Properties of Poly(ethylene glycol)-Based Bioelastomers

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ABSTRACT: In this article, a series of poly(ether ester) bioelastomers, poly(PEG-co-CA)s (PECs), were synthesized by the melt polycondensation of citric acid (CA) and poly(ethylene glycol) (PEG) with molecular weights of 150, 200, 300, and 400. The measurements of the mechanical properties of the PEC series testified that these polymers were elastomers with a low hardness and high elongation, and the hydrolytic degradation of polymer films in a buffer of pH 7.4 at 37°C showed that the PECs had excellent degradability. The molecular weight of PEG had a strong influence on the degradation rates, water absorption rates, and mechanical performance of the PECs. The materials are expected to be useful for pressure hemostasis implementation in lacuna and other biomedical applications. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 118: 2442–2447, 2010

Key words: biodegradable; biomaterials; biopolymers

INTRODUCTION

As important biomaterials, bioelastomers are widely used in the medical field, from treatment apparatus to artificial organs to tissue engineering.[1] Degradable bioelastomers have been a research focus because of their various applications in biomaterial areas, such as scaffolds for the regeneration of soft tissue *in vivo* or *in vitro*[2–6] and depot systems for localized drug delivery.[7–9] Four classes of biodegradable elastomers have been reported in literature: hygrogels, elastin-like peptides, polyhydroxyalkanoates, and network polyesters. Wang and coworkers reported a network polyester-poly(glycerol sebacate) (PGS), which chose non-toxic monomers, glycerol and sebacic acid, as novel elastomeric materials for potential use in soft-tissue engineering.[10,11] Other kinds of promising network polyesters are poly(diol citrate)s. Yang et al.[12] did most efforts on the development of network polyester based on citric acid (CA)–poly(1,8-octanediol citrate) (POC). The synthesis of POC is simple and can be conducted under very mild conditions. The biodegradable PGS and POC elastomers have been proven to have good flexibility, biocompatibility, and biodegradation. However, the long degradation times of PGS and POC are usually a disadvantage for some medical applications, such as drug-carrying devices.

Our study was aimed at the development of a novel biodegradable elastomer with a good elasticity and a fast degradation ratio under mild conditions. Previously, we reported the preparation of a degradable bioelastomer, poly(PEG-co-CA) [PEC; PEC_{200}, made with poly(ethylene glycol) (PEG) with a molecular weight of 200 by condensation with CA].[13] The mechanical properties and degradable properties of the elastomer were adjusted by altering the monomer ratio or changing the postpolymerization time. The relatively simple synthesis of PEC, especially without crosslinking reagents, makes it a good candidate for biomaterials. The low cost of the monomers for the synthesis of PEC also increases its potential for future commercialization.

In this study, a series of poly(ether ester) bioelastomers, PECs, were synthesized by the melt polycondensation of CA and PEGs with molecular weights of 150, 200, 300, and 400. The effects of the molecular weight of the PEGs on the thermal and mechanical properties of the material and *in vitro* degradation were investigated.

EXPERIMENTAL

Materials

PEGs with molecular weights of 150, 200, 300, and 400 were obtained from Shanghai Chemical Reagent

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Co. (Shanghai in China) and were dried *in vacuo* at 25°C overnight before use. CA (Tianjin Chemical Reagent Co., Tianjin in China) was used without further purification.

Preparation of the PECs

PEG and CA (PEG/CA molar ratio = 1 : 1) were added to a 250-mL, three-necked, round-bottom flask fitted with an inlet and an outlet adapter. The mixture was melted under the protection of nitrogen gas by stirring at 150–155°C. Then, the mixture was stirred at 140°C under atmospheric pressure for 6 h to create the prepolymers. PEC bioelastomers were prepared by the postpolymerization of prepolymers at 120°C in a polytetrafluoroethylene model under nitrogen for a period of time.[13] Here, PEC_{200}24h denotes the elastomer synthesized with a molar ratio of PEG with a molecular weight of 200 to CA of 1 : 1 and a postpolymerization time of 24 h. Other samples were named similarly.

Characterization

Differential scanning calorimetry (DSC) thermograms were recorded in the range −80 to 150°C on a PerkinElmer DSC (USA) instrument at a heating rate of 10°C/min under nitrogen.

Tensile tests were performed on a CMT4104 testing machine (SANS, ShenZhen in Chian) equipped with a 50-N load cell at 21°C. Briefly, the dog-bone-shaped sample (35 × 2 × 1 mm^3 length × width × thickness) was tested at a rate of 50 mm/min until break. The stress–strain curve and Young's modulus were determined. The results were based on the average of four to six samples. The crosslink density (n) was calculated by eq. (1)[11]:

$$n = \frac{E_0}{3RT} \tag{1}$$

wherein n represents moles of active network chains per unit volume, E_0 is Young's modulus (Pa), R is the universal gas constant (8.3144 J mol^{-1} K^{-1}), and T is the absolute temperature (K).

Water uptake experiments

Disc samples (10 mm in diameter, approximately 1 mm thick) were placed in 100-mL Erlenmeyer flasks containing deionized water (20 mL) and were kept for 24 h in an incubator maintained at room temperature (21°C). The samples were removed after 24 h, wiped gently with filter paper to remove excess liquid on the surface, and immediately weighed (W_2). Then, the samples were dried to a constant weight (W_1) in a vacuum oven. Each experiment was performed with three samples, and then, an average value was gained. The water uptake ratio was calculated according to the following formula:

$$\text{Water uptake ratio} = \frac{(W_2 - W_1)}{W_1}\,(\text{g/g}) \tag{2}$$

Swelling test

Disc samples prepared in a similar manner were immersed in phosphate buffered saline (PBS; pH 7.4) in an incubator at 37°C. The samples were removed at various time points. The volume swelling degree (Q) was determined from the volume differences of the swollen samples and the dry samples, as shown in eq. (3). The final value given was an average of the results from three determinations:

$$Q = \frac{V_{\text{swell}} - V_{\text{origin}}}{V_{\text{origin}}} \times 100 \tag{3}$$

where V_{origin} and V_{swell} are the elastomer volumes before and after equilibration at the determined intervals in PBS, respectively.

In vitro degradation

The disc specimen (10 mm in diameter, approximately 1 mm thick) was placed in a small bottle containing 20 mL of PBS (pH 7.4). The bottle was incubated at 37°C for certain periods of time. After incubation, the film was washed with water and dried at 40°C *in vacuo*. The weight loss was calculated by a comparison of the initial mass (W_0) with the mass measured at a given time point (W_t), as shown in eq. (2). Three individual experiments were performed for degradation testing, and then, an average value was gained:

$$\text{Weight loss}(\%) = \frac{W_0 - W_t}{W_0} \times 100 \tag{4}$$

RESULTS AND DISCUSSION

Characterization

The typical DSC heating thermograms of the PEC elastomers are depicted in Figure 1. All of the polymers were amorphous, with glass-transition temperatures (T_g's) ranging from −28.2 to −0.4°C, and no crystallization melting peaks were found. Additionally, the T_g values of the polymers increased with decreasing molecular weight of PEG. The change in the T_g of the polymers occurred because the PEG monomer took part in the condensation reaction

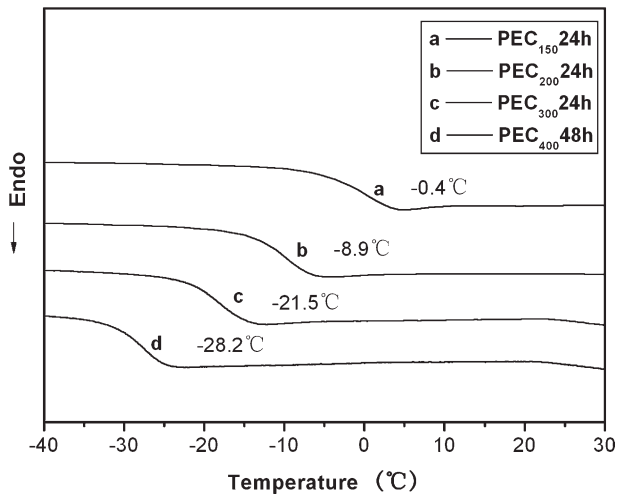

Figure 1 DSC curves of the PEC elastomers.

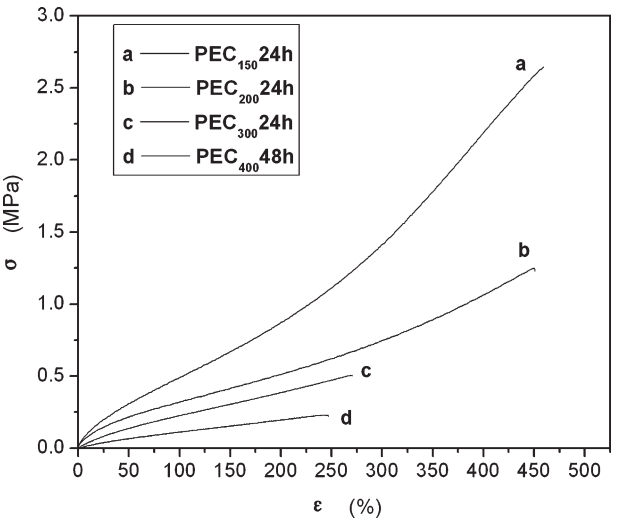

Figure 2 Typical stress–strain curves of the PEC films.

and, thus, was incorporated into the final elastomer. As shown in Table I, the lower molecular weight of PEG led to a higher crosslinking density of the elastomer. As the crosslinking density of the elastomer increased, the length of the molecular chain between crosslinking points decreased, and the thermal motion of the polymer chains was more constrained, which resulted in an increasing T_g. Because the T_g values of the new amorphous polymers were lower than room temperature, all of them were considered to be elastomers.

Mechanical properties

The typical stress–strain curves of the polymer films are depicted in Figure 2. The main mechanical properties of the elastomers are also summarized in Table I. As the molecular weight of PEG increased, the elastomer became softer (the Young's modulus and tensile stress at break decreased). We believe that the increased molecular weight of PEG resulted in a decrease in the moles of active network chains per unit volume. That is, this decreased the crosslinking density of polymer, which resulted in a decrease of the Young's modulus and tensile stress at break. As the molecular weight of PEG changed from 150 to 400, the Young's modulus and tensile stress at break changed from 1.26 ± 0.08 and 2.66 ± 0.011 MPa to 0.10 ± 0.01 and 0.21 ± 0.04 MPa, respectively. At the same time, the elongation at break of the elastomer became shorter (it changed from 458.9 ± 10.4 to 248.1 ± 7.1%). Therefore, it was possible to manipulate the mechanical properties of the elastomers by the alteration of the molecular weight of PEG. Moreover, as shown in Figure 3, the permanent set of the film was zero, which showed that these elastomers possessed excellent elastic resilience.

As is apparent from the data listed previously, PEC displayed mechanical properties markedly superior to those exhibited by other biodegradable elastomers developed recently. For example, PGS exhibited a tensile strength slightly above 0.5 MPa and an elongation at break value below 350%, respectively,[10] whereas $PEC_{150}24h$ attained UTS (Ultimate Tensile Strength) levels above 2.66 MPa and an elongation of about 458.9%.

Water uptake experiment

The hydrophilicity of elastomers is an important characteristic for controlled release and other medical applications. Figure 4 shows the relationship between the postpolymerization time and water uptake ratio of the PEC_{200} elastomer. Figure 5 displays a set of pictures of $PEC_{300}24h$ in the water

TABLE I
Mechanical Properties and Crosslinking Densities of the PEC Films

PEC	σ (MPa)	ε (%)	E_0 (MPa)	n (mol/m^3)	Permanent set (%)
$PEC_{150}24h$	2.66 ± 0.11	458.9 ± 10.4	1.26 ± 0.08	170.9 ± 10.6	0
$PEC_{200}24h$	1.16 ± 0.08	451.5 ± 9.2	0.75 ± 0.10	99.6 ± 13.2	0
$PEC_{300}24h$	0.53 ± 0.05	265.2 ± 9.6	0.42 ± 0.06	60.3 ± 7.9	0
$PEC_{400}48h$	0.21 ± 0.04	248.1 ± 7.1	0.10 ± 0.01	13.8 ± 1.3	0

σ = tensile stress at break, ε = elongation at break.

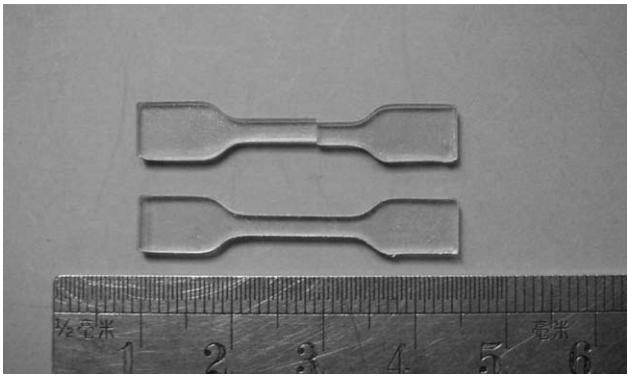

Figure 3 Picture of the $PEC_{150}24h$ elastomer before and after the mechanical property experiment.

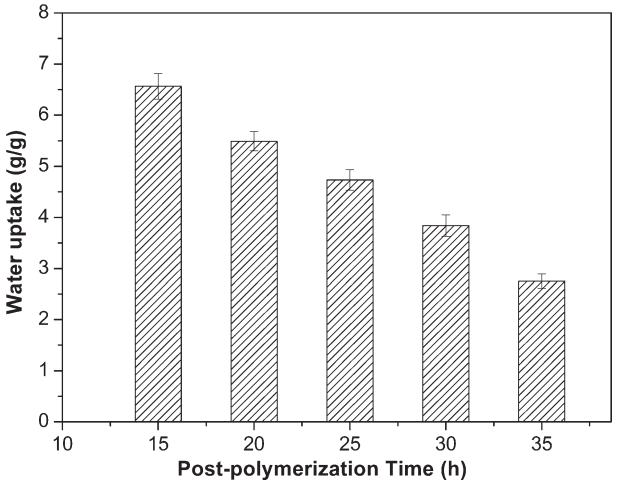

Figure 4 Relationship of the postpolymerization time and the water uptake ratio of the PEC_{200} elastomer.

uptake experiment. As shown in Figure 4, the increase in postpolymerization time resulted in a reduction of the water uptake ratio of PEC_{200}. As the postpolymerization time of PEC_{200} changed from 15 to 36 h, the value of the water uptake ratio changed from 6.6 to 2.7 g/g. The water uptake increased with decreasing postpolymerization time, which could have been due to the decreased crosslinking density.[10] As postpolymerization time decreased, the network space increased; this facilitated the permeation of water into the film. Therefore, it was possible to adjust the water uptake ratio of these elastomers by the alteration of the postpolymerization time.

Figure 5 is a set of pictures of the $PEC_{300}24h$ elastomer in the water uptake experiment. The diameter of the specimen increased with prolonged time in deionized water. When the immersion times were 0, 2, 12, and 24 h, the diameters of the specimen were 10, 18, 19.6, and 20 mm, respectively. After it was dipped in deionized water for 24 h, the water uptake ratio of $PEC_{300}24h$ was 6.1 g/g.

Swelling test

Figure 6 shows the relations between the soaking time and Q of these elastomers in PBS(pH 7.4) at 37°C. Q increased dramatically in the first few hours and then became mild up to 20 h because of the balance of osmotic forces determined by the affinity to

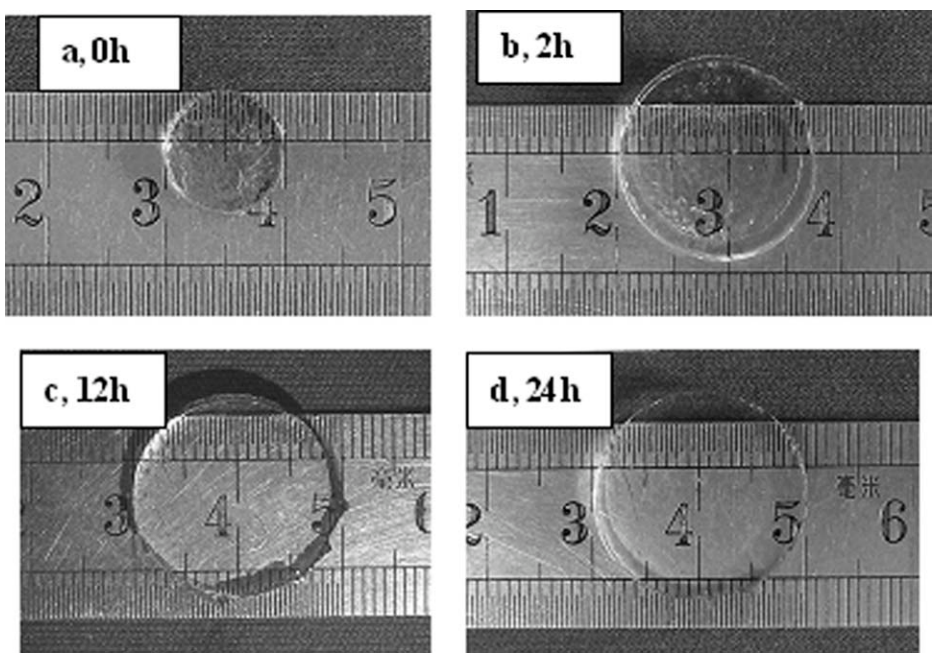

Figure 5 Pictures of $PEC_{300}24h$ in the water uptake experiment: immersion time = (a) 0, (b) 2, (c) 12, and (d) 24 h.

the solution and the network limitations.[14] After 20 h, the crosslinking framework of the elastomer was broken down because of gradual degradation in PBS, and the change trend of Q became fleet again. As shown in Figure 6, Q of $PEC_{400}48h$ was always larger than that of $PEC_{300}24h$ under the same conditions. The reason for this was that crosslink density of $PEC_{400}48h$ was lower than that of $PEC_{300}24h$ (see Table I).

As indicated by the above data, the PEC elastomer could be suitable for pressure hemostasis implements in lacuna. On the one hand, PEC, with elasticity and good volume swelling in body fluids, could bring extrusion power to attain a homeostasis effect in lacuna. On the other hand, the change trend of Q became subsequently mild, which could help to prevent local tissue necrosis because of excess pressure.

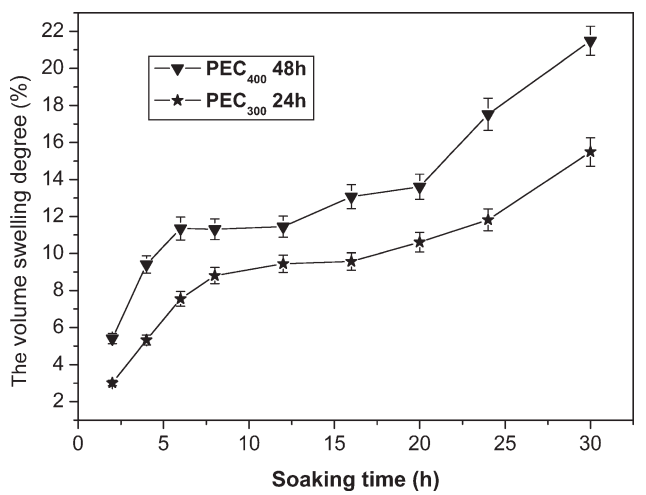

Figure 6 Q curves of the PEC elastomer (37°C, pH 7.4 PBS).

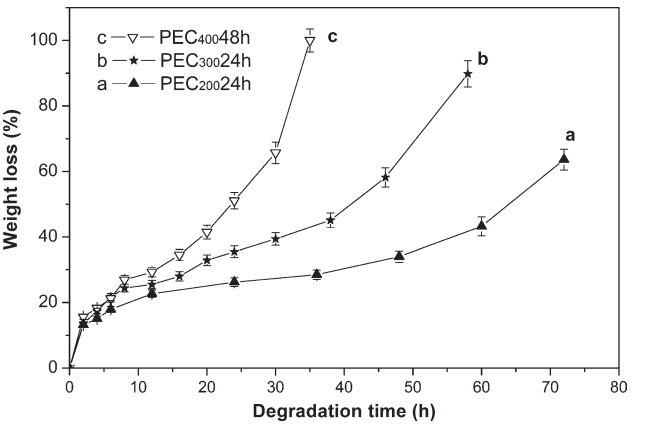

Figure 7 *In vitro* degradation weight loss versus time curves of the PEC elastomers: (a) $PEC_{200}24h$, (b) $PEC_{300}24h$, and (c) $PEC_{400}48h$.

In vitro degradation

Figure 7 shows the weight losses of the PEC elastomers with different PEG monomers degraded in PBS (pH 7.4) at 37°C. The weight loss increased with increasing molecular weight of PEG, which was ascribed to the decreased crosslinking density (Table I). When the weight loss was 50%, $PEC_{200}24h$ needed about 70 h, whereas $PEC_{400}48h$ only needed about 24 h under the same conditions. The reason was that, as molecular weight of PEG increased, the network space increased; this facilitated the diffusion of PBS into the film. On the other hand, the increase of PEG molecular weight could have resulted in the decrease in the density of the ester bond in the polymers. These results indicate that it was possible to manipulate the elastomer degradable properties by altering the molecular weight of PEG. Furthermore, all of the polymers prepared in this study degraded faster than other biodegradable elastomers recently developed elsewhere. For instance, PGS[13] and POC[14] degraded completely in more than 2 and 6 months, respectively, under the same conditions.

CONCLUSIONS

The PEC possessed good mechanical and swelling properties, which could be manipulated by controlling the molecular weight of the PEG monomer. Meanwhile, the degradation rate of the elastomers could be varied in a comparatively wide time range from 24 to 70 h. The material is expected to be useful for pressure hemostasis implements in lacuna. Additionally, the prepolymers of PEC had a low viscosity, which would allow easy part manufacture by the injection of the prepolymers into molds. Compared to existing biodegradable elastomers in biomaterials, PEC is inexpensive and easy to synthesize and process. The relatively simple synthesis under mild conditions without the addition of toxic catalysts or crosslinking reagents and its good degradation properties make it a good candidate for biomedical applications and coatings for food and drug materials.

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