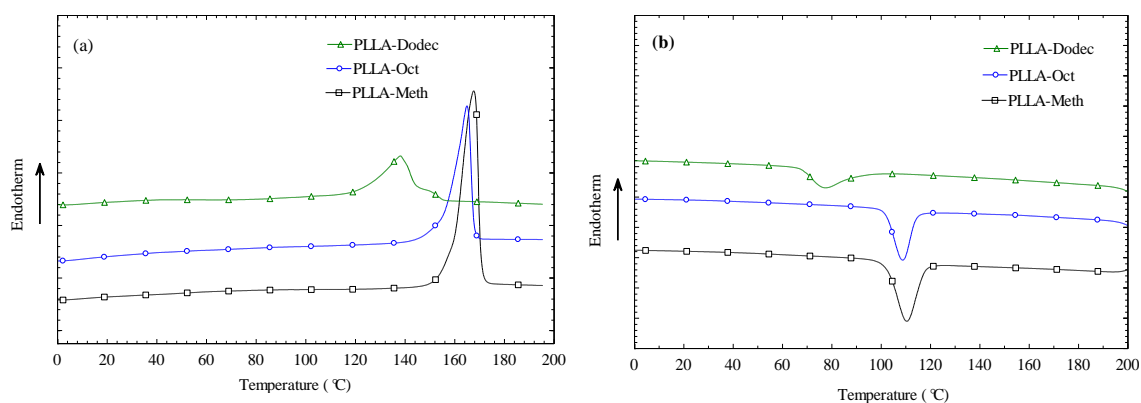
**Figure 5.** Molecular weight distribution graphs of PLLAs.

### 3.4. Thermal properties

Melting and crystallization behaviours were investigated using DSC. The temperatures obtained from the first heating, second heating and cooling cycles at rates of 10 degC/min. The first heating scan data was discarded because it included the previous thermal history [10]. The results are shown in Figure 6 and Table 2. The data obtained from second heating scan (Figure 6(a)) indicates the effect of the initiator on formation and crystallization during polymerization. PLLA synthesized in other laboratories showed melting temperatures ( $T_m$ ) in the range 150-170°C [1, 7], while our experiments showed values in the range 130-160°C. It was observed that all PLLA samples have a single melting

peak. It is notable that PLLA-Meth showed  $T_m$  at 167°C higher than other samples. Melting temperature differences correlated with their molecular weight (as shown in Table 1). For low molecular weight, mostly less than 10,000 g/mol, the polymer crystallinity will decrease and melting temperature also reduce, because the molecular surface is more irregular and individual polymer molecules do not pack together as well as longer strands leading to lower melting temperature. Saeidlou et al showed that the PLA melting temperature varies with number average molecular weight and reaches steady state about 100,000 g/mol [11]. Our experiments had number average molecular weights less than 10,000 g/mol and thus still in the rising part of Saeidlou et al's PLA melting point as a function of molecular weight curve (figure 5 in [11]). Polymer crystallization is made more difficult by long chains, which make exact chain alignment difficult. On the other hand, too low molecular weight polymers, eg. PLLA-Oct (5,460 g/mol), are difficult to crystallize because the short chains cannot fit into existing crystal locations, so the PLLA-Oct crystallinity was lowest.

The crystallization behaviour of all synthesized PLLAs were distinguished on cooling cycle, the thermograms shown in Figure 6(b). The crystallization temperature ( $T_c$ ) of PLLA-Meth was 110°C and the PLLA-Oct was 108°C consistent with other results, eg. Zhanxin et al. found, for PLLA (Mw 200,000 g/mol, NatureWorks),  $T_c$  at 110°C [1]. This is expected because crystal growth is achieved by further addition of folded polymer chain segments and only occurs for temperatures below the melting temperature ( $T_m$  of PLLA ~ 160°C) and above the glass transition temperature ( $T_g$  of PLLA ~ 50°C). However, it is clear that  $T_c$  of PLLA-Dodec shows an unusual value (77°C), which correlates with its crystallization behavior. In summary, PLLA initiated by methanol has the best combination of thermal properties, including melting temperature, crystallization temperature and degree of crystallinity.



**Figure 6.** DSC thermograms of PLLAs: (a) second heating scan and (b) cooling scan.

**Table 2.** Thermal parameters of lactide and PLLAs obtained from DSC.

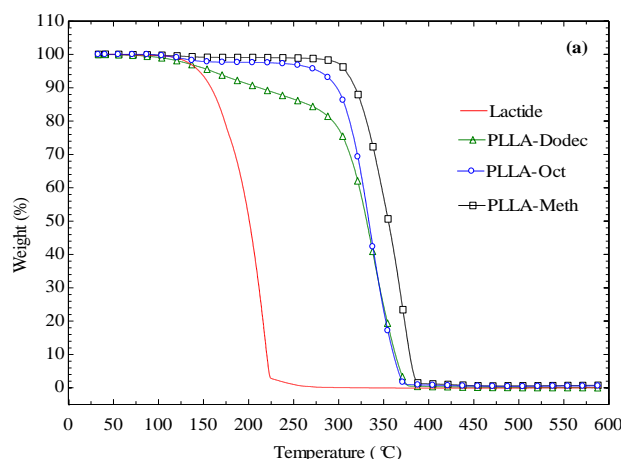
Sample	$T_m$ (°C)	$\Delta H_m$ (J/g)	$\chi_c$ (%)	$T_c$ (°C)	$\Delta H_c$ (J/g)
PLLA-Dodec	138	39	42	77	29
PLLA-Oct	165	50	54	108	39
PLLA-Meth	167	72	77	110	56

### 3.5. Thermal stability

Thermal decomposition was observed when the temperature exceeds 200°C. The TGA curves of temperature decomposition are shown in Figure 7 and the nominal values of the 10% weight loss temperature ( $T_{10}$ ) are in Table 3. Lactide begins to decompose at 158°C. All PLLAs showed a single decomposition process and it was clear that PLLA-Meth had higher decomposition temperature (317°C). This indicates that PLLA-Meth had the highest thermal stability as well as the best values of



other properties. PLLA-Meth showed the highest molecular weight which could undergo the high formation of chain entanglements [12]. The lowerer chain entangled PLA gets fragmented easily and subsequent volatilisation of the degradation products is easier. On the other hand, the higher entanglement, PLLA-Meth, makes the bond rupture difficult and increased the thermal stability [12-14].



**Figure 7.** TGA curves of lactide and PLLAs.

**Table 3.** Degradation temperature of PLLAs.

Sample	$T_{10}$ (°C)
Lactide	158
PLLA-Dodec	223
PLLA-Oct	299
PLLA-Meth	317

#### 4. Discussion

Masutani and Kimura [6] Ryner et al [5] discussed coordination-insertion mechanism of ring opening and suggested that the first step of reaction is that the alcohol attacks the octoate ligand (catalyst). Our results showed that methanol was more effective. We attribute the strongest effect of methanol, the smallest alcohol, to lower steric hindrance when attacking the octoate ligand, resulting in a more complete polymerization, because it can attack the substrate more easily than longer primary alcohols (1-octanol and 1-dodecanol) which have more steric hindrance.

#### 5. Conclusion

We concluded that methanol was the most effective of the alcohols studied as initiators for synthesis of L-polylactide (PLLA) through ring opening polymerization using stannous octoate as a catalyst: it led to the highest molecular weight, melting temperature, thermal stability and degree of crystallinity as well as the highest yield. Our study included 1-dodecanol, 1-octanol and methanol. Further, FTIR and XRD results verified that, when the reactions were initiated with those alcohols, it achieved a complete polymerization and perfect structure of PLLA. This implies that the methanol based PLLA would better qualify for a variety of applications.

#### Acknowledgement

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