Characterization of Novel Biodegradable Segmented Polyurethanes Prepared from Amino-Acid Based Diisocyanate

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Summary: Segmented polyurethanes (SPUs) which were expected to yield non-toxic degradation products were synthesized from lysine-based diisocyanate (LDI), 1,3-propanediol (PDO), and polycaprolactone diol (PCL). SPUs were synthesized via a standard two-step prepolymer method. The hard segment fraction was changed in order to tune the mechanical properties and the degradability. The aggregation structures of the SPUs were characterized by infrared spectroscopy and differential scanning calorimetry (DSC), temperature dependence of dynamic viscoelasticity, and small-angle X-ray scattering (SAXS). DSC and dynamic viscoelastic measurements revealed that the glass transition temperature (T_g) of the soft segment increased with an increase in the hard segment fraction. SAXS of SPUs revealed the aggregation states of hard and soft segments. Furthermore, the degradation of SPUs was investigated by exposing the polymers to a buffer solution at 310 K (pH=7.6). The degradation rate of SPUs increased with an increase in the soft segment fraction. This is because the soft segment has the hydrolyzable ester linkages and the ester linkages are susceptible to hydrolysis compared with the urethane linkages. Finally, an electrospray deposition method was used to fabricate biodegradable SPU micro-fibers. FE-SEM images showed that higher concentration of solution favored the formation of uniform biodegradable micro-fibers without beads-like structure.

Keywords: biodegradation; electro-spray deposition; lysine-based diisocyanate; microfiber; segmented polyurethane

Introduction

A variety of biodegradable polymers have been developed in the last two decades. However, the majority of these polymers are typically hard and brittle plastics and few biodegradable elastomeric polymers have been synthesized so far.[1-3] The recent

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development of diisocyanates based on lysine has removed an obstacle to synthesize biodegradable segmented polyurethane (SPU) elastomers expected to yield non-toxic degradation products.[4] If the lysine-based diisocyanate component in SPU was liberated by hydrolysis of the urethane bonds of the polymer during degradation, the product would be a lysine derivative, an essentially non-toxic product.

In this study, the segmented polyeurethanes (SPUs) were synthesized from lysine-based diisocyanate. The physical and structural characterizations of SPU were performed. The degradation behavior of SPUs was also investigated. Finally, in order to discuss the possibility of the design of a tissue-engineering scaffold, the electro-spray deposition (ESD) technique was used to fabricate biodegradable microfibers and microfiber mesh.

Experimental

Materials. 2,6-Diisocyanatohexanoate (LDI), polycaprolactone diol (PCL), and 1,3-propandiol (PDO) were used for the preparation of SPU. PCL with M_n of 1250 was obtained from Aldrich Chemical (Milwaukee, WI, USA). PCL was placed in a vacuum oven at 333 K to remove residual water before reaction. PDO and LDI were obtained from Kanto Chemical Co. (Tokyo, Japan) and Kyowa Hakko Kogyo Co. (Tokyo, Japan), respectively, and they were distilled under vacuum before use. Their chemical structures were summarized in Figure 1.

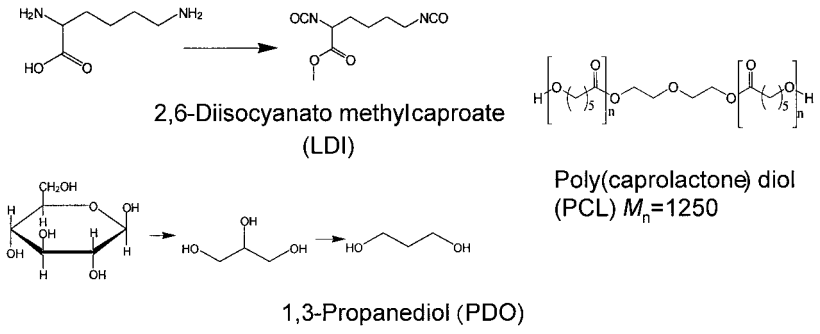

Figure 1. Chemical structures of components of SPU. LDI and PDO can be synthesized from lysine and glucose, respectively.

Synthesis of segmented polyurethanes. SPUs were synthesized via a standard two-step prepolymer method[5,6,7] and the ratio of soft segment to chain extender was changed in order to control the mechanical properties and degradation behavior. Figure 2 shows a schematic representation of the synthesis of segmented polyurethane(SPU). Excess LDI was reacted with PCL as a prepolymer reaction for 150 min at 358 K. Then, the PDO chain extender was added to the prepolymer and allowed to react for 48 h in the presence of dibutyltin dilaurate (0.1 mol%) as a catalyst in *N*,*N*-dimethylformamide (DMF). The resultant polymer was precipitated by slowly pouring the solution into water and the obtained polymer powder was washed with methanol and water. Then, the polymer was dried under vacuum at 353 K for 24 h to remove water. The obtained polymers were multi-block copolymers of hard and soft segments. The soft segment consists of PCL and LDI, whereas the hard segment consists of LDI and PDO. Gel permeation chromatography (GPC) was used to determine the molecular weight of SPU. M_w of SPU was in the range of 53k to 86k with M_w/M_n of ca.1.75. Samples were designated as "PCL (M_n of PCL) (PCL fraction) PDO". All solid films were prepared by solution casting from THF solution. The cast films were dried under vacuum at 393 K for 24 h.

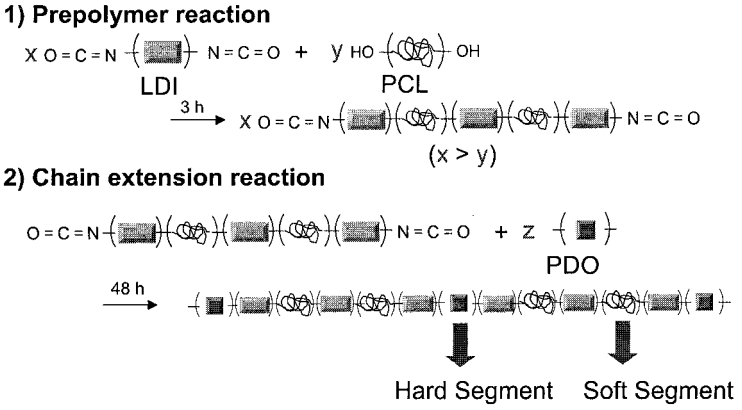

Figure 2. Schematic representation of synthesis of segmented polyurethane(SPU).

Characterization. SPU films were characterized by dynamic viscoelastic measurement, small-angle X-ray scattering (SAXS), Fourier transform infrared (FT-IR) spectroscopy, differential scanning calorimetry (DSC), and tensile tests.

Degradation behavior. Degradation studies were performed using tris-buffered saline (TBS, 0.05 M Tris, 0.1M NaCl, pH=7.6). Each SPU film with the dimensions of 10 mm x10 mm x 0.9 mm was placed into an individual vial containing 10 mL TBS, and incubated at 310 K. Samples were removed from buffer following 7, 21, 35, and 70 days. After drying under vacuum for 72 h, samples were reweighed to determine total percentage of weight loss.

Electro-spray deposition. Chloroform was used as the solvent to prepare the polymer solutions at different concentration for ESD. The details of the ESD equipment were reported elsewhere.[8] The polymer solution was delivered by a programmable pump to the exit hole of the electrode. A positive high-voltage supply was used to supply the voltage. The flow rate was 1 mL h^{-1} and the distance of the electrode was 300 mm. The electrosprayed mesh was prepared on to the substrate through continuous deposition with transverse movement of the substrate. All the samples were observed with a FE-SEM (Hitachi, S-4300) under the accelerating voltages of 1 kV without conductive over-coating.

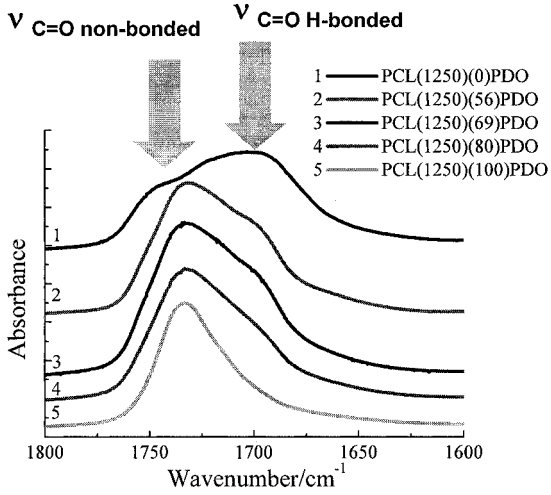

Figure 3. Transmission IR spectra of SPU in the carbonyl stretching region.

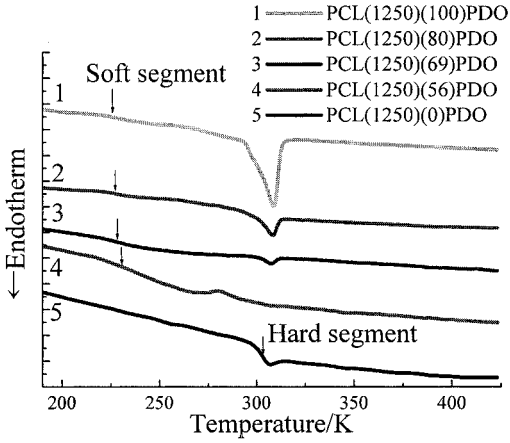

Figure 4. DSC thermograms for SPU with various soft segment contents.

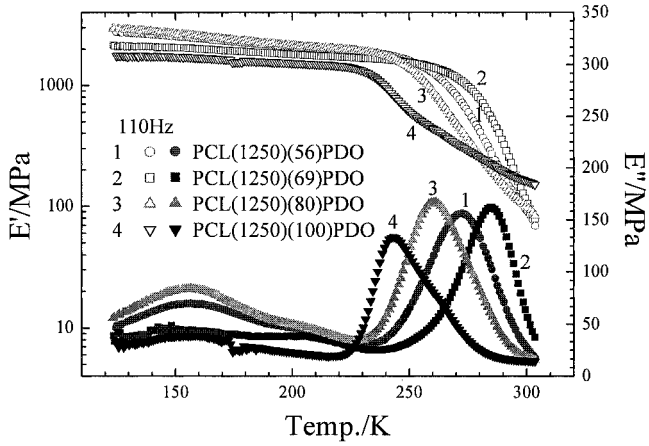

Figure 5. Temperature dependence of dynamic storage modulus, E' and dynamic loss modulus, E" for SPU with various soft segment content.

Results and Discussion

Characterization. FT-IR spectroscopy was used to investigate the structural difference in hard and soft segments of SPUs with various PCL fractions. Figure 3 shows the IR spectra of SPUs. The broad shoulders detected at 1730-1750 and 1680-1710 cm^{-1} are assigned to the free and hydrogen-bonded urethane and ester carbonyl groups, respectively. The relative intensity of the bands attributed to hydrogen-bonded carbonyl groups increased with an increase in the hard segment fraction. This result suggests that hydrogen bonding of carbonyl groups increases with an increase in the fraction of the PDO chain extender.

The difference in state of molecular aggregation of SPUs was confirmed by DSC. Figure 4 shows DSC thermograms for SPU with various soft segment contents. A base line shift corresponding to the hard segment T_g was observed at 302 K. It seems that the non-symmetric diisocyanate (LDI) produces hard segments that were unable to pack efficiently to form a crystalline hard segment domain. This also gives the low T_g of the hard segment compared with that of the aromatic diisocyanate-based hard segment. T_g and crystal melting of PCL in the soft segment were observed in the ranges of 225 K to 235 K and 283 K to 320 K, respectively. Crystallinity of PCL in SPUs decreased with a decrease in PCL fraction. This is because of the partial solubilization of the hard segment in the PCL phase.

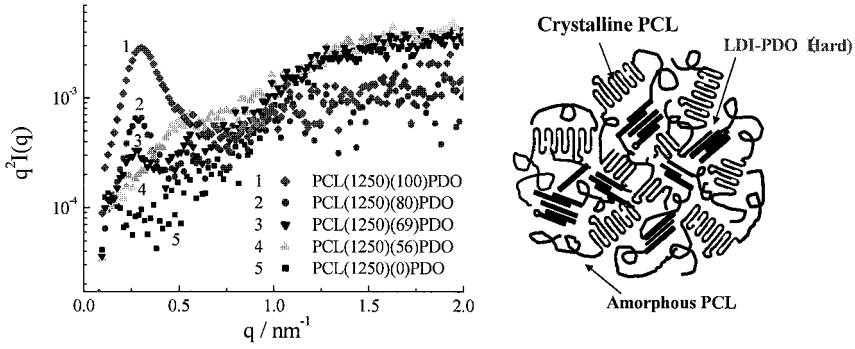

Figure 6. (a) Dependence of corrected intensity on scattering vector for PCL(1250)(X)PDO and (b) structure model of PCL(1250)(X)PDO.

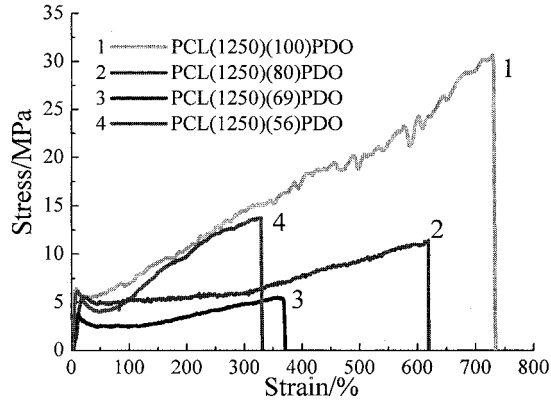

Figure 7. Stress-strain curves for SPU with various soft segment fraction.

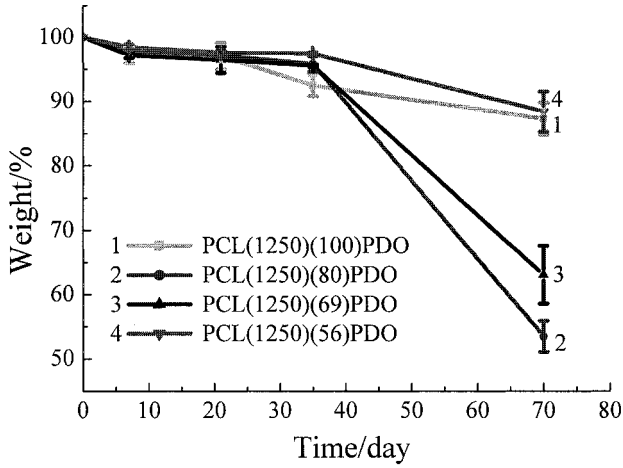

Figure 8. The change in weight with time after immersion in Tris-buffer solution at 310K for SPUs with various soft segment contents.

The state of thermal molecular motion of SPUs was characterized by the dynamic viscoelastic measurement. Temperature dependence of dynamic viscoelasticity was measured at 110 Hz from 130 to 310 K under dried nitrogen purge. Figure 5 shows the

temperature dependence of dynamic storage modulus, E' and dynamic loss modulus, E" for SPUs with various soft segment contents. A large decrease in E' was observed due to the onset of micro-Brownian motion of the PCL soft segment following by the melting of the PCL crystallite. Since more than two relaxations were overlapped at around 300 K, it is difficult to separate the relaxation mechanisms at this temperature region. Since the hard segment T_g and melting temperature of PCL were located at ca.300 K, a constant modulus at rubbery plateau was not observed for SPU at above room temperature. Since PCL(1250)(100)PDO does not have a low T_g hard segment, a crossover of E' was observed at 280-300 K. A broad peak observed at ca.150 K is assignable to γ-absorption of the PCL soft segment.

The phase structure of SPUs was characterized by synchrotron SAXS. SAXS was measured on a BL10C at Photon Factory, KEK, Tsukuba, Japan. Figure 6 (a) shows the dependence of the corrected intensity on a scattering vector of PCL(1250)(X)PDO. q is defined as $4\pi\sin\theta/\lambda$, where θ and λ are the Bragg angle and wavelength of the X-ray, respectively. Lorentzian factor was corrected by multiplying q^2 to the intensity. A large peak observed at q=ca.0.27 nm^{-1} is attributed to the long period between the PCL crystallite. Even for the PCL(1250)(100)PDO without the hard segment component, the long period was clearly observed. The intensity of this peak decreased with an increase in the hard segment fraction and finally disappeared for the LDI-PDO homopolymer. The scattering peak corresponding to the distance between hard segment domains was not observed in SPUs. This can be explained either by the partial phase mixing of hard and soft segments or the absence of the difference in electron density between hard and soft segments. The structure model of PCL(1250)(X)PDO based on the above mentioned characterization is depicted in Figure 4(b). PCL formed folded lamellar crystal between hard segment domains. A fairly large amount of amorphous PCL might be present in the soft segment phase. Since the PCL forms the large crystallite, PCL(1250)(X)PDO forms three phase structure consists of a glassy hard segment, an amorphous PCL and a crystalline PCL phase.

The mechanical properties of SPUs were investigated by stress-strain measurement. Figure 7 shows the stress-strain curves for SPUs with various PCL fractions. Below T_g of the hard segment (302K) and T_m of PCL(283-320K), both the hard segment and crystalline PCL phase can act as a crosslink at low elongation. However, the PCL crystallite is easily deformed at this temperature, the yielding was observed in the low elongation region.

Beyond the yielding point, the amorphous PCL phase with low T_g act as a rubber elastic component. On the other hand, the elongation at break increased with an increase in the soft segment fraction.

Degradation behavior. The degradation characteristics of a series of SPUs were evaluated. Figure 8 shows the change in weight with time after immersion in Tris-buffer solution at 310 K for SPUs with various soft segment contents. At 310 K, the PCL phase in SPU might be melted and the hard segment is in a leather-like state. The magnitude of degradation in SPUs was increased with an increase in the soft segment fraction. This is because the soft segment has the hydrolyzable ester linkages and the ester linkages are susceptible to hydrolysis compared with the urethane linkages. On the other hand, the PCL-LDI soft segment homopolymer showed a small magnitude of degradation. This can be ascribed to the presence of PCL crystallites at 310 K.

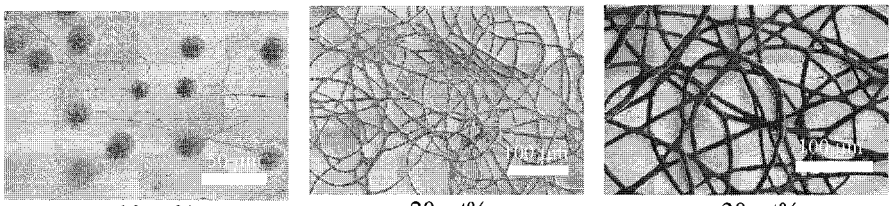

Figure 9. FE-SEM images of microstructure of PCL(1250)(80)PDO ESD microfibers prepared at 10-30 wt% chloroform solution under voltage of 12 kV.

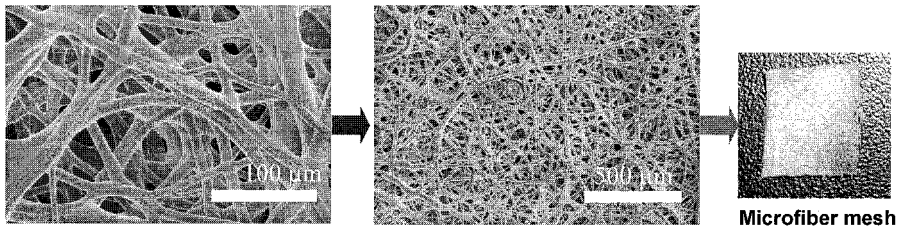

Figure 10. FE-SEM images of SPU microfiber mesh prepared by ESD.

Electro-spray deposition. In the ESD experiment, the morphological change of the electrospray deposited microstructure is expected when the concentration of polymer solutions was changed. Figure 9 shows FE-SEM images of PCL(1250)(80)PDO ESD microfibers deposited from 10-30wt% solution under 12 kV. FE-SEM images showed that a mixture of large beads and fibers were formed by ESD at 10 wt% PCL(1250)(80)PDO solution under a voltage of 12 kV. In contrast, fine fibers were formed at 20 wt% and 30wt% PCL(1250)(80)PDO solution. The average diameters of the fibers prepared at 10wt%, 20wt%, and 30wt% were 1.0 μm, 7.5 μm, and 7.7 μm, respectively. It was shown that a higher concentration of solution favored the formation of uniform fibers without a bead-like structure. This is because the critical viscosity in solution needs to be exceeded in order to fabricate fibers. Below this viscosity chain entanglements are insufficient to stabilize the jet, leading to spraying of droplets. A repeated deposition of microfiber with transverse movement of the substrate gives a mesh of SPU microfibers. Figure 10 shows FE-SEM images of PCL(1250)(80)PDO microfiber mesh prepared from 35 wt% solution under 12 kV with a flow rate of 1 ml h^{-1}. The average diameter of the fibers was 11.6 μm As shown in Figure 10, a self-standing microfiber mesh with high porosity was successfully obtained from ESD of SPU.

Conclusion

Novel biodegradable segmented polyurethanes were prepared from lysine-based diisocyanate, PCL, and PDO chain extender. DSC, dynamic viscoelastic measurements, and small-angle X-ray scattering experiment revealed that the SPU has amorphous PCL, crystalline PCL, and a glassy hard segment structure. The degradation rate of SPUs was confirmed by the exposure of SPU film to buffer solution. Microfibers and a microfiber mesh of SPU were successfully prepared by electro-spray deposition.

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