

## Biodegradable Copolymers Obtained by Solution Polymerization

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This study aims the synthesis of copolymers of poly (l-lactic acid) and polycaprolactone by ring opening polymerization. The reactions between l-lactide (LLA) and  $\epsilon$ -caprolactone (CL) monomers, in 100/0, 95/5, 90/10 and 80/20 LLA/CL mass ratios, were conducted in refluxing toluene, using Stannous octoate as initiator, methanol as co-initiator and inert atmosphere ( $N_2$ ). The reaction medium was maintained under stirring at 120 °C for 24 hours. The samples were characterized by carbon-13 and proton nuclear magnetic resonance ( $C^{13}$ -NMR and  $H^1$ -NMR), and gel permeation chromatography (GPC). Monomers were characterized by thermogravimetry (TG). Copolymers were formed only in samples containing 20 wt%  $\epsilon$ -caprolactone. NMR spectra of the other samples showed no evidence of CL units. This fact may be associated with the low-temperature volatilization of monomers. The GPC analysis showed that the increase of CL concentration decrease the molecular weight of copolymers.

**Keywords:** ring opening polymerization, copolymer, poly(l-lactide acid), polycaprolactone

### 1. Introduction

Various aliphatic polyesters, such as poly (lactic acid) (PLA) and poly ( $\epsilon$ -caprolactone) (PCL), have been of great interest due to their biocompatibility, biodegradability and mechanical strength<sup>1-5</sup>. PLA can be obtained from renewable resources, however, it is a brittle material which represents an important handicap for further applications in biomedical area, packaging, industrial and agricultural fields<sup>6</sup>. On the other hand, PCL is characterized by a relatively low glass transition temperature ( $\sim 60$  °C); thus, at room temperature it behaves as a tough plastic<sup>7</sup>. PLA and PCL copolymers have been developed in order to take advantage of synergistic improvement in properties offered by both polymers<sup>8</sup>.

The PLLA and PCL can be obtained by ring-opening polymerization of L-lactide (LLA) and  $\epsilon$ -caprolactone (CL), respectively, using Stannous octoate as the initiator and low molecular weight alcohols. The most used technique for that is mass polymerization, which employs only monomer and catalysts<sup>9,10</sup>.

The advantages of mass polymerization are the high polymer purity and the easy production. On the other hand, the reaction control becomes difficult due to the formation of hot spots during the synthesis, which causes heat dissipation problems. The solution polymerization technique can reduce this difficulty since a solvent is added to the reaction medium, despite the few papers developed in this area used toxic organic solvents<sup>11</sup>. However, when it is interesting to modify the properties of these polymers by adding nanoparticles *in situ*, the presence of a solvent can make the process easier.

In the last two decades, there is growing interest in the modification of the properties of PLLA, which is rigid and brittle, either by obtaining copolymers with other monomers to provide flexibility, or by adding nanoparticles to improve its tensile strength and lower its gas permeability<sup>12-14</sup>.

The objective of this study was to synthesize a copolymer of PLLA and PCL by solution polymerization, using toluene as solvent. Evidence of copolymer formation is discussed in terms of carbon and hydrogen nuclear magnetic resonance analysis, while the molar masses were evaluated by gel permeation chromatography.

### 2. Material and Methods

The monomers employed in this work were  $\epsilon$ -caprolactone (CL) 97% (Sigma Aldrich) and the L-lactide (LLA) (Purac<sup>®</sup>). The initiator stannous octoate,  $Sn(Oct)_2$ , was purchased from Sigma Aldrich<sup>®</sup>. Toluene and methanol, both in spectrophotometric grade, were obtained from Merck<sup>®</sup>.

#### 2.1. Synthesis of PLLA and copolymers of PLLA-co-PCL

The synthesis of copolymers from L-lactide (LLA) and  $\epsilon$ -caprolactone (CL) was carried out in a three-necked bottom flask (250 mL) with the central neck adapted to a Graham condenser. The side necks were coupled to a thermometer (ETS IKA) connected to the heating plate with magnetic stirrer. The copolymerization was carried out in different feed ratios of LLA to CL (100/0, 95/5, 90/10, 85/15 and 80/20, w/w).  $Sn(Oct)_2$ , toluene and methanol were added to

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carbonyl carbon, at 68.9 ppm related to tertiary carbon, and at 16.6 ppm related to the methylene group -CH-. Chemical shifts of caprolactone unit (CL) were only presented in the 80/20 sample. In Figure 2 there is a comparison between the  $C^{13}$ -NMR spectra for samples of PLLA (100/0) and PLLA-co-PCL (80/20).

The areas of the  $C^{13}$ -NMR signals related to  $\epsilon$ -CL-CH<sub>2</sub> groups (20.2 ppm) and the -CH<sub>3</sub> groups of the LLA (16.2 ppm) were calculated, and the ratio between them expresses the percentage of  $\epsilon$ -CL chemically bound to LLA, according to Equation 1.

$$\begin{aligned} \% \epsilon CL &= \frac{\text{Integral da área do pico da } \epsilon CL}{\text{Integral da área do pico do LLA}} \cdot x \\ 100 \% \epsilon CL &= \frac{\text{Integral } \epsilon CL}{\text{Integral LLA}} \cdot 100 \end{aligned} \quad (1)$$

It is observed that in the synthesis of the 85/15 copolymer, only 2.7% of the final product consists of CL units, whereas in the synthesis of 80/20 copolymer, 30.3% of the final product consists of CL units.

During solution polymerization, the temperature (120 °C) used for the synthesis is sufficient to volatilize the molecules of  $\epsilon$ -caprolactone (CL) and L-lactide (LLA), which possibly has hindered the reactivity between the two monomers. Thermogravimetric analysis of monomers (Figure 3) showed that the starting temperature of mass loss ( $T_{\text{onset}}$ ) is 64 °C for CL and 104 °C for the LLA, and the two monomers lose mass by volatilization. Even if the system is heated under reflux, monomers may remain in dynamic equilibrium, and as the temperature of volatilization of CL

is lower, the gaseous state is richer in CL, decreasing the reactivity of this monomer.

Castro<sup>10</sup> studied random copolymers of poly(L-lactic acid) and polycaprolactone via mass polymerization without the addition of solvents. The researcher varied the L-lactide/ $\epsilon$ -caprolactone ratios, and observed by  $C^{13}$ -NMR that the synthesis fed with less than 20 wt% of  $\epsilon$ -caprolactone produced structures with 100% of poly(L-lactic acid). The author also used a temperature of 120 °C and a closed vacuum system.

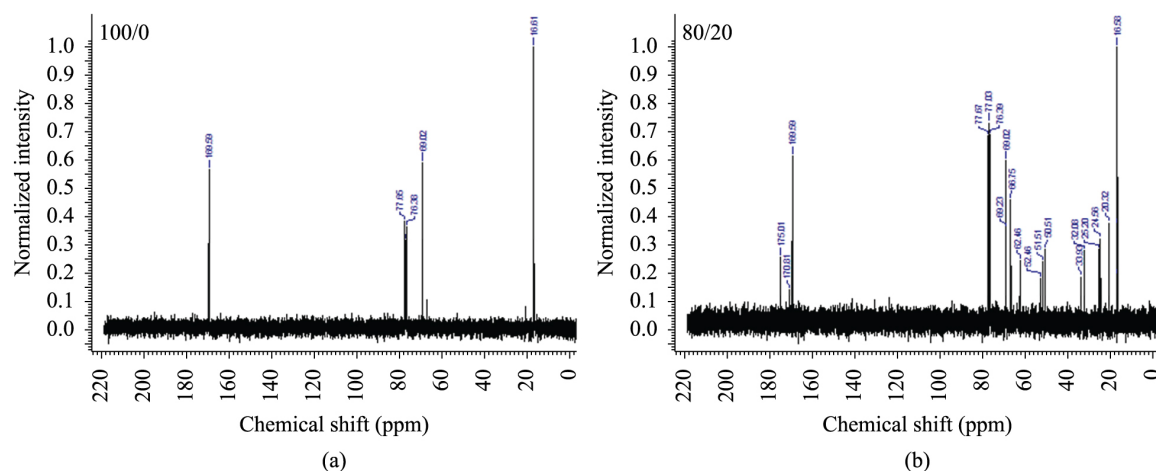
Some studies on the synthesis of aliphatic polyesters have been carried out in recent years and the NMR technique has been used to confirm the formation of polymers. The  $^1\text{H}$ -NMR signals for the pure PCL and PLLA based on these works are presented in Table 3.

Figure 4 shows the  $^1\text{H}$ -NMR spectra of PLLA 100/0 samples. The  $^1\text{H}$ -NMR spectra for samples with less than 20 wt% of CL showed only signals referring to the LLA units. For PLLA (100/0), a major intensity doublet at 1.62 and 1.59 ppm refers to the signals of methyl groups (-CH<sub>3</sub>). Two doublets of lower intensity appeared at 1.54 and 1.53 ppm, and at 1.51 and 1.50 ppm, which can be assigned to methyl groups bonded to the terminal carbons. A quadruplet related to groups -(CH-CH<sub>3</sub>) appeared at 5.14, 5.17, 5.21 and 5.24 ppm. A second quadruplet assigned to terminal groups -(CH-CH<sub>3</sub>) was recorded at 4.34, 4.38, 4.41, 4.45 ppm.

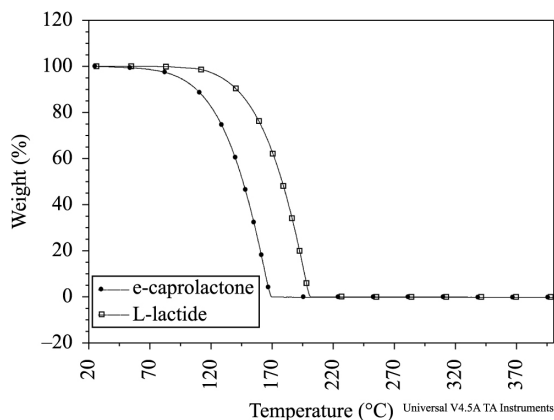
Motta & Duek<sup>4</sup> studied the synthesis of PLLA using the same catalyst, but via mass polymerization. The researchers prepared polymers with molar ratio monomer/catalyst between 4,000 and 5,500, and obtained polymers with molecular

**Table 3.** Signals of  $^1\text{H}$ -NMR for PCL and PLLA, obtained from reactions of ring-opening using  $\text{Sn}(\text{Oct})_2$ <sup>[2,15,17]</sup>.

PCL		Poly(lactide acid)	
Signal	Hydrogens	Signal	Hydrogens
2.64	-C(O)-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-	1.6	-C(O)-CH(CH <sub>3</sub> )-O-C(O)-CH(CH <sub>3</sub> )-O-H
1.77	-C(O)-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-	1.5	-C(O)-CH(CH <sub>3</sub> )-O-C(O)-CH(CH <sub>3</sub> )-O-H
1.86	-C(O)-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-	5.1	-C(O)-CH(CH <sub>3</sub> )-O-C(O)-CH(CH <sub>3</sub> )-O-H
1.77	-C(O)-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-	4.4	-C(O)-CH(CH <sub>3</sub> )-O-C(O)-CH(CH <sub>3</sub> )-O-H
4.43	-C(O)-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -O-		



**Figure 2.**  $C^{13}$ -NMR spectra for samples of (a) PLLA (100/0) and (b) PLLA-co-PCL (80/20).



**Figure 3.** TG curves of LLA and CL monomers.

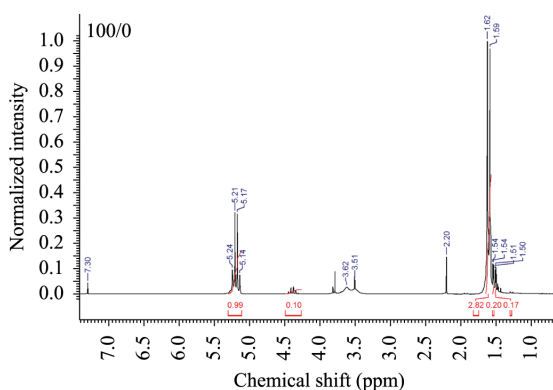
weights between 75,000 and 150,000 g/mol. The  $^1\text{H-NMR}$  spectra show chemical shifts ( $\delta$ ) at 5.15 ppm for the CH groups and at 1.58 ppm for  $\text{CH}_3$  groups, both singlet signals<sup>4</sup>.

The 95/5, 90/10 and 85/15 samples showed similar spectra and none of them indicate any evidence of the presence of CL units. For the 85/15 sample (Figure 5), a major intensity doublet at 1.58 and 1.55 ppm refers to groups ( $-\text{CH}_3$ ) and another of lower intensity at 1.48 and 1.44 ppm is assigned to terminal groups ( $-\text{CH}_3$ ). Quadruplets were recorded at 5.10, 5.13, 5.17 and 5.20 ppm, and at 4.05, 4.08, 4.12 and 4.15 ppm, corresponding to the groups ( $-\text{CH}-\text{CH}_3$ ) and terminals ( $-\text{CH}-\text{CH}_3$ ), respectively. All obtained data are in accordance to the literature<sup>2,4</sup>.

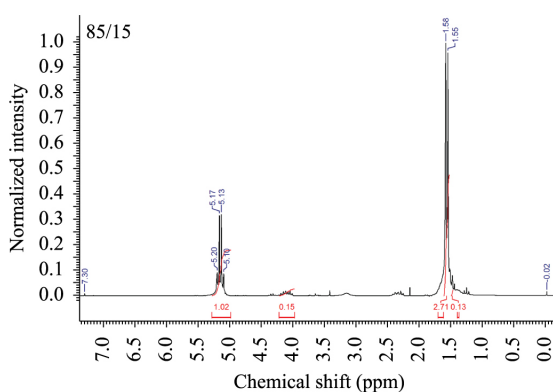
The 80/20 sample, however, presents several peaks such as singlet and duplets in the region between 1.71 and 1.45 ppm. The duplets at 1.57 and 1.56, and at 1.49 ppm and 1.48 ppm can be assigned to the group ( $-\text{CH}_3$ ) of LLA units, suggesting that copolymers with different sequences of two monomers can be obtained (Figure 6). The peaks of highest intensity at 1.53 and 1.16 ppm can be assigned to methylene hydrogens ( $-\text{CH}_2-$ ) bonded to the  $\beta$  carbon and to the  $\gamma$  carbon of CL unit, respectively. A peak around 2.34 ppm can be assigned to  $\alpha$  methylene hydrogens of CL unit. The peak related to hydrogens bonded to the  $\delta$  carbon of CL units arises at 4.96 ppm. Two quadruplets between 5.13 and 5.25 ppm refer to the hydrogens of the groups ( $-\text{CH}-\text{CH}_3$ ) of LLA units. Once again, the signal split can indicate two different configurations for the copolymer of PLLA-co-PCL.

However, the  $^1\text{H-NMR}$  spectrum for the obtained PLLA has a quadruplet with chemical shifts ( $\delta$ ) at 5.14, 5.17, 5.21 and 5.24 ppm for the CH group, and a doublet at 1.59 and 1.62 for  $\text{CH}_3$  groups. It is noteworthy that the polymerization technique employed in this study is the solution polymerization and the molar ratio of monomer/catalyst is 1825, which can lead to the formation of polymers of low molecular weight.

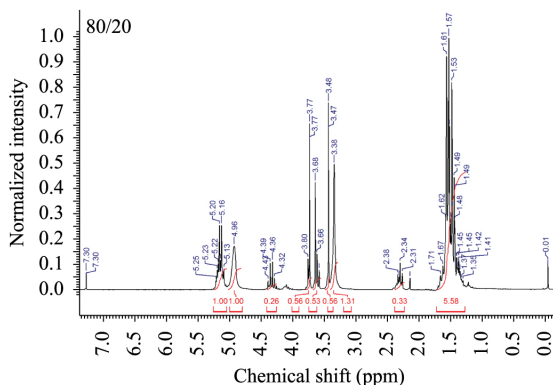
Table 4 presents the molecular weight ( $M_n$  and  $M_w$ ) of PLLA and copolymers as well as polydispersity ( $M_w/M_n$ ). Except from sample 80/20 ( $1.6 \cdot 10^3$  g/mol), the molecular weights ranged from  $1.0 \cdot 10^4$  to  $1.3 \cdot 10^4$  g/mol, showing that the increase CL concentration affects the molecular weight of copolymers, difficult to obtain poly(LLA-co-CL) with desired high molecular weight<sup>10,18</sup>. Samples 100/0, 95/5,



**Figure 4.**  $^1\text{H-NMR}$  spectrum of a sample of PLLA 100/0 obtained by solution polymerization after 24 hours of reaction at 120 °C.



**Figure 5.**  $^1\text{H-NMR}$  spectrum of a sample of PLLA 85/15 obtained by solution polymerization after 24 hours of reaction at 120 °C.



**Figure 6.**  $^1\text{H-NMR}$  spectrum of a PLLA 80/20 sample obtained by solution polymerization after 24 hours of reaction at 120 °C.

**Table 4.** PLLA and copolymers molecular weight ( $M_n$  and  $M_w$ ), polydispersity ( $M_w/M_n$ ) obtained by GPC.

Samples	$M_n$	$M_w$	( $M_w/M_n$ )
100/0	$1.14 \times 10^4$	$2.89 \times 10^4$	1.70
95/5	$1.01 \times 10^4$	$1.60 \times 10^4$	1.58
90/10	$1.35 \times 10^4$	$2.00 \times 10^4$	1.48
85/15	$1.21 \times 10^4$	$2.14 \times 10^4$	1.76
80/20	$1.65 \times 10^3$	$2.10 \times 10^3$	1.27

90/10, showed a bimodal molecular weight distribution characteristic of PLLA synthesis, according to the literature. This behavior was not observed for samples 85/15, 80/20. Low molar ratio monomer / initiator, humidity and the presence of oxygen are factors that may have contributed to the reduction in molecular weight<sup>19,20</sup>.

#### 4. Conclusion

The technique of polymerization, employing toluene as solvent at 120 °C, is effective for obtaining PLLA and the copolymer of PLLA-co-PCL, if CL mass fractions are above 20%. These results were confirmed by <sup>13</sup>C-NMR and <sup>1</sup>H-NMR techniques, since the signals in chemical shifts related to CL units were identified only for the 80/20 sample.

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