Effect of glycolide dosage on molecular weight of poly (lactic-co-glycolic acid)

Xiaoqi Chen1, Lu Bai2, Jia Tian2, Haijun Zhou4, Mengmeng Zhou1, Jijun Xiao2 and Yantao Li1,*

1 Institute of Energy Source, Hebei Academy of Sciences, Shijiazhuang, China
2 Hebei University of Science and Technology, Shijiazhuang, China

*Corresponding author e-mail: xiaojj@hebust.edu.cn

Abstract. A series of biodegradable polymers, poly (lactic-co-glycolic acid) (PLGA) were prepared by ring-opening polymerization with racemic lactide and glycolide as main raw materials. Gel Permeation Chromatography (GPC), differential scanning calorimetry (DSC) and ubbelohde viscometer were used for the characterizations of the PLGA. And the effect of glycolide’s (GA) content on molecular weight (Mw), vitrification transition temperature (Tg), intrinsic viscosity [η] of PLGA was discussed. The results show that the GA’s content in PLGA molecular structure is higher than the actual feeding ratio. Meanwhile, with the increase of GA’s content, the Mw, [η] and Tg of PLGA decreased.

1. Introduction
Polylactic acid has good biocompatibility and biodegradability, so it is widely used in biomedicine, disposable products, electronics and other fields. However, due to the limitation of polylactide (PLA) structure, it also shows certain defects, such as strong hydrophobicity, lack of active groups, and difficult to control the degradation cycle. Copolymerization modification has always been an important direction to improve performance in the synthesis of polymer materials. By introducing new polymer chains, the performance defects of the original can be modified by introducing new polymer segments. Polyglycolic acid is the simplest linear aliphatic polyester, which molecular structure is less methyl groups than polylactic acid, and it has high crystallinity, good mechanical properties, good hydrophilicity, and its degradation rate in the body is much faster than polylactic acid. Therefore, the introduction of polyglycolic acid into polylactic acid can improve the shortcomings of polylactic acid. [1-6]

In this paper, through the ring-opening copolymerization of glycolide and racemic lactide, prepared PLGA biodegradable materials with different GA’s content. The effects of glycolide’s content on molecular weight (Mw), vitrification transition temperature (Tg) and intrinsic viscosity ([η]) of poly (lactic-co-glycolic acid) were mainly studied.
2. Experimental

2.1. Materials
Racemic lactide (DL-LA), glycolide (GA), purity >99.5%, provided by Jinan Daigang Biotechnology Co., Ltd. Recrystallize in ethyl acetate before used. The amount of ethyl acetate was 1.1 times of the unit, and it is dried under reduced pressure to constant weight for used. Ethyl acetate, dichloromethane, absolute ethanol, stannous octoate (SnOct₂) and dodecanol are all analytically pure (AR), which are obtained from Sinopharm Chemical Reagent Co., Ltd, and need to be dried before used.

2.2. Equipment
Vacuum drying oven (Shanghai Senxin experimental instrument), fourier transform infrared spectrometer (FT-IR 100, Perki Elmer Co.), nuclear Magnetic Resonance (DRX 400MHz, Germany Bruker Co.), differential scanning calorimetry (DSC 214, Germany Netzsch Co.), etc.

2.3. Preparation of PLGA biodegradable material
At first, according to a certain proportion, dry DL-LA, GA, SnOct₂ and initiator are added into an ampoule bottle with a rotor, and the tube is sealed in vacuum. Then react at 175°C for 8h to obtain crude PLGA. A series of biodegradable materials with different GA’s content were obtained by extracting and purifying the prepared PLGA. The reaction equation was shown in Figure 1.

\[
R\text{-OH} + n\begin{array}{c}
\text{O} \\
\text{O}
\end{array} + m\begin{array}{c}
\text{O} \\
\text{O}
\end{array} \xrightarrow{\text{Cat}} H\begin{array}{c}
\text{O} \\
\text{O}
\end{array} \begin{array}{c}
\text{O} \\
\text{O}
\end{array} \begin{array}{c}
\text{O} \\
\text{O}
\end{array} \begin{array}{c}
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\end{array} \begin{array}{c}
\text{O} \\
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\end{array} \begin{array}{c}
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\text{O} \\
\text{O}
\end{array} \begin{array}{c}
\text{O} \\
\text{O}
\end{array}
\]

Figure 1. Reaction equation of PLGA

2.4. Characterization
The molecular structure of polymer was measured by Fourier transform infrared spectrometer (FT-IR). The molecular structure of polymer was measured by nuclear magnetic resonance (¹H-NMR), using deuterated CCL₄ as solvent and tetramethylsilane (TMS) as internal standard. The intrinsic viscosity[η] of polymer was measured by Ubbelohde viscometer in a water bath at 25°C, the solvent is chloroform, and calculated it by extrapolation. Vitrification transition temperature (Tᵥ) was measured with a differential scanning calorimetry, nitrogen atmosphere, and the heating rate was 20°C/min.

3. Results and discussion

3.1. The characterization of molecular structure
The molecular structure of poly (lactide) was quantitatively determined by using nuclear magnetic resonance hydrogen spectrometer, according to the ¹H-NMR spectrometer of PLGA with different GA’s contents, calculated the proportion of n (GA)/ n (LA) in molecular chain of poly (lactide). The results were shown in Figure 2 and Table 1.
As the $^1$H-NMR spectrum of PLGA shown in Figure 2, the characteristic groups: 1.57 (LA-CH$_3$), 4.80 (GA-CH$_2$) and 5.20 (LA-CH) can be identified from the chemical shift value, $^1$H-NMR initially confirmed the structure of the synthesized polymer. It can be seen from Table 1 that the GA structure in the molecular chain of PLGA is slightly higher than the feeding ratio. It is mainly because the reactivity ratio of the two monomers is quite different, $r$(GA)=2.8, $r$(LA)=0.2, GA has high reactivity and is easy to react completely.

Fourier transform infrared spectrometer was used to qualitatively determine the molecular structure of PLGA. The results are shown in Figure 3.

| Numble | GA/(mol%) | n(GA)/n(LA)   |
|--------|-----------|---------------|
| 1      | 20        | 20.93/79.07   |
| 2      | 24        | 24.52/74.48   |
| 3      | 28        | 28.58/69.42   |
| 4      | 32        | 32.52/62.48   |

Figure 2. The $^1$H-NMR spectrum of PLGA

Table 1. GA/LA ratio in PLGA molecular structure
The FT-IR spectrum of PLGA is shown in Figure 3. The stretching vibration absorption peak of linear C=O bond is 1748 cm\(^{-1}\), the stretching vibration absorption peak of C-C is on 1451 cm\(^{-1}\), the stretching vibration absorption peak of C-O-C is on 1176 cm\(^{-1}\), but there are no GA and DL-LA’s absorption peaks on 1210 cm\(^{-1}\) and 1240 cm\(^{-1}\). It can be confirmed that the target polymer has been obtained with NMR.

3.2. Influence of GA’s content on the physical and chemical properties of PLGA
Intrinsic viscosity, copolymer composition, molecular weight and its distribution are important indexes of PLGA biodegradable materials. In this paper, we study the influence of GA’s content on the M\(_w\) and \([\eta]\) of PLGA, and the results are shown in Table 2.

| Numble | GA/(mol\%) | M\(_w\) | \([\eta]/(dl/g)\) |
|--------|------------|---------|------------------|
| 1      | 20         | 67767   | 0.4365           |
| 2      | 24         | 67544   | 0.3823           |
| 3      | 28         | 67344   | 0.3427           |
| 4      | 32         | 64205   | 0.3195           |

As shown in Table 2, with the increase of GA’s content, the M\(_w\) and \([\eta]\) of PLGA decreased, and the \([\eta]\) decreased significantly, while the M\(_w\) measured by GPC decreased slightly. This was due to polyglycolide acid(PGA) with poor solubility was easy to be produced with the increase of GA’s content, and the retention time is affected by incompletely dissolved PGA in GPC determination, which leads to the high molecular weight of the measured polymer; when we measured\([\eta]\), because of the homopolymer PGA with incompletely dissolved in PLGA solution, lead to the viscosity of polymer solution was low, then the measured \([\eta]\) is also low.

3.3. Effect of GA Content on Tg of Polylactide
In the research on the modification of polylactic acid, the vitrification transition temperature is an important physical and chemical parameter to characterize its performance. Therefore, the T\(_g\) of research materials has an important guiding significance for correct use and development research. This paper studied the influence of different GA’s content on the T\(_g\) of PLGA, as shown in Table 3.

| Numble | GA/(mol\%) | T\(_g\) |
|--------|------------|--------|
| 1      | 20         | 54.82  |
| 2      | 24         | 52.55  |
| 3      | 28         | 51.52  |
| 4      | 32         | 50.29  |

It can be seen from Table 3 that as the GA’s content increased, the T\(_g\) of PLGA significantly decreased. This is because that the T\(_g\) of poly(lactide) (PLA) is 60–65\(^\circ\)C, and the T\(_g\) of poly(glycolide) (PGA) is 35–40\(^\circ\)C. With increasing of GA’s content, the T\(_g\) of PLGA decreased.

4. Conclusion
In this paper, the direct ring-opening reaction of racemic lactide and glycolide successfully introduced GA segments into the molecular structure of polylactic acid, and obtained PLGA biodegradable materials. The molecular weight of it more than 600,000, which has excellent hydrophilicity, good biocompatibility, and bioabsorbability, can be used in medical fields such as surgical sutures and pharmaceutical carriers, etc.
References

[1] NN W, CH Ma, PY Zhang. Study on Hydrophilicity of Poly(glycolide-co-lactide) [J]. Polymer bulletin, 2012, 06:83-86.

[2] Z Guo, PH Zhang. The Recent Advances in PGA, PLA and PGLA Fibers [J]. Synthetic Fiber in China, 2009, 03:7-11.

[3] Fang X, Xiao M, Wang S, et al. Synthesis and characterization of high molecular weight polyglycolide [J]. Gaofenzi Cailiao Kexue Yu Gongcheng/polymeric Materials Science & Engineering, 2012, 28(1):1-4.

[4] Estelle G, Patrick F, Philippe C, et al. Synthesis and rheology of biodegradable poly (glycolic acid) prepared by melt ring-opening polymerization of glycolide [J]. Journal of Polymer Science: Part A: Polymer Chemistry, 2009, 47:1440-1449.

[5] WANG Ning and YIN Huihui. Review on the preparation method of lactic acid-glycolic acid copolymer [J]. Wool Textile Journal, 201846(9): 84-90.

[6] GKTRK E, PEMBA A G, MILLER S A. Polyglycolic acid from the direct polymerization of renewable C1 feedstocks [J]. Polymer Chemistry, 2015, 6(21): 3918-3925.