

Synthesis and Characterization of Poly (Lactic Acid) for Use in Biomedical Field

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The development of biomaterials for application in medicine is one of the great challenges of research in material science. Bioabsorbable polymers have been identified as alternative materials for biomedical applications, since these polymers are degraded by simple hydrolysis to products that can be metabolized by the human body. Among the biomaterials (biopolymers) used in the medical field, the poly (lactic acid) (PLA) has received significant attention. It is produced from lactic acid, a naturally occurring organic acid that can be produced by fermentation. PLA and its copolymers are being used in biomedical area in the form of implants or devices due to its excellent biocompatibility and biodegradability. The objective of this study was to investigate the PLA synthesis in laboratory scale in order to characterize the PLA according the needs for biomedical use. Characterization by DSC and FTIR of the PLA obtained was made to know the required properties for biomedical use.

1. Introduction

Biomaterials are substances of natural or synthetic origins that can interact with biological systems on a temporary or permanent. These offer a possible alternative to treat and to repair the loss of tissues and organs from trauma or diseases. There are a lot of biomedical applications in which biomaterials are been used as a drug delivery system, cell scaffold and suture in tissue engineering, prostheses for tissue replacements like intraocular lens, dental implant, and breast implant, and artificial organs for temporary or permanent assist (e. g. artificial kidney, artificial heart, and vascular graft) (Y. Cheng et al, 2009). Moreover, biomaterials are derived from biological sources in an eco-friendly way. Biosourced materials will gradually replace the currently existing family of oil-based polymers as they become cost- and performance-wise competitive (Lunelli et al, 2010).

Variety materials have been used for medical care including metals, ceramics and polymers. Biodegradable and bioabsorbable polymers have excellent characteristics for certain applications. Resorbable polymers gradually dissolve and are eliminated through the kidneys or other means. Among the main polymers used in medicine there are the poly (α -hydroxy acids). Poly (lactic acid) or polylactide (PLA) is becoming to be the

most important bio-based polyester due to its favorable properties widely investigated as support material for tissue regeneration. The attractive price and commercial availability of lactic acid are important reasons for PLA development.

In this work, the reaction mechanism PLA synthesis was investigated in order to find useful information for determining the kinetic parameters of the process. For the polymerization were used intermediate temperatures, nitrogen atmosphere, vacuum and short reactions times. Some properties of the PLA synthesized were studied to determinate the possible applications for biomedical area.

1.1 PLA chemistry

The basic building block of PLA is the lactic acid (LA). It is a simple chiral molecule which exists as two enantiomers, L- and D-lactic acid, optically active. It is can be produced by fermentative or chemical synthesis. The petrochemical scheme of monomer production was prevalent until about 1990. Today the most popular route is fermentation, in which sugars and starches are converted into lactic acid by bacterial fermentation using an optimized strain of *Lactobacillus* (Gupta et al, 2007; Adsul et al., 2007).

The PLA is a semi-crystalline polymer with glass transition temperature around 55 to 59°C and melting point 174-184 ° C. It shows a good mechanical strength, high Young's modulus, thermal plasticity and has good processability (Auras et al, 2010). It is relatively hydrophobic polyester, unstable in wet conditions, which can undergo chain disruption in the human body and degrades into nontoxic byproducts, lactic acid, carbon dioxide and water which are subsequently eliminated through the Krebs cycle and in the urine.

1.2 PLA synthesis

There are two important methods for PLA synthesis: direct polycondensation of lactic acid and ring opening polymerization of lactic acid cyclic dimer, known as lactide. Figure 1 shows the reaction mechanism for both of them. In direct condensation, solvent is used and higher reaction times are required. The resulting polymer is a material of low to intermediate molecular weight.

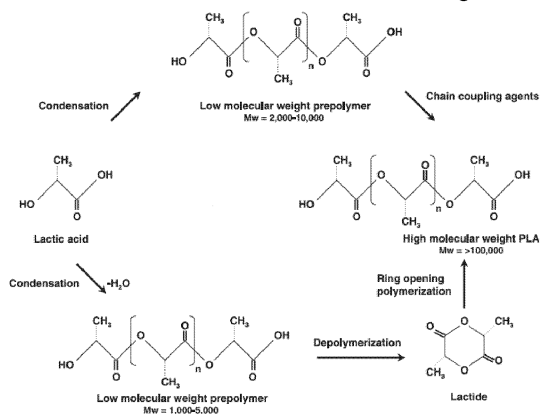


Figure 1: PLA synthesis methods (Gupta et al, 2007)

Ring-opening polymerization (ROP) of the lactide needs catalyst but results in PLA with controlled molecular weight (Gupta et al, 2007). Depending on monomer used and controlling reactions conditions, it is possible to control the ratio and sequence of D- and L-lactic acid units in the final polymer. This polymerization route was select for this study.

2. Materials and Methods

Lactic acid (LA reagent grade) with 85 wt% of purity was used in the polymerization process, and Stannous octoate ($\text{Sn}(\text{Oct})_2$) was used as catalyst.

The polymerization process was carried out in a bench top system (see Fig. 3), composed by two flasks of 0.5 L, a mechanical stirrer, temperature control system, condenser connected to a vacuum pump. The reaction was conducted with and without nitrogen gas to control the system inert atmosphere.

Differential Scanning Calorimetric (DSC) was used to obtain thermal transitions and properties of products . This procedure was performed using a first heating ramp to reach 200°C followed by a cooling to 25°C to erase the thermal history, then a second heating was made to 200°C . Heating and cooling rate was always of $10^\circ\text{C}/\text{min}$ under nitrogen flow of 40 ml/min. The functional groups of PLA and LA were analyzed by Fourier Transform Infrared Spectroscopy (FTIR).

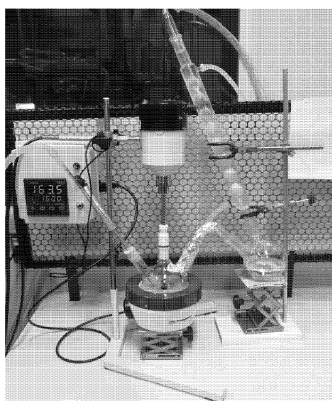


Figure 2: Polymerization experimental system

3. Results and Discussion

PLA polymerization by ROP from lactic acid was carried out in two steps. In the first part of the synthesis occurs the lactide formation, in which lactic acid is heated and, vacuum is used to remove water generated by the union of the monomer molecules. Second part is the disruption of the cyclic ring formed and, the union of open chains of lactide to form the polymer. In this step stannous octoate ($\text{Sn}(\text{Oct})_2$) was used as catalyst to promotes the esterification reaction.

There is not a standard methodology to synthesize PLA, therefore several experiments were made with different conditions in order to determinate suitable reaction temperature for each stage. The conditions were set as 200°C and 4 hr for first step and 160°C and 24 hr for the second one. For each trial around 450 grams of LA was added to the flask then, the monomer was heated to first step temperature gradually to avoid degradation of the reagent. The total condensate was measured at the end of each stage. At the end of the reaction, the product was deposited in a Petri dish and cooled to room temperature. Throughout the process it was observed that most of the condensate was obtained in the first stage, indicating the lactide formation and its subsequent polymerization in the second stage.

During tests we observed that when the reaction was carried out without nitrogen, the water removal was slower, i.e, the nitrogen flow helped in removing the water vapor formed in reactor.

DSC analysis made of products obtained show similar thermal behavior for all samples. Figure 3 shows typical thermograms of DSC run. From the graph can observe a deviation from the baseline that was attributed to the glass transition temperature (T_g) of the material around 40-42 °C. On the other hand, sign of crystallization temperature (T_c) and melting temperature (T_m) were observed around 106 °C and 142 °C respectively.

FTIR analyses were made to determine the functional groups of the products obtained in order to understand more deeply what happens in the polymerization of lactic acid. A qualitative analysis of absorption bands with reaction time shows a decrease in the intensity of some bands and, the formation of new ones, indicating the end groups which decrease and those formed due to the polymerization reaction progress.

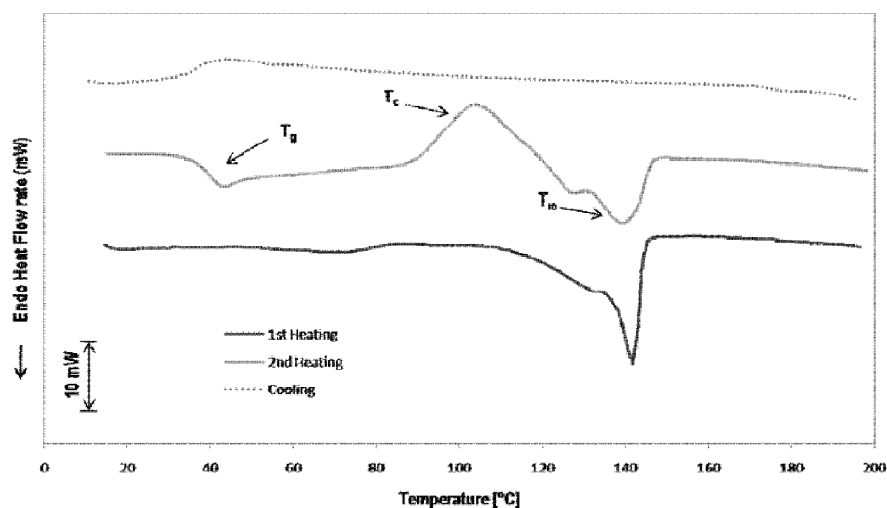


Figure 3: DSC thermogram

Figure 4 shows the FTIR spectrums of the monomer and the poly(D,L-lactic acid) which was obtained from 24h of reaction. The PLA spectrum shows the bands at

2,754.94 and 2,766.51 cm^{-1} from symmetric and asymmetric valence vibrations of C-H from CH_3 , respectively. It is possible to observe a band shift related to the C=O stretch in the monomer in 1,727.06 to 1,757.92 cm^{-1} in the polymer. These bands that show shifts of monomer to polymer also show a difference in the peak intensity which suggests the arrangement of molecules in the polymer chain. Bands corresponding to bending vibrations of CH_3 (asymmetric and symmetric) were found in 1,433.94 and 1,511.08 cm^{-1} in the polymer spectrum as greater intensity peaks compared with those from monomer found in 1,408.87 and 1,476.37 cm^{-1} . C-O-C asymmetrical and symmetrical valence vibrations were found at 1,250.73 and 1,200.59 cm^{-1} respectively; at 1,333.68 cm^{-1} is detected the C-O-C stretching vibration. The band around 3200 cm^{-1} is related to the stretching of OH group and this decreases from the monomer to the polymer due to reaction polyesterification that consumes the OH groups when they react with the acid groups to form the ester bond. These statements are similar those described by Nikolic et al., 2010 and Jahno et al., 2006.

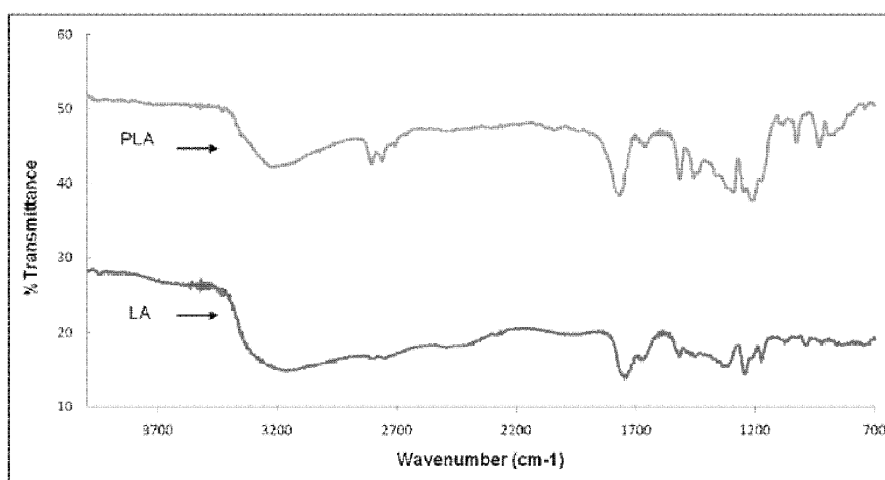


Figure 4: FTIR of PLA and lactic acid

4. Conclusion

Lactic acid polymerization by ring-opening (ROP) was performed in two steps, at 200 °C for 4 hours in step 1 followed by 160 °C for 24 hours in step 2, resulting in a polymer with $T_g = \sim 42$ °C and $T_m = 142$ °C. The use of nitrogen provided an inert atmosphere favorable to the occurrence of the polymerization reaction. By means of FTIR spectra comparisons, it was possible to observe the formation of poly-lactic acid from the monomer.

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