Synthesis and Properties of Poly (DL-lactide)/ Poly (Ethylene Glycol) Diblock Copolymer

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Abstract. Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer is successfully synthesized with mPEG and DL-LA as main raw materials. FT-IR, 1H-NMR and DSC are used to study the influence of precipitant species and dosage on the properties of copolymer; and the effects of the m (mPEG)/ m(LA) ’s ratio on the copolymer’s molecular weight (Mn), glass transition temperature (Tg) and the properties of residual monomers. The results showed that the precipitant was ether, dichloromethane / ether was 1/6, m (mPEG)/ m(LA) was 2/1.8, the synthesized Poly (DL-lactide)/ Poly (Ethylene Glycol) Diblock Copolymers, the residual monomer was only 0.26 and the solvent residue was only 0.04.

Keywords: Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer; DL-LA; mPEG.

1. Introduction

Polylactic acid (PLA) was a hydrophobic substance and its degradation cycle was difficult to control. By copolymerizing with other monomers, the hydrophilicity and hydrophobicity, crystallinity and degradation rate can be changed to overcome the limitation of molecular weight and distribution alone to regulate degradation rate alone. Polyethylene Glycol (PEG) was a widely used polyether polymer compound, which had excellent biological compatibility and blood compatibility, as well as good hydrophilicity and softness. By introducing PEG into PLA molecular structure, amphiphilic block copolymers containing hydrophilic PEG segment and hydrophobic PLA segment were obtained, which improved PLA hydrophilicity and poor compliance, degradation cycle difficult to control and other shortcomings. Moreover, the copolymer can self-assemble in water medium to form a core hydrophobic, shell hydrophilic micelles, which can assemble hydrophobic drug molecules into the micelle interior, which had the function of improving the circulation time of drugs in blood, prolonging the biological half-life, controlling drug release and targeting distribution of specific tissues. Therefore, the study of Polylactic acid-Polyethylene Glycol degradable amphiphilic block copolymers was very important for...
its application in controlled release drug delivery system, which provided a meaningful new carrier material for the research of biomedicine and tissue engineering. [1-6].

In this paper, the Polylactide/Polyethylene Glycol Diblock Copolymer (Poly) Poly (DL-lactide) Diblock Copolymer m) was prepared by copolymerization of Polylactide/Polyethylene Glycol monomethyl ether as the main raw material, and the effect of m ratio (m PEG)/ m (DLLA) on the structure and properties of block copolymer was studied; The effect of different kinds of precipitant on the residual monomer for block copolymers and productivity was studied.

2. Experimental

2.1. Materials
Racemic lactide (DL-LA) purity >99.5%, provided by jinan daigang biotechnology limited public Company. Poly (Ethylene Glycol) methyl ether (mPEG, Mn=2000), ethyl acetate, dichloromethane, Stannous caprylate (SnOct2), ethyl ether, n-hexane, anhydrous ethanol, etc. are all analytically pure (AR), which are provided by Sinopharm Chemical Reagent Co., Ltd. All raw materials must be dried before used.

2.2. Instruments and Equipment
Vacuum drying oven, Shanghai Senxin Laboratory Instrument; Fourier transform infrared spectrometer, model FT-IR 100, Perkin Elmer Company; Nuclear magnetic resonance instrument, model DRX 400MHz, Bruker Company, Germany; Differential scanning calorimeter, DSC 214, Netzsch Company, Germany, etc.

2.3. Preparation of Poly(DL-lactide)/Poly(Ethylene Glycol) Diblock Copolymer
Adding DL-LA, mPEG and SnOct2 into an ampoule bottle with a rotor according to a certain proportion, vacuum sealing the tube, stirring at 170℃ for 8 hours, and cooling to obtain crude Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer. A series of Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymers with different m(mPEG)/m(DL-LA) ratios were obtained by extraction and purification. The polymerization equation was shown in Figure 1.

![Figure 1. Polymerization equation](image)

2.4. Performance Characterization
Fourier transform infrared spectroscopy (FT-IR): The molecular structure of polymer was determined by FT-IR. Nuclear magnetic resonance (1H-NMR): The molecular structure of the polymer was determined by NMR. Deuterium CCL4 was used as solvent and tetramethylsilane (TMS) was used as internal standard. Glass transition temperature (Tg): Nitrogen atmosphere was measured by differential scanning calorimeter, and the heating rate was 20℃/min.

3. Result and Discussion

3.1. Molecular Structure Characterization
The prepared Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer was extracted and purified by CHCl3 and petroleum ether for three times, removed the residual monomer, and its molecular structure was determined by Nuclear magnetic resonance hydrogen spectrometer and Fourier transform infrared spectrometer. The molecular structure of Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock
Copolymer was quantitatively determined by Nuclear magnetic resonance hydrogen spectrometer, and the results were shown in Figure 2.

**Figure 2.** $^1$H-NMR of Poly (DL-lactide)/ Poly (Ethylene Glycol) Diblock Copolymer

From the $^1$H-NMR spectra of Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer, it is shown that the quadruple splitting peak at $\delta = 5.17$ is caused by the hydrogen proton on -CH in PLA, the double splitting peak at $\delta = 1.57$ is caused by the hydrogen proton on -CH$_3$ in PLA, and the single peak at $\delta = 3.643$ is caused by the hydrogen proton on -CH$_2$ in mPEG segment. The structure of the synthesized polymer was confirmed by $^1$H-NMR.

**Figure 3.** FT-IR of Poly (DL-lactide)/ Poly (Ethylene Glycol) Diblock Copolymer

The molecular structure of Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer was qualitatively determined by Fourier transform infrared spectrometer, and the results were shown in Figure 3.

As shown in Figure 3, the stretching vibration characteristic peak of -CH$_3$ is at 2997cm$^{-1}$, the stretching vibration characteristic peak of -CH is at 2947cm$^{-1}$, and the characteristic absorption peak of -CH$_2$ is at 2882cm$^{-1}$. The 1095cm$^{-1}$ and 1278cm$^{-1}$ are C-O-C asymmetric telescopic vibration absorption peak and symmetric telescopic vibration absorption peak respectively. The stretching vibration characteristic peak of C=O appears at 1751cm$^{-1}$. There is no vibration absorption peak of ring skeleton at 934cm$^{-1}$, which explained that there was no ring structure and lactide basically reacted completely.

It can be seen from the analysis of $^1$H-NMR and FT-IR spectra that the synthesized products were all Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer with predetermined structure.
3.2. Selection of Precipitant Varieties
We adopted direct melt polymerization to get the PLA- mPEG block copolymer, which may have some impurities, such as lactide monomer, mPEG, PLA, low molecular polymer, oxidation impurities, etc. It was necessary to purify the Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer. The polymer was completely dissolved in dichloromethane and then precipitated with different precipitating agents to obtain purified Poly (DL-lactide)/ Poly (Ethylene Glycol) Diblock Polymers. The effects of several different precipitants on the properties of copolymers were compared, as shown in Table 1.

| Precipitant            | mDCM/m (Precipitant) | Appearance    | LA Residue/(wt%) | Productivity/(wt%) |
|------------------------|----------------------|---------------|------------------|--------------------|
| n-hexane               | 1/3                  | white solid   | 1.32             | 89.0               |
| ethyl ether            | 1/6                  | Buff solid    | 0.26             | 81.1               |
| anhydrous ethanol      | 1/12.5               | white powder  | 0.36             | 82.3               |

It can be seen from Table 1 that when the precipitant was n-hexane, the amount of the precipitator was the least and the Productivity was the highest, but the DL-LA residual amount was up to 1.32%, the resulting sediment sticks to the bottom of the bottle and was hard to filter out and clean; When the precipitant was anhydrous ethanol, the amount was the highest, and the Productivity was 82.3%, the monomer residue was 0.36%, However, the amount was large, which increases the raw material cost; When the precipitant was ethyl ether, the dosage was 6 times that of dichloromethane, and the Productivity and residual monomer were the lowest. Overall, the precipitation effect of ethyl ether was better than that of n-hexane and anhydrous ethanol.

3.3. Determination of Poly(DL-lactide)/Poly(Ethylene Glycol) Diblock Copolymer’s Properties
According to the test results of nuclear magnetic spectrum, m(mPEG)/m(DLLA) values in molecular chains of Poly (DL-lactide)/ (Ethylene Glycol) Diblock Copolymers with different m (m PEG)/ m (DLLA) ratio were calculated, and its performance was measured. the results were shown in table 2.

As shown in Table 2, with the decrease of m (mPEG)/ m (DL-LA) ratio and the amount of DL-LA increased, the obtained molecular weight of PLA chain segment in the Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer increased. However, the PLA segments in the Diblock copolymer are lower than the actual input, it’s possibly because that the system contains unreacted DL-LA, PLA homopolymer and other impurities, which were removed after extraction and purification, and reduced the proportion of PLA segments in Poly Diblock copolymers. Table 2 also showed that the Tg of Diblock copolymer increased with the decrease of m(mPEG)/m(DL-LA) ratio. Meanwhile, the prepared Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer had lower solvent residues, monomer residues, and higher productivity, all of which are above 80%.

| Numble | m(mPEG)/m (LA) | Mn(mPEG)/Mn (PLA) | LA Residue/(wt%) | Solvent Residue/(wt%) | Tg/℃ | Productivity/(wt%) |
|--------|----------------|-------------------|------------------|-----------------------|------|--------------------|
| 1      | 2/2            | 2000/1890         | 0.13             | 0.024                 | -40.2| 83.0               |
| 2      | 2/1.8          | 2000/1676         | 0.26             | 0.04                  | -41.6| 81.1               |
| 3      | 2/1.6          | 2000/1488         | 0.36             | 0.1                   | -42.3| 82.3               |

4. Conclusion
In this paper, Poly (DL-lactide)/Poly (Ethylene Glycol) Diblock Copolymer was successfully synthesized with mPEG and DL-LA as main raw materials, in which m(mPEG)/ m(LA) was 2/1.8, and the precipitant was ethyl ether. The copolymer had excellent hydrophilicity and flexibility, and can be used as a pliable modifier for the modification of postoperative suture lines and isolation materials,etc. Meanwhile, the copolymer also had hydrophilic and hydrophobic chain segments, and they can form
micelles in water medium, which can be used in the fields of controlled release of drugs, targeted drug application and so on, all of which had broad application prospects.

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