

# Studies on the Block Copolymerization of D,L-Lactide and Poly(ethylene glycol) with Aluminum Complex Catalyst

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## SYNOPSIS

A series of block copolymers from D,L-lactide and poly(ethylene glycol) (PEG) with different molecular weights were synthesized by using  $\text{Al}(\text{i-Bu})_3\text{-H}_3\text{PO}_4\text{-H}_2\text{O}$  as the initiator and identified by  $^1\text{H-NMR}$ , GPC, and DSC. The elongation at break of the material increased when PEG was introduced, but the strength of the material decreased. The copolymers degrade more smoothly *in vitro* than did the PLA homopolymer. © 1995 John Wiley & Sons, Inc.

## INTRODUCTION

Poly(lactide) (PLA) is a biodegradable material that is nontoxic and biocompatible. To adapt the properties of PLA for clinical use, many efforts have been made to improve this family of the polymer since the 1970s. For example, the lactide- $\epsilon$ -caprolactone copolymer<sup>1</sup> and lactide-glycolide copolymer<sup>2</sup> have been investigated for drug-delivery systems and surgical application. The main purpose of all the efforts is to introduce other monomers with different characters so that the degradation, drug delivery, and mechanical properties of copolymers can be improved.

Polyethers, especially poly(ethylene glycol) (PEG), are hydrophilic and biocompatible and may be used in copolymerization with D,L-lactide for improving the brittleness and hydrophobic property of PLA. It is possible to control the degradation and delivery of the material by changing the composition. It is also expected to reduce the amount of surfactant needed in producing the polymer-drug microsphere. Thus, this kind of biodegradable polyester-polyether block copolymers has been given much attention.<sup>3-5</sup> The purpose of this article was to synthesize D,L-lactide-PEG block copolymers (PELA) using the  $\text{Al}(\text{i-Bu})_3\text{-H}_3\text{PO}_4\text{-H}_2\text{O}$  complex catalyst and to investigate the mechanical properties and degradation *in vitro* of the copolymer.

## EXPERIMENTAL

D,L-Lactide was added into a dried polymerization tube and mixed with a prescribed amount of PEG and the catalyst.<sup>6</sup> The copolymerization was carried out under nitrogen atmosphere at the temperature above the melting point of D,L-lactide. When the copolymerization was completed, the reaction product was dissolved in acetone, precipitated in a large amount of water, and washed in hot water to remove the PEG homopolymer. The resulting product was dried in vacuum and readied for characterization.

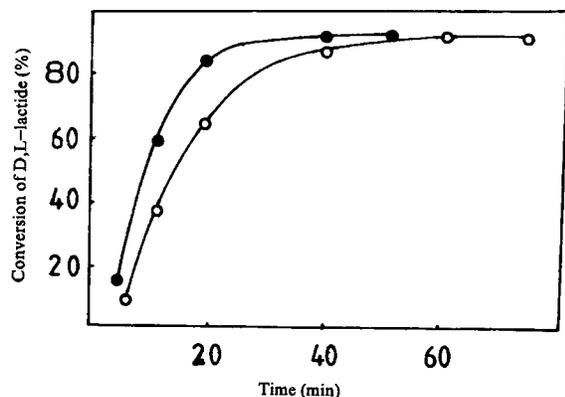
$^1\text{H-NMR}$  spectra were recorded on a Varian FT-80A NMR spectrometer at room temperature in  $\text{CDCl}_3$ , with TMS as the internal standard. The glass transition temperature was obtained using a Perkin-Elmer DSC7 thermal analysis apparatus. Molecular weights and weight distribution were evaluated by means of GPC using a Water Associates Model Alc/gpc 244 apparatus. Molecular weight was calibrated relative to monodispersed polystyrene.

## RESULTS AND DISCUSSION

### Copolymerization

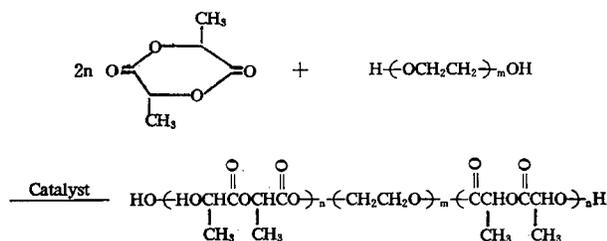
Many catalysts can be utilized to initiate the ring-opening polymerization of D,L-lactide, such as stannous chloride, tetraphenyltin, zinc oxide, and metal alkoxide, preferably stannous octoate. Here, we used a complex catalyst of triisobutylaluminum together

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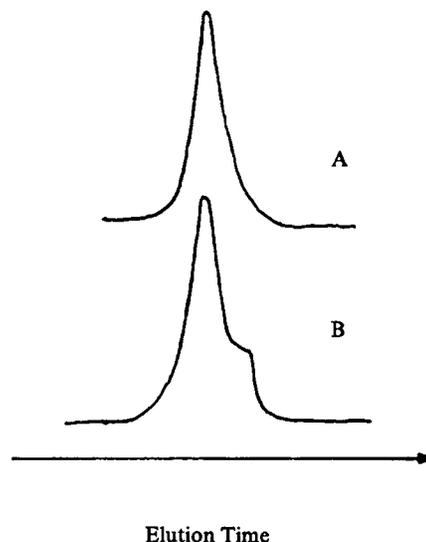


**Figure 1** Time-conversion curve for the copolymerization of D,L-lactide with PEG4000 at (O) 140°C and (●) 160°C.

with phosphoric acid and water to initiate the copolymerization of D,L-lactide with PEG. The following equation schematizes the process of the polymerization of D,L-lactide with the aluminum catalyst:



In Figure 1, the relationship between the conversion of D,L-lactide and polymerization time at different temperatures is presented. The influence of temperature on the conversion rate of the monomer is identical. The reaction rate increased with the rise of polymerization temperature. After 1 h, the



**Figure 2** GPC traces of (A) PLA/PEG (90/10) block copolymer and (B) PELA/PEG (90/10) blend mixture.

conversion rate of the monomer did not rise again in either case.

The PELA copolymers with different compositions are given in Table I. The molecular weight of the copolymers changed with the composition and was almost in accordance with the results by the calculation on the assumption that all PEG was incorporated into the polymer product. The most important factors that have a great influence on the molecular weight of the product are the feed ratio of PEG and the quality of the catalyst itself.

### Characterization

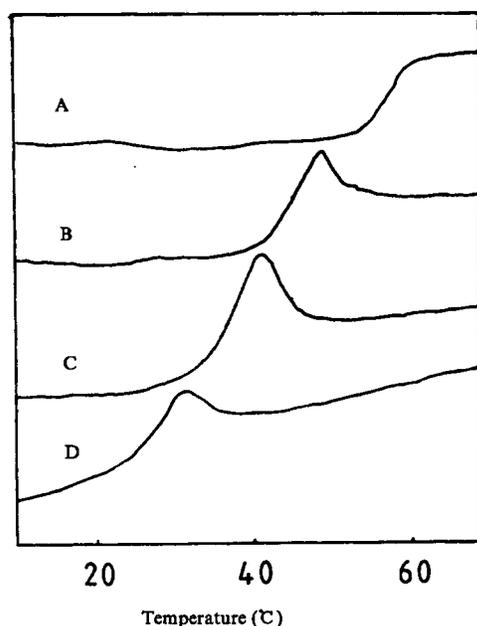
The GPC traces of the crude copolymers are shown in Figure 2. Only a single peak appeared, which is

**Table I** Block Copolymerization of D,L-Lactide and PEG

| Samples | PEG in Feed (%) | Conversion (%) | $M_n^a$ ( $\times 10^{-4}$ ) | $M_n^b$ ( $\times 10^{-4}$ ) | $M_w/M_n$ |
|---------|-----------------|----------------|------------------------------|------------------------------|-----------|
| 1       | PEG1500         |                |                              |                              |           |
|         | 6               | 92             | 2.7                          | 2.6                          | 1.56      |
| 2       | 10              | 89             | 1.3                          | 1.5                          | 1.42      |
| 3       | PEG4000         |                |                              |                              |           |
|         | 5               | 97             | 7.8                          | 8.0                          | 1.83      |
| 4       | 10              | 95             | 4.5                          | 4.0                          | 1.65      |
| 5       | 15              | 91             | 3.3                          | 2.7                          | 1.47      |
| 6       | PEG6000         |                |                              |                              |           |
|         | 20              | 91             | 4.9                          | 3.0                          | 1.29      |

<sup>a</sup> By GPC in THF with polystyrene as the reference.

<sup>b</sup> Calculated from the composition.



**Figure 3** DSC traces of PLA/PEG block copolymers containing PEG4000 (A) 0%, (B) 5%, (C) 10%, and (D) 15%.

due to the copolymer's elution volume peak. The elution volume peak of the PEG homopolymer was undetected except for the case of the blend mixture of PELA and PEG (trace B). This was evidence to identify which block copolymer had been produced.

As PEG can dissolve in water, it is possible to isolate the unreacted PEG from the copolymer by the dissolution-precipitation method in the acetone-water system. The  $^1\text{H-NMR}$  spectrum of the PELA copolymer purified in this way shows that the peaks at 5.10 and 1.50 ppm are assigned to methine protons and methyl protons of PLA homopolymer units, and the peak at 3.57 ppm is due to the methylene protons of homosequences of PEG oxyethylene units.

The dependence of the thermal behavior of the copolymers on the composition was investigated by DSC analyses. The results are shown in Figure 3. Poly(D,L-lactide) is an amorphous polymer with a glass transition temperature of about 59°C.

PEG4000 belongs to a crystalline material with a melting point at about 50°C. But the copolymers from D,L-lactide and PEG4000 have no melting endotherms in the DSC curves, only having a glass transition temperature, i.e., PELA copolymers obtained in this way also belong to an amorphous polymer. As expected, the glass transition temperature of the copolymers decreased with increase of PEG in the copolymers. The incorporation of PEG gives the PLA-PEG copolymers some extent of soft properties.

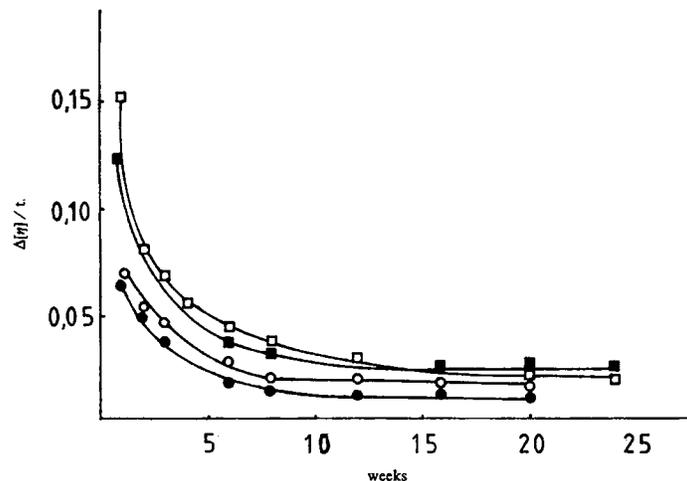
The mechanical properties of the PLA homopolymer and PELA copolymers are described in Table II. They seem to be identical. The PLA homopolymer has a much higher mechanical strength than that of PELA copolymers. This is due to the drop of molecular weight in copolymers and the employment of the flexible PEG chain segment. The elongation at break of the material increased sharply with increase in the amount of PEG in the polymers.

*In vitro* degradation of polymer films was evaluated in a 0.9% sodium chloride solution of water at 37°C. Three copolymer samples with different compositions and one of the PLA homopolymers were investigated. The results are shown in Figure 4. Except during the several weeks of the initial stage, the copolymers degraded more smoothly. But the degradation lifetime of the PLA homopolymer was longer in water, which was about 43 weeks for complete degradation. The degradation lifetime of PELA copolymers was no longer than 25 weeks and decreased with increase of the amount of PEG in the copolymers. This is because the PLA homopolymer and the PELA copolymers had different molecular weights, which for PLA was about  $3.2 \times 10^5$ . On the other hand, a main pattern of the degradation occurring through the polymer matrix is by diffusion-controlled hydrolysis. With introducing the hydrophilic PEG segments, the diffusion and the permeability of water through the block copolymer PELA is facilitated. Therefore, the hydrolytic erosion of the copolymer is well distributed in the process and, also, the degradation rate of PELA is smoother

**Table II** Mechanical Properties of PLA and PELA

| Material                              | PEG4000 (%) | $T_g$ (°C) | Stress (max) (MPa) | Modulus (GPa) | Elongation at Break (%) |
|---------------------------------------|-------------|------------|--------------------|---------------|-------------------------|
| D,L-PLA ( $M_v$ 320,000) <sup>a</sup> | 0           | 59         | 108.8              | 2.84          | 136.0                   |
| PELA                                  | 5           | 44         | 40.2               | 0.98          | 306.0                   |
|                                       | 10          | 36         | 13.7               | 0.03          | 650.0                   |

<sup>a</sup> Measured at 37°C in THF from the relation<sup>7</sup>  $[\eta] = 1.04 \times 10^{-4} M_v^{0.75}$ .



**Figure 4** Degradation of (□) PLA and three block copolymers comprising PEG4000 (■) 5%, (○) 10%, and (●) 15%.

than that of PLA. The molecular weight of polymers may influence only the degradation period, but the composition of copolymers may also influence the degradation rate.

## CONCLUSION

Block copolymers from D,L-lactide and PEG can be synthesized by a *tiisobutylaluminum*–phosphoric acid–water complex catalyst. The molecular weight of copolymers varied with the change of composition. The glass transition temperature of copolymers changed from 59 to 24°C when the amount of PEG4000 in copolymers increased from 0 to 15%. Mechanical property analyses indicated that some soft characteristics had been produced while the strength of copolymers decreased. An *in vitro* degradation test of the copolymers showed that they degraded at a smooth rate. Thus, this kind of copolymer might be very useful in biomedical applications.

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