Physicochemical Properties and Bio-degradation of Segmented Polyurethane and Poly(urethane-urea) Derived from Lysine-Based Diisocyanate

Tomohiro Yamaguchi[1], Hideyuki Otsuka[1,2], Satoru Kidoaki[3],
Takehisa Matsuda[3], Atsushi Takahara[1,2]*

[1]Graduate School of Engineering, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812-8581, JAPAN
[2]Institute for Materials Chemistry and Engineering, Kyushu University, Hakozaki, Higashi-ku,
Fukuoka 812-8581, JAPAN
[3]Biomedical Engineering, Graduate School of Medicine, Kyushu University, Maidashi, Higashi-ku,
Fukuoka 812-8582, JAPAN
Tel: 81-92-642-2721, Fax: 81-92-642-2715, e-mail: takahara@cstf.kyushu-u.ac.jp

Segmented polyurethanes (SPU) and poly(urethane-urea)s (SPUU) which were expected to yield non-toxic degradation products were synthesized from lysine-based diisocyanate (LDI), 1,3-propanediol (PDO), 1,4-butanediamine (BDA), and polycaprolactone diol (PCL). SPU and SPUU 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 SPU and SPUU were characterized by IR spectroscopy and DSC. IR spectroscopy revealed that fraction of hydrogen bonded urethane and urea carbonyl groups increases with an increase in hard segment fraction. DSC thermogram revealed that the glass transition temperature of BDA-based hard segment is higher than that of PDO-based one. Tensile tests revealed the excellent elastic properties of PCL(1250)(71)BDA. Furthermore, the degradation of SPU and SPUU were investigated by exposing the polymers to buffer solution at 310 K (pH=7.6). The degradation rate of SPU increased with an increase in soft segment fraction. This is because the soft segment has the hydrolyzable ester linkages and is susceptible to hydrolysis compared with that of the urethane linkage. Finally, an electrospray deposition method was used to fabricate biodegradable SPU micro-fibers. FE-SEM images showed that higher concentration of solution favored to form of uniform biodegradable micro-fibers without beads-like structure.
Key words: Degradation, Lysine-based diisocyanate, Polyurethanes, Poly(urethane-urea)s, Electrospray Deposition

1. INTRODUCTION

The use of degradable polymers in tissue engineering for replacement or repair of wide range of tissues is an area of intensive research in recent years. A variety of biodegradable polymers have been developed in the last two decades. However, the majority of these polymers are typically hard and brittle plastic and few biodegradable elastomeric polymers have been synthesized.[1]

The recent development of diisocyanates based on lysine has removed an obstacle to synthesizing biodegradable elastomers expected to yield non-toxic degradation products.[2] It was surmised that if the diisocyanate were liberated by hydrolysis of the urethane bonds of the polymer during degradation the isocyanate functionalities would react with water to regenerate the lysine derivative, an essentially non-toxic products.

Recently, there has been growing interest in a fiber production technology known as electrospray deposition (ES). ES is unique as a fiber spinning process because it can change the morphology and diameter depending on the processing parameter such as solution concentration and applied electric field strength.[3] ES can produce highly porous non-woven fabrics consisting of well-defined fibers which are used for tissue engineering.

In this study, the segmented polyurethanes (SPU) and segmented poly(urethane-urea)s (SPUU) were synthesized from lysine-based diisosyanate. The physical and structural characterizations of SPU and SPUU were performed using differential scanning calorimetry and IR spectroscopy. Then the mechanical properties were investigated by stress-strain measurement. The degradation behavior of SPU and SPUU were also investigated. ES technique was used to fabricate biodegradable fibers. The morphology of electrospray deposited fiber was investigated by field-
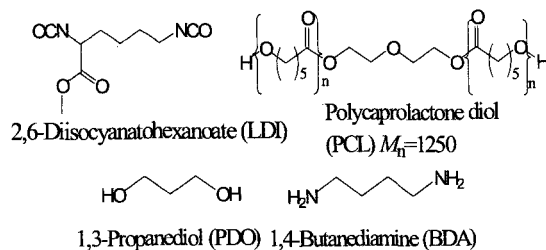
Figure 1 Chemical structures of diisosyanate, soft segment polyol, and chain extenders.

Table 1 Ratio of LDI, PCL, and chain extenders and soft segment concentration of SPU and SPUU.

Sample	LDI: PCL: Chain Extender	Chain Extender	Soft Segment Fraction (wt%)
PCL(1250)(100)PDO	4:4:0	PDO	100
PCL(1250)(80)PDO	4:2:2	PDO	80
PCL(1250)(69)PDO	4:1.5:2.5	PDO	69
PCL(1250)(56)PDO	4:1:3	PDO	56
PCL(1250)(0)PDO	4:0:4	PDO	0
PCL(1250)(80)BDA	4:3:1	BDA	80
PCL(1250)(75)BDA	4:2.5:1.5	BDA	75
PCL(1250)(71)BDA	4:2:2	BDA	71
PCL(1250)(64)BDA	4:1.5:2.5	BDA	64
PCL(1250)(53)BDA	4:1:3	BDA	53
PCL(1250)(0)BDA	4:0:4	BDA	0

emission scanning electron microscopy (FE-SEM).

2. EXPERIMENTAL

2.1 Materials

Fig. 1 shows the chemical structures of 2,6-diisocyanatohexanoate (LDI), polycaprolactone diol (PCL), 1,3-propandiol (PDO), and 1,4-butanediamine (BDA). 2,6-Diisocyanatohexanoate (LDI, Kyowa Hakko Co., Ltd.), polycaprolactone diol (PCL, Aldrich Chemical), 1,3-propandiol (PDO, Kanto Chemical. Co., Ltd.), and 1,4-butanediamine (BDA, Aldrich Chemical) were used for the preparation of SPU and SPUU.

LDI, PDO, and BDA were purified by vacuum distillation. PCL was placed in a vacuum oven at 353 K for 24 h to remove residual water before reaction. Dimethylformamide (DMF, Nacalai Tesque, Co., Ltd) was purified by vacuum distillation. Di-n-butyltin dilaurate (Tokyo Kasei Kogyo Co., Ltd.) was used as a catalyst for the synthesis of SPU.

2.2 Synthesis of SPU and SPUU

SPU and SPUU were synthesized via a standard two-step prepolymer method and the ratio of soft segment to chain extender was changed.[4] Excess LDI was reacted with PCL. The prepolymer reaction proceeded for 150 min at 358 K. Then the chain extenders (PDO for SPU and BDA for SPUU) was added to the prepolymer and allowed to react for 48 h (SPU) in the presence of 0.1 % of catalyst and for 1 h (SPUU) in DMF. The polymer was then immersed in distilled water for 48 h and dried under vacuum at 353 K for 24 h to remove water.[5] The composition of SPU and SPUU was given in Table 1. Sample names were designated as soft segment (soft segment M_n) (soft segment fraction) chain extender.

All solid films were prepared by solution casting. The SPU and SPUU were dissolved in THF (SPU) and DMF (SPUU). The cast films were dried under vacuum at 393 K for 24 h.

2.3 Characterization of SPU and SPUU

Fourier transform infrared (FT-IR) spectra were obtained with a Spectrum One (Perkin-Elmer. Co., Ltd.) infrared spectrometer. Spectra were generated from 64 scans at 0.5 cm⁻¹ resolution. 5 % THF solution of SPU was placed directly onto NaCl and 5 % DMF solution of SPUU were placed directly onto CaF₂. Subsequent evaporation of the DMF at 393 K under vacuum was

performed for 24 h.

DSC thermograms from 173 K to 423 K were obtained using a differential scanning calorimeter DSC8230B (Rigaku Denki Co. Ltd.) at a heating rate of 15 K min⁻¹ under a dried nitrogen purge. The sample weight was around 8 mg.

Stress-strain measurements were obtained at room temperature using an RTC-1250 (ORIRNTEC. Co., Ltd.). Samples were cut from films cast to 90-120 μm thickness. A cross-head speed of 200 mm min⁻¹ was used.

2.4 SPU and SPUU degradation

Degradation studies were performed using tris-buffered saline (TBS, 0.05 M Tris, 0.1M NaCl, pH=7.6).[5] Each samples were 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 mass loss.

2.5 Electrospray Deposition (ES)

For SPU, THF was used as the solvent to prepare the polymer solutions at different concentration for ES. A schematic diagram of the ES device for manufacturing fibers was shown in Fig. 2. The polymer solution was delivered by a programmable pump to the exit hole of the stainless-steel blunt-ended needle electrode (inner diameter; 0.8 mm). An aluminum plate was used as a lower electrode. A positive high DC voltage supply was used to apply the voltage. The flow rate was 1 ml/h. The distance of electrode was 350 mm. The sample solution was electrostatistically drawn from the needle tip and deposited on the lower electrode.
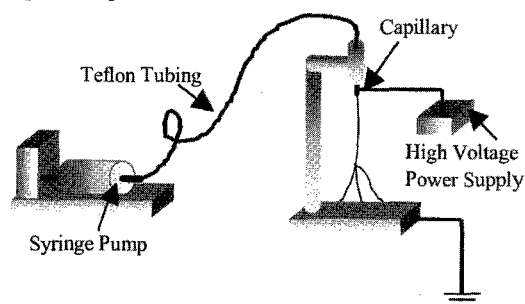

Figure 2 Schematic diagram of the ES apparatus for manufacturing fiber structure.

All the samples were observed with FE-SEM (S-4300SE, Hitachi Co., Ltd.) under the accelerating voltages of 1 kV. The samples were observed without conductive over-coating.

3. RESULTS AND DISCUSSION

3.1 Characterization of SPU and SPUU

Fourier transform infrared (FT-IR) spectroscopy was used to investigate the structural difference in hard and soft segments of SPU and SPUU. IR spectra for the SPU and SPUU are shown in Fig. 3. The absorption bands at 1735 cm^{-1} to 1720 cm^{-1} are associated with the ester carbonyl groups of PCL. The broad shoulders detected at 1670 cm^{-1} to 1710cm^{-1} are assigned to the hydrogen bonded urethane carbonyl group (Fig. 3a). The shoulder from 1620 cm^{-1} to 1680cm^{-1} is ascribed urea carbonyl group (Fig. 3b). The relative intensity of the bands attributed to hydrogen bonded urethane and urea linkage increased with a decrease in hard segment fraction. This result shows that the increase of hydrogen bonding among hard segments with an increase in fraction of chain extender.

The difference in state of molecular aggregation between SPU and SPUU was confirmed by the DSC. The hard segment is amorphous because of the non-symmetric molecular structure of LDI. Fig. 4 shows the DSC thermograms for SPU and SPUU, respectively. A base line shift corresponding to the hard segment glass transition temperature (T_g) was observed in the 308 K in SPU (Fig. 4a). It seems that the non-symmetric diisocyanate (LDI) produces hard segment that was unable to pack efficiently. However, the hard segment T_g was observed 379 K in DSC curves of SPUU. This is because the urea linkage has strong hydrogen bonding

compared with that of the urethane linkage. Soft segment crystal melting was observed in the range of 283 K to 320 K (Fig.4a). Crystallinity of SPU decreased
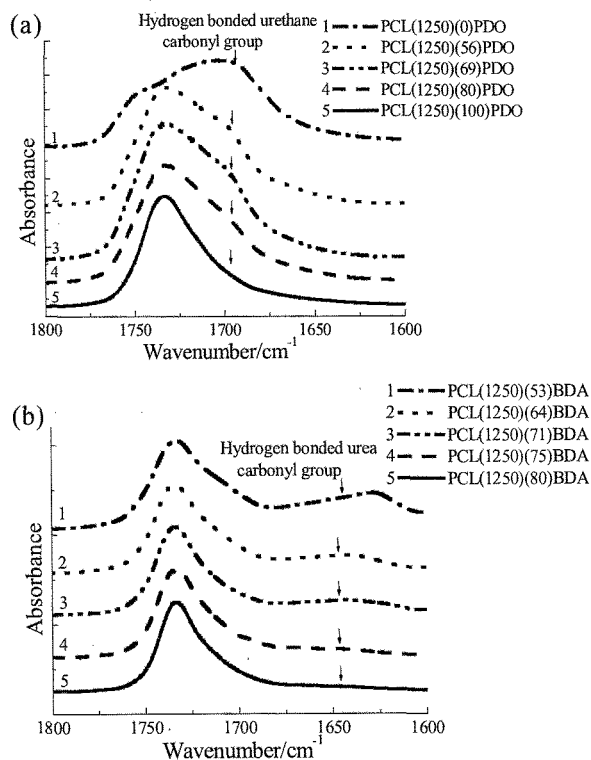

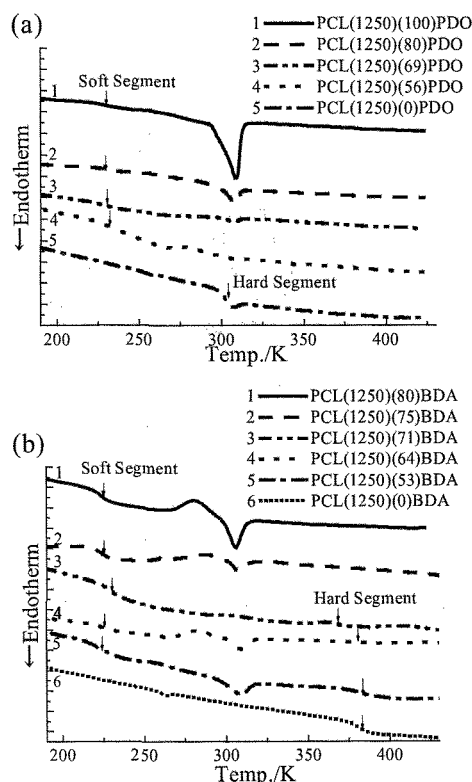Figure 4 DSC scans of (a) SPU series and (b) SPUU series.

Figure 3 FT-IR absorbance spectra of (a) SPU series and (b) SPUU series.
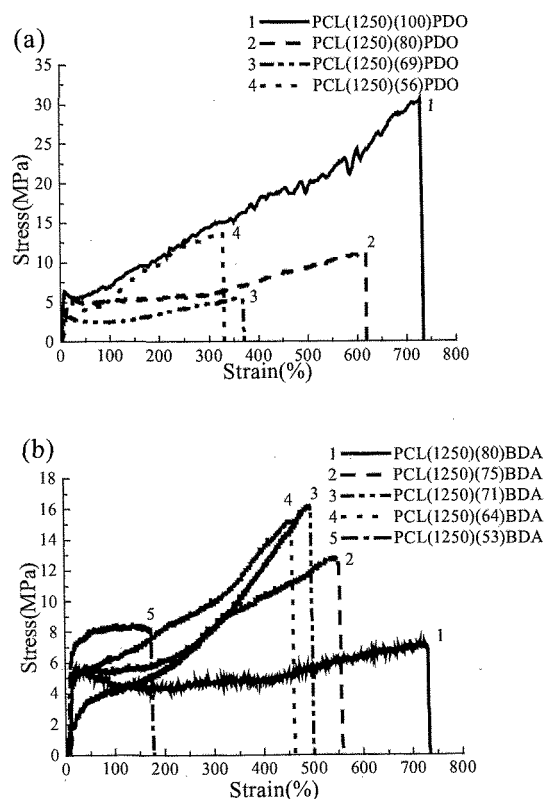

Figure 5 Uniaxial stress-strain curves for (a) SPU series and (b) SPUU series.

with a decrease in PCL fraction. This is due to the partial solubilization of hard segment into PCL phase. PCL(1250)(71)BDA showed higher soft segment T_g than other SPUU's (Fig. 4b). These shifts of T_g are attributed to the partial solubilization of hard segment into PCL phase. Phase separation proceeded with the increase of hard segment because of strong hydrogen bonding.

3.2 Mechanical properties of SPU and SPUU

The mechanical properties of SPU and SPUU were investigated by stress-strain measurement. Typical stress-strain curves for SPU and SPUU are shown in Fig. 5. The results suggested that the increasing modulus and decreasing the ultimate strain with increasing the hard segment fraction of SPU (Fig. 5a). This result showed that the PCL crystallites may act as physical cross-links. In contrast, PCL(1250)(71)BDA showed the excellent elastic properties (Fig. 5b). This is because the BDA formed strong aggregated hard segment and the loss of crystallinity of PCL soft segment.

3.3 Degradation of SPU

The degradation characteristics of a series of SPU were evaluated. The mass loss data for SPU samples were shown in Fig 6. The magnitude of degradation in SPU was increased with an increase in the soft segment fraction. This is because the soft segment has the hydrolyzable ester linkages and is susceptible to hydrolysis compared with that of the urethane linkage.
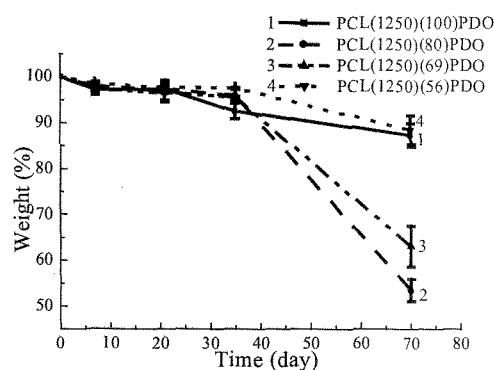

Figure 6 Degradation behavior of SPU in pH=7.6 at 310 K.

3.4 Electrospray deposition (ES)

In ES experiment, morphological change of the deposited ES microstructure is expected when the concentration of polymer solutions were changed. Fig. 7 showed FE-SEM images of SPU. FE-SEM images showed that a mixture of large beads and fibers were formed by ES at 20 wt% PCL(1250)(80)PDO solution under voltage of 13.5 kV (Fig. 7a). In contrast, fine fibers was formed at 30 wt% PCL(1250)(80)PDO solution under voltage of 15.4 kV (Fig. 7b). It was shown that higher concentration of solution favored to form of uniform fibers without beads-like structure. This is because the critical viscosity in solution needs to be exceeded in order to fabricate fibers.[6] Below this viscosity chain entanglement are insufficient to stabilize the jet, leading to spraying of droplets.
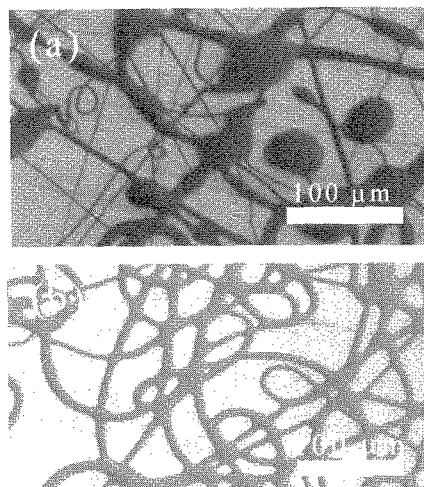

Figure 7 FE-SEM images of microstructure of electrospray deposited PCL(1250)(80)PDO. (a) 20 wt% under voltage of 13.5 kV and (b) 30 wt% under voltage of 15.4 kV.

4. CONCLUSION

Biodegradable segmented polyurethanes (SPU) and segmented poly(urethaneurea)s (SPUU) derived from a lysine-based diisocyanate were synthesized and characterized. IR spectroscopy revealed that the increase of hydrogen bonding among the hard segment with an increase in chain extender fraction. DSC thermogram revealed that the BDA-based hard segment T_g is higher than that of PDO-based one. Tensile tests revealed the excellent elastic properties of PCL(1250)(71)BDA. The magnitude of degradation of SPU was increased with an increase in the soft segment fraction. ES technique was used to fabricate biodegradable fibers. It was shown that higher concentration of solution favored to form of uniform biodegradable micro-fibers without beads-like structure.

References
[1] K. A. Athanasiou, G. G. Niederauer and C. M. Agrawal, *Biomaterials.*, **17**, 93(1996).
[2] P. Bruin, G. J. Veenstra, A. J. Nijenhuis, A. J. Pennings, *Makromol Chem Rapid Commun.*, **9**, 589(1988).
[3] J. M. Deitzel, J. Kleinmeyer, D. Harris, N. C. Beck Tan, *Polymer*, **42**, 261(2001).
[4] D. J. Lyman, *J.Polym.Sci.*, **45**, 49(1960).
[5] G. A. Skarja and K. A. Woodhouse, *J. Biomater. Sci. Polymer Edn*, **13**, 391(2002).
[6] E. Kenawy, J. M. Layman, J. R. Watkins, G. L. Bowlin, J. A. Matthews, D. G. Simpson, G. E. Wnek, *Biomaterials*, **24**, 907(2003).