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 ε-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 iniciator, methanol as co-iniciator and inert atmosphere (N₂). 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 (C¹³-NMR and H¹-NMR), and gel permeation chromatography (GPC). Monomers were characterized by thermogravimetry (TG). Copolymers were formed only in samples containing 20 wt% ε-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 (ε-caprolactone) (PCL), have been of great interest due to their biocompatibility, biodegradability and mechanical strength ¹-⁵. 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. On the other hand, PCL is characterized by a relatively low glass transition temperature (~60 °C); thus, at room temperature it behaves as a tough plastic. PLA and PCL copolymers have been developed in order to take advantage of synergistic improvement in properties offered by both polymers ⁶-⁷. The PLLA and PCL can be obtained by ring-opening polymerization of L-lactide (LLA) and ε-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 ⁸,⁹. 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 ¹⁰. 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 ¹¹-¹³. 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 (C¹³-NMR and H¹-NMR), and gel permeation chromatography (GPC). Monomers were characterized by thermogravimetry (TG). Copolymers were formed only in samples containing 20 wt% ε-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.

2. Material and Methods

The monomers employed in this work were ε-caprolactone (CL) 97% (Sigma Aldrich) and the L-lactide (LLA) (Purac®). The initiator stannous octoate, Sn(Oct)₂, was purchased from Sigma Aldrich®. Toluene and methanol, both in spectrophotometric grade, were obtained from Merck®. Toluene and methanol, both in spectrophotometric grade, were obtained from Merck®.

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

The synthesis of copolymers from L-lactide (LLA) and ε-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
monomers and maintained under dry nitrogen atmosphere at 120 °C for 24 hours. The compositions of the reaction media is described in Table 1.

After 24 hours, the polymer solution was precipitated in cold methanol, the filtered solvent was removed. Then, the polymer was dried under vacuum.

2.2. Characterization

The samples of PLLA and PLLA-co-PCL were subjected to carbon-13 nuclear magnetic resonance analysis (13C-NMR) in a Varian Mercury Plus spectrometer operating at 500 MHz, 294 K, for 1 hour. In addition, 1H nuclear magnetic resonance (1H-NMR) was performed in a Bruker AC 200 at 294 K. The solvent used was deuterated chloroform (CDCl3), and tetramethylsilane (TMS) was used as an internal standard.

TG curves to l-lactide and ε-caprolactone were obtained in TA Q20 equipment, operating from 20 to 400 °C, at 10 °C/min. The monomers samples were conditioned in a platinum sample holder and analyses were conducted under N2 atmosphere with a flow of 40 mL/min.

Gel Permeation Chromatography (GPC) was performed using Waters 1525-detector ELSD 2424, Styragel HR3ETHF and Styragel HR5RTHF (4.6 × 300 mm) columns. All samples were dissolved in chloroform at a concentration of 1.0% (w/v) and analyzed at 40 °C. Chloroform was used as eluent (flow rate = 0.5 mL/min). Molecular weights (Mn and Mw) and polydispersity (Mw/Mn) were determined with respect to the polystyrene standard.

3. Results and Discussion

Figure 1 shows the chemical reaction between the monomers of L-lactide and ε-caprolactone in order to obtain the copolymer of PLLA-co-PCL. The letters in the chemical structure of copolymer indicate potential signals emitted by 13C-NMR and 1H-NMR techniques, respectively.

Table 1. Mass and molar composition of reaction media for the preparation of PLLA and its copolymers with PCL.

<table>
<thead>
<tr>
<th>Reagents</th>
<th>100/0</th>
<th>95/05</th>
<th>90/10</th>
<th>85/15</th>
<th>80/20</th>
</tr>
</thead>
<tbody>
<tr>
<td>m (g)</td>
<td>n (mol)</td>
<td>m (g)</td>
<td>n (mol)</td>
<td>m (g)</td>
<td>n (mol)</td>
</tr>
<tr>
<td>LLA</td>
<td>50.0</td>
<td>0.3472</td>
<td>47.5</td>
<td>0.3298</td>
<td>45.0</td>
</tr>
<tr>
<td>εCL</td>
<td>-</td>
<td>-</td>
<td>2.5</td>
<td>0.0219</td>
<td>5.0</td>
</tr>
<tr>
<td>CH3OH</td>
<td>7.8×10^-3</td>
<td>2.3×10^-4</td>
<td>7.8×10^-3</td>
<td>2.3×10^-4</td>
<td>7.8×10^-3</td>
</tr>
<tr>
<td>Sn(Oct)2</td>
<td>7.3×10^-3</td>
<td>2.3×10^-4</td>
<td>7.3×10^-3</td>
<td>2.3×10^-4</td>
<td>7.3×10^-3</td>
</tr>
<tr>
<td>CH2Cl2</td>
<td>43.3</td>
<td>0.4706</td>
<td>43.3</td>
<td>0.4706</td>
<td>43.3</td>
</tr>
</tbody>
</table>

Table 2. Chemical shifts (ppm) from 13C-NMR spectra cited in literature and obtained experimentally.

<table>
<thead>
<tr>
<th>Signal</th>
<th>Literature</th>
<th>Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B</td>
<td>173.50</td>
<td>175.01</td>
</tr>
<tr>
<td>b1</td>
<td>169.60</td>
<td>169.59</td>
</tr>
<tr>
<td>C</td>
<td>69.06</td>
<td>69.02</td>
</tr>
<tr>
<td>cl</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D</td>
<td>16</td>
<td>16.61</td>
</tr>
<tr>
<td>e</td>
<td>64.14</td>
<td>-</td>
</tr>
<tr>
<td>f</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>g</td>
<td>24</td>
<td>-</td>
</tr>
<tr>
<td>h</td>
<td>28</td>
<td>-</td>
</tr>
<tr>
<td>i</td>
<td>33</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 1. Chemical structure of PLLA-co-PCL copolymer with carbons marked for identification by 13C-NMR.
carbonyl carbon, at 68.9 ppm related to tertiary carbon, and at 16.6 ppm related to the methylene group -CH₂. Chemical shifts of caprolactone unit (CL) were only presented in the 80/20 sample. In Figure 2 there is a comparison between the C¹³-NMR spectra for samples of PLLA (100/0) and PLLA-co-PCL (80/20).

The areas of the C¹³-NMR signals related to ε-CL -CH₂ groups (20.2 ppm) and the -CH₃ groups of the LLA (16.2 ppm) were calculated, and the ratio between them expresses the percentage of ε-CL chemically bound to LLA, according to Equation 1.

\[
\%_{\text{CL}} = \frac{\text{Integral da área do pico da εCL}}{\text{Integral da área do pico do LLA}}
\]

\[
100.\%_{\text{CL}} = \frac{\text{IntegralCL}}{\text{IntegralLLA}}.100
\]

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 ε-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_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.

Castro¹⁰ studied random copolymers of poly(l-lactic acid) and polycaprolactone via mass polymerization without the addition of solvents. The researcher varied the L-lactide/ε-caprolactone ratios, and observed by C¹³-NMR that the synthesis fed with less than 20 wt% of ε-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 ¹H-NMR signals for the pure PCL and PLLA based on these works are presented in Table 3.

![Figure 2. C¹³-NMR spectra for samples of (a) PLLA (100/0) and (b) PLLA-co-PCL (80/20).](image)

Table 3. Signals of ¹H-NMR for PCL and PLLA, obtained from reactions of ring-opening using Sn(Oct)₂.[¹²,¹⁵,¹⁷]

<table>
<thead>
<tr>
<th>Signal (ppm)</th>
<th>Hydrogens</th>
<th>Signal (ppm)</th>
<th>Hydrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.64</td>
<td>-C(O)-CH₂CH₂-CH₂CH₂CH₂O-</td>
<td>1.6</td>
<td>-C(O)-CH(CH₃)O-C(O)-CH(CH₃)O-H</td>
</tr>
<tr>
<td>1.77</td>
<td>-C(O)-CH₂CH₂-CH₂CH₂CH₂O-</td>
<td>1.5</td>
<td>-C(O)-CH(CH₃)O-C(O)-CH(CH₃)O-H</td>
</tr>
<tr>
<td>1.86</td>
<td>-C(O)-CH₂CH₂-CH₂CH₂CH₂O-</td>
<td>5.1</td>
<td>-C(O)-CH(CH₃)O-C(O)-CH(CH₃)O-H</td>
</tr>
<tr>
<td>1.77</td>
<td>-C(O)-CH₂CH₂-CH₂CH₂CH₂O-</td>
<td>4.4</td>
<td>-C(O)-CH(CH₃)O-C(O)-CH(CH₃)O-H</td>
</tr>
<tr>
<td>4.43</td>
<td>-C(O)-CH₂CH₂CH₂CH₂CH₂O-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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weights between 75,000 and 150,000 g/mol. The 1H-NMR spectra show chemical shifts (δ) at 5.15 ppm for the CH groups and at 1.58 ppm for CH₃ groups, both singlet signals.

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 (-CH₃) and another of lower intensity at 1.48 and 1.44 ppm is assigned to terminal groups (-CH₃). 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 (-CH-CH₃) and terminals (-CH-CH₃), respectively. All obtained data are in accordance to the literature.

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 (-CH₃) 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 (-CH₂-) bonded to the β carbon and to the γ carbon of CL unit, respectively. A peak around 2.34 ppm can be assigned to α methylene hydrogens of CL unit. The peak related to hydrogens bonded to the δ 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 (-CH-CH₃) of LLA units. Once again, the signal split can indicate two different configurations for the copolymer of PLLA-co-PCL.

However, the 1H-NMR spectrum for the obtained PLLA has a quadruplet with chemical shifts (δ) 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 CH₃ groups. It is noteworthy that the polymerization technique employed in this study is the solution polymerization and the molar ratio of monomer/catalyst is 18/25, which can lead to the formation of polymers of low molecular weight.

Table 4 presents the molecular weight (Mₐ and Mₘ) of PLLA and copolymers as well as polydispersity (Mₘ/Mₐ). Except from sample 80/20 (1.6.10^3 g/mol), the molecular weights ranged from 1.0.10^3 to 1.3.10^4 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. Samples 100/0, 95/5, 90/10, 85/15, and 80/20 obtained by solution polymerization after 24 hours of reaction at 120 °C.
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\textsuperscript{19,20}.

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 \textsuperscript{13}C-NMR and \textsuperscript{1}H-NMR techniques, since the signals in chemical shifts related to CL units were identified only for the 80/20 sample. This can be related to the fact that the monomers volatilize at temperatures below 120 °C, generating a dynamic equilibrium between the gas and liquid phases in the reaction system, and as the CL presents a volatilization temperature lower than that of the LLA, the former can be in greater amount in the vapor phase.

The \textsuperscript{13}C-NMR signal intensities of (-CH\textsubscript{3}) and (-CH\textsubscript{2}CH\textsubscript{2}) groups of LLA units, and (-CH\textsubscript{2}CH\textsubscript{2}) groups of CL units are lower than the values mentioned by other authors, which suggests that the full area of these peaks is also smaller and therefore the molecular weights of both PLLA and PLLA-co-PCL (80/20) are low. This fact may be associated with the solvent chosen for the synthesis\textsuperscript{13}. The present study shows that higher CL concentrations and smaller headspace can facilitate obtaining copolymers.

References