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### Degradable Polymers. II. Synthesis, Characterization, and Degradation of an Aliphatic Thermoplastic Block Copolyester

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## **Degradable Polymers. II. Synthesis, Characterization, and Degradation of an Aliphatic Thermoplastic Block Copolyester**

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### ABSTRACT

A degradable aliphatic thermoplastic elastic block copolymer, poly(ethylene glycol)/poly(ethylene succinate), was synthesized by a two-step process with polycondensation and chain extension. Fibers of the block copolymer were extruded at 95°C and cold drawn to yield an oriented product. These fibers degraded in vitro at 37°C. The degradation process was hydrolysis of the amorphous parts which induced a rapid loss of tensile strength (to 7% of the original value in 10 days) but no significant weight loss. The hydrolysis involved chain scission, as shown by GPC, and "selective" degradation, as shown by DSC and <sup>1</sup>H-NMR.

### INTRODUCTION

There is a great need in surgery for materials that are similar to human tissue with respect to tensile strength and elasticity [1]. Polyurethanes can be made with a variety of properties, but they may show adverse tissue reactions due to residual isocyanate groups, and they are not inert in human tissue.

Biodegradable aromatic block copolyesters have previously been made [2] but, to our knowledge, no aliphatic types have been produced. These materials can be made as thermoplastic elastomers, thus making it possible to construct devices by the usual methods, such as fiber extrusion or injection molding.

Another application of biodegradable block copolymers made from polyethylene glycol is as the substrate for the attachment of drugs. These so-called functional polymers can then release their drug at a controlled rate [3].

Crosslinked aliphatic polyester elastomers have been synthesized from a 1:1 mixture of valerolactone and caprolactone with biscaprolactone as a crosslinking agent [4]. We have chosen poly(ethylene glycol)/poly(ethylene succinate) (PEG/PES) as a model because of the degradability of the aliphatic polyester block [5, 6].

## EXPERIMENTAL

### Materials

Dimethyl succinate (synthesis grade), ethylene glycol (p.a.), poly(ethylene glycol) MW = 400 (GC grade), and tetraisopropyl orthotitanate (synthesis grade) were obtained from E. Merck (West Germany). The glycols were used as received. The titanate and the succinate were purified by distillation and the titanate was stored under nitrogen in sealed amber bottles.

### Synthesis

The reagents (dimethyl succinate (0.6 mol, 87.63 g), ethylene glycol (0.9 mol, 55.86 g) and poly(ethylene glycol) (0.05 mol, 21 g)) were added to a carefully dried 3-necked kettle, and nitrogen was bubbled through for a minimum of 15 min with rapid stirring. The temperature was then raised over 30 min to 180°C, and this condition was held for 2 h. The catalyst (tetraisopropyl titanate, 0.5 wt% of the reagents) was added immediately before vacuum was applied by replacing the combined distilling head and nitrogen inlet with a vacuum line. The pressure was lowered to <1 torr over 30 min. The temperature was then raised to 240°C, and this condition was maintained for 6 h.

The resulting brown viscous product was dissolved in dichloromethane and precipitated into methanol with a yield of 60%. This purified block copolymer was then chain extended with adipoyl chloride by the following procedure.

### Chain Extension (Example)

The polymer (5 g) was dissolved in 100 mL dry dichloromethane and 10 mL dry pyridine. A solution of 0.5 g adipoyl chloride in 10 mL dry dichloromethane was slowly added to the polymer solution at room temperature with stirring and nitrogen bubbling. When the addition was completed, the solution was refluxed for 5 h. The extended polymer was precipitated into methanol. The yields were  $75 \pm 2\%$ .

### Polymer Characterization

The block copolymer was characterized by GPC, DSC, IR, NMR, and tensile strength measurements. A Waters 6000 A pump with 6 columns ( $100\text{-}10^6$  Å) connected to a differential refractometer was used for GPC, with THF as the solvent, and the flow rate was 1 mL/min. The apparatus was run at room temperature with the solvent pressure at 6.9 MPa (1000 psi). The apparatus used for DSC was a Perkin-Elmer DSC-2 with a heating rate of  $10^\circ\text{C}/\text{min}$ . The sample weight was 5 mg. The IR used was a Perkin-Elmer 580B, with sample films on NaCl windows. The NMR was a Bruker WP 200. Tensile strength was measured with an Instron 1122 equipped with pneumatic grips (No. 2714-002).

### Polymer Degradation

Fibers of the block copolymer were extruded at  $95^\circ\text{C}$  in an extrusion device made in our workshop. The fibers were then necked at room temperature, and the oriented products had diameters of  $0.45 \pm 0.05$  mm. The tensile strength was  $6.3 \pm 0.6$  N at fracture with  $100 \pm 20\%$  elongation. These fibers were placed in test tubes containing 7.5 mL pseudoextracellular fluid [7] (Table 1) thermally stabilized at  $37^\circ\text{C}$ . Samples were taken after 3, 7, 18, 39, and 77 days, cleaned with distilled water, and dried to constant weight, then characterized in the following order: tensile strength (if possible), DSC, GPC, IR, and NMR.

The water in the pseudoextracellular fluid from the 77-day sample was evaporated, and the resulting mixture of materials was extracted with 1 mL chloroform. This solution was used for the GPC measurement of the water-soluble fraction.

## RESULTS AND DISCUSSION

The  $^{13}\text{C}$ -NMR spectra (Fig. 1) show the different steps in block copolymerization and chain extension, and the peak assignments are shown

TABLE 1. Composition of the Pseudoextracellular Fluid<sup>a</sup>

Salt <sup>b</sup>	Concentration, meq/L
NaCl	95
KCl	5
Ca(Ac) <sub>2</sub> ·H <sub>2</sub> O	4
MgSO <sub>4</sub> ·7H <sub>2</sub> O	2
Na <sub>2</sub> HPO <sub>4</sub> ·7H <sub>2</sub> O	2

<sup>a</sup>NaOH to adjust to pH 7.4.

<sup>b</sup>Analytical reagent grade.

in Table 2. The ratio polyether/ester in the monomer feed was 0.083 mol polyether per mol ester and, since the molecular weight of the polyether was 400, the carbon ratio was 0.758 mol polyether carbon per mol ester carbon. This is confirmed by the intensity ratio of 0.796 for the corresponding <sup>13</sup>C-NMR peaks (B/D, Fig. 1b).

The DSC curves (Fig. 2) show that the crystallinity and the melting point decrease when the polyether is introduced into the system but increase during the extension. Molecular weight increases and GPC curves before and after the reaction are shown in Fig. 3.

Since the polyether is very sensitive to thermal oxidation [8], the polycondensation cannot be driven far enough without degradation. It is, therefore, necessary to use a two-step synthesis with chain extension to get polymers that are fiber forming.

### Degradation

The tensile strength of the fibers decreases rapidly due to hydrolysis of the ester linkages and the resulting decrease of molecular weight (Fig. 4). The decrease of the molecular weight levels off (Fig. 5), due probably to solubilization of the low molecular weight products. The GPC curve of the water-soluble part is shown in Fig. 4 (Curve 7). The weight loss is not prominent until Day 40 when the fiber has become much too fragile for tensile strength measurements. During the decrease of molecular weight, there is an increase of the heat of fusion (Fig. 6).

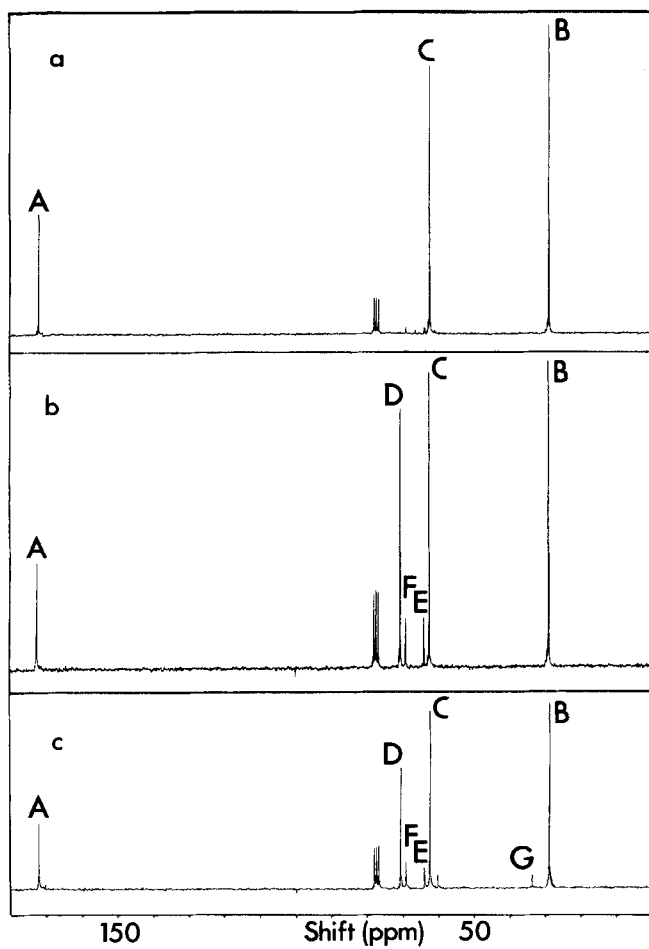
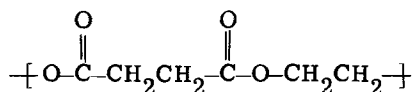


FIG. 1.  $^{13}\text{C}$ -NMR spectra of (a) poly(ethylene succinate) (PES) homopolymer, (b) poly(ethylene succinate)/poly(ethylene glycol) (PES/PEG) block copolymer, (c) chain-extended block copolymer. Peak assignments in Table 2.

TABLE 2. Assignment of  $^{13}\text{C}$ -NMR Peaks

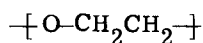
Carbon type	Calculated shift	Observed shift
A	165-175	172
B	29.3	28.9
C	63.5	62.4
D	72.5	70.6
E	65.5	63.9
F	70.5	69.1
G	33.4	33.7
H	26.0	-
C'	66.5	-
C''	60.5	-
D'	74.5	-
D''	62.5	-



Carbon: A B

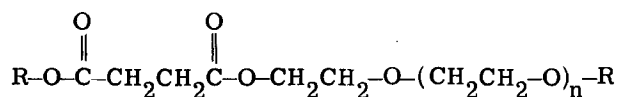
C

Polyester part



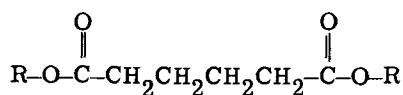
Carbon: D

Polyether part



Carbon:

E F

Link between  
polyester and  
polyether

Carbon: G H

Chain extension,  
adipic acid unit

(continued)

TABLE 2 (continued)

$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{O}-\text{CH}_2-\text{CH}_2-\text{OH} \end{array}$	Ethylene glycol endgroup
Carbon:    C'    C''	
$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{O}-(\text{CH}_2\text{CH}_2-\text{O})-\text{CH}_2\text{CH}_2-\text{OH} \end{array}$	Poly(ethylene glycol) end- group
Carbon:                    D'   D''	

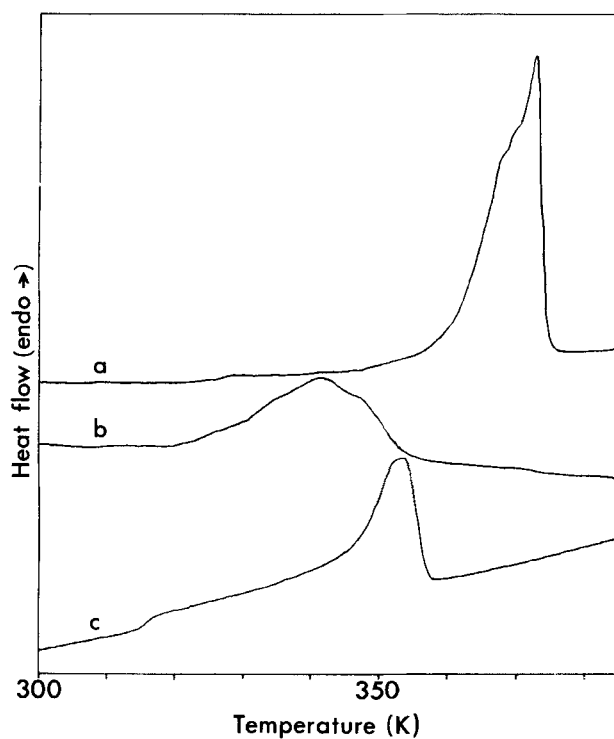


FIG. 2. DSC curves of (a) PES homopolymer, (b) PES/PEG block copolymer, (c) chain-extended block copolymer.



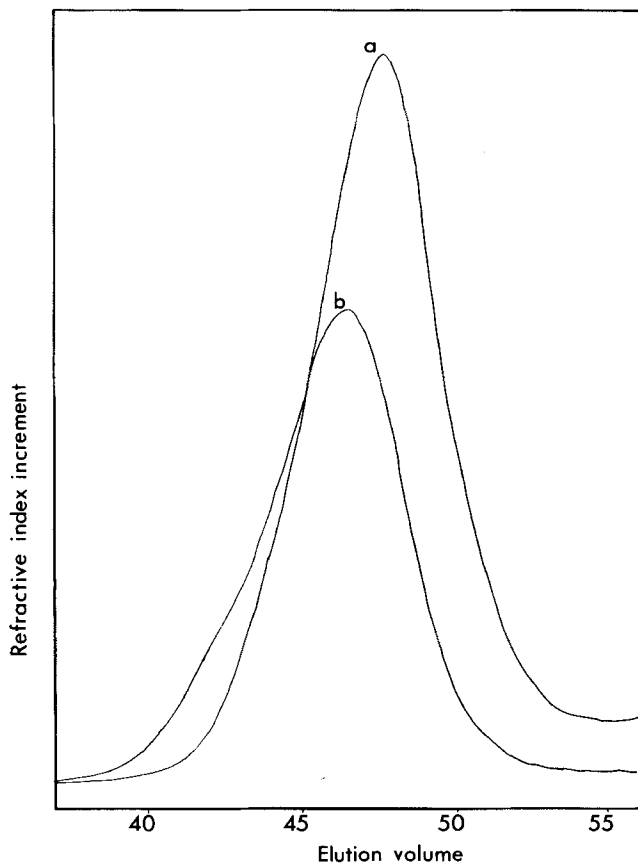


FIG. 3. GPC chromatograms of (a) PES/PEG block copolymer, (b) chain-extended block copolymer.

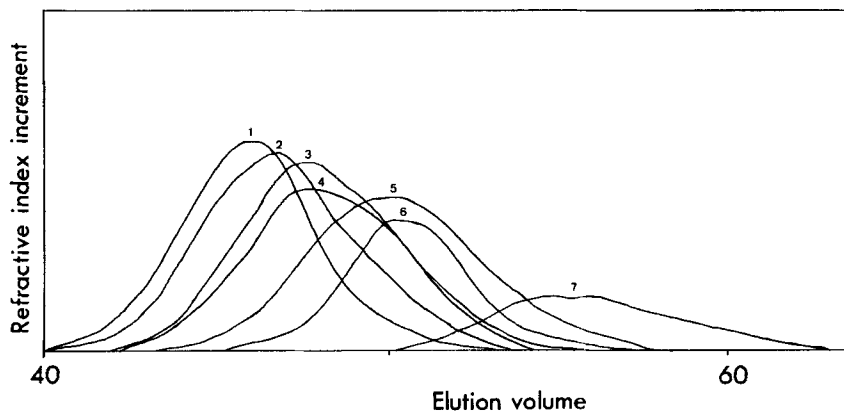


FIG. 4. GPC chromatograms of chain-extended block copolymer after 0 (Curve 1), 3 (2), 7 (3), 18 (4), 39 (5), 77 (6), and 77 days degradation, water-soluble part (7).

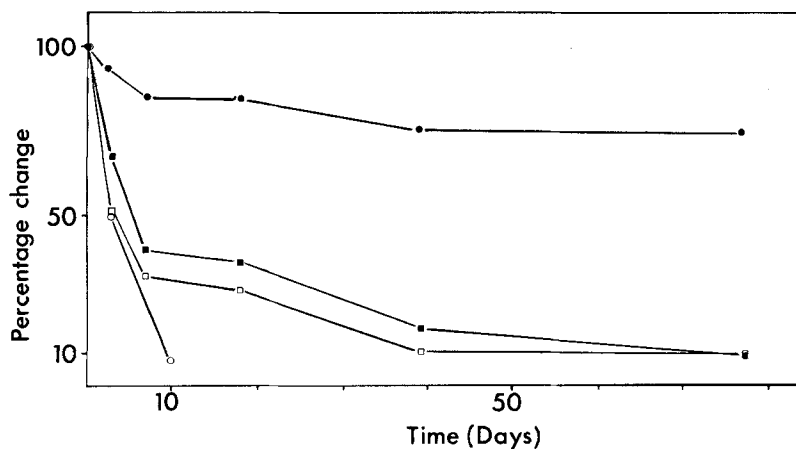


FIG. 5. Degradation results versus days of degradation: % remaining weight (●), % retention of tensile strength (○),  $M_n/M_n^0$  (□),  $M_w/M_w^0$  (■).

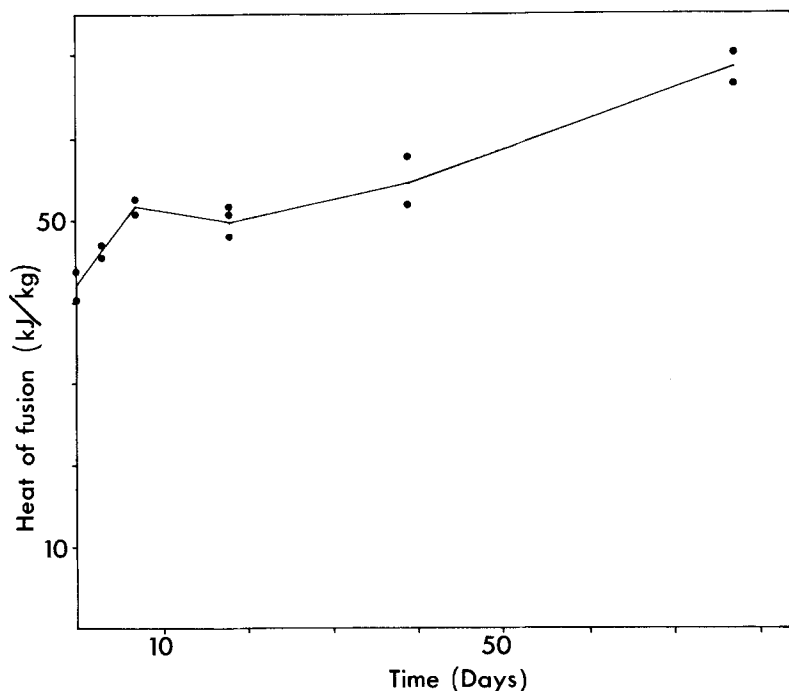


FIG. 6. Heat of fusion versus days of degradation.

### CONCLUSIONS

The amorphous component of the polymer is more sensitive to hydrolysis due to less structural hindrance compared with the crystalline components [9]. Tie chains between the crystallites are destroyed, and this explains the rapid loss in tensile strength while there is no significant weight loss of the fiber.

The elastic properties, which reflect a combination of the amorphous and crystalline fractions of the polymer, are therefore decreased, and the material becomes brittle. This "selective" hydrolysis is shown in Fig. 7, where the ratio of polyether (amorphous component) to polyester (crystalline component) is plotted versus time.

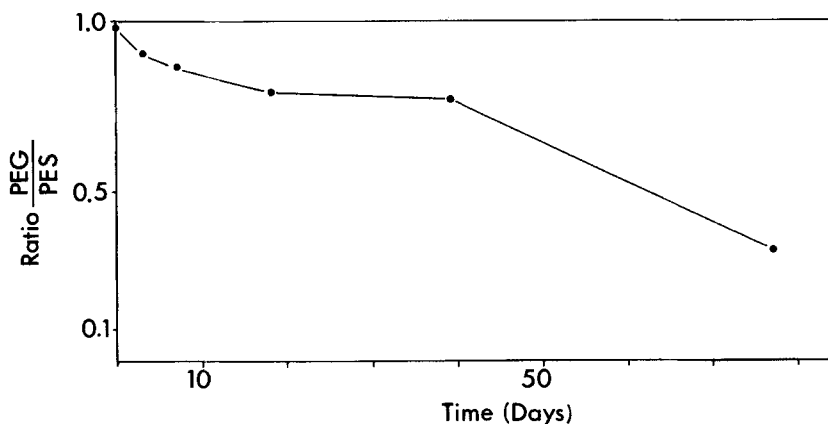


FIG. 7. The ratio of polyether/polyester (as determined by NMR) versus days of degradation.

#### ACKNOWLEDGMENT

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