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Synthesis and Characterization of Biodegradable Poly(ε-caprolactone)-b-Poly(L-lactide) and Study on Their Electrospun Scaffolds

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A series of multi-block copolymers, poly(L-lactide)-b-poly (ε-caprolactone) (PLLA-b-PCL) were synthesized. The first step of the synthesis consisted of the transesterification between the PLLA and 1,4-Butanediol, followed by the copolymerization of PLLA-diols and PCL, using isophorone diisocyanate (IPDI) as a coupling agent. The synthesized polymers were characterized by Fourier transform infrared (FTIR) spectra, differential scanning calorimetry (DSC) and wide angle X-ray diffraction (WAXD). PLLA/PCL block copolymers were electrospun into ultrafine fibers. The morphology of the electrospun fibrous scaffolds were investigated by Scanning Electron Microscopy (SEM). Results showed that the morphology and diameter of the fibers were affected by the electrospinning solution concentrationan and different weight ratio of PLLA/PCL. These electrospun PLLA-b-PCL fibrous membranes exhibited good flexibility and deformability. In comparison with the electrospun PLLA membrane, the electrospun fibrous membranes of PLLA-b-PCL demonstrated an enhanced elongation with still high tensile strength and Young's modulus to be beneficial for tissue engineering scaffolds.

Keywords: Poly(L-lactide), poly(ε-caprolactone), block copolymer, electrospinning, fiber

1 Introduction

Over the past decade, considerable efforts have attempted to develop scaffolds for tissue engineering, using biodegradable and biocompatible polymers (1–4). Tissue engineering is a multidisciplinary area that has evolved in parallel with recent advances of materials and biotechnology. Particularly, electrospun nano-/micro-scale non-woven polymer fibrous mats are widely used as scaffolds for tissue engineering (5,6). Electrospinning is a simple, relatively efficient, technique to fabricate polymer fibers with less than 50 nm to over 1 μm diameter which are mostly spun from polymer solutions (7,8). Because of their small size, high specific surface areas and high porosity, the ultrafine electrospun fibers is different from the polymer itself so that the ultrafine fibers exhibit a variety of potential applications, including filtration membrane, sensors, protective clothes and biomaterial applications (e.g., wound dressing, drug delivery system, scaffold in tissue engineering, etc.) (9–11).

As the core of tissue engineering, polymers used in tissue engineering serve as a physical support for seeded cells and provide a template for three dimensional organization to enable cell adhesion, migration, proliferation, differentiation, and eventually tissue regeneration. Recently, aliphatic polyesters, including poly(lactic acid) (PLA), poly(glycolic acid) (PGA), poly((R)-3-hydroxybutyrate) (PHB), poly(ε-caprolactone) (PCL) and their copolymers have attracted great attention due to their distinctive degradation and excellent biocompatibility (12–14). Of these, PLA is the most promising and widely used as the candidate scaffolds for tissue engineering(15). However, its application is limited by its brittleness. This weakness might be improved by blending PLA with lower glass-transition temperature polymers, such as biodegradable PCL (16–18). PCL is known to be susceptible to biological degradation, Nevertheless, this material suffers from its low glass transition (~-50°C) and low melting point ($\sim$60°C), limiting its wide application(19). It is noted that the miscibility of PLA and PCL is very poor due to their widely different physiochemical properties. Our objective was to find chemical methods which can combine PLA and PCL to improve their miscibility, without affecting the desirable biocompatible and biodegradable properties. L-lactide and

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ε-caprolactone (PLCL) copolymers have been reported previously (14,20). Huang et al. (13) reported a PLA–PCL–PLA triblock copolymer was synthesized by ring-opening polymerization of successively added ε-caprolactone and DL-lactide in the presence of ethylene glycol, using zinc powder as catalyst. Cohn et al. (12) reported a series of PCL/PLA biodegradable poly(ester-urethane)s synthesized by the ring opening polymerization of L-lactide, initiated by the hydroxyl terminal groups of the PCL chain, followed by the chain extension of these PLA-PCL-PLA triblocks with hexamethylene diisocyanate. These block copolymers have the advantage that both the permeation rate of steroids and the degradation rate are between their homopolymers which can be controlled by adjusting their composition of the copolymer (21). On the other hand, the block copolymer P (LLA-CL) in acetone and chloroform was successfully prepared in the form of fibers to be used for smooth muscle cell and endothelial cell proliferation (22). Vaz et al. (23) reported that the electrospun PLA/PCL bi-layered tube presents appropriate characteristics to be considered as a candidate scaffold for blood vessel tissue engineering.

Our work aimed at developing biodegradable PLLA/PCL multi-block copolymers by combining phase-segregated PLLA and PCL directly. PLLA/PCL block copolymers were synthesized from diol-terminated PLLA (PLLA-diols), as hard segments and PCL, as soft segments. As a junction, isophorone diisocyanate (IPDI) was employed as a nontoxic connecting unit. With the intention of seeking wide applications in tissue engineering, PLLA/PCL multi-block copolymers were prepared in the form of better-defined fibers by electrospinning.

2 Experimental

2.1 Materials

PLLA with an average molecular weight of 10×10^4 g/mol was purchased from Shenzhen Guanghua Co., Ltd., China. PCL with an average molecular weight of 1000 g/mol was purchased from Slovey Co., Korean. IPDI, Dibutyltin dilaurate, and *p*-toluene sulfonic acid were used as received. 1,4-Butanediol and 1,2-dichloroethane were dried using 4-Å molecular sieves. The solvents, chloroform, 1,2-dichloroethane and methanol were analytical grade reagents.

2.2 Synthesis of PLLA/PCL Multi-block Copolymers

The synthesis of the PLLA/PCL multi-block copolymers were conducted through a two-stage method, First, PLLA-diols of the desired molecular weights were prepared by transesterification between the PLLA and 1,4-butanediol with *p*−toluenesulfonic acid as catalyst (24). The reaction was carried out in dry 1,2-dichloroethane at 60°C under argon atmosphere. After 20 h, the reaction was stopped by pouring the product in cold methanol, the solid formed was separated by filtration and washed successively with methanol, acetone, and diethyl ether, and then dried under vacuum. After drying, PLLA-diols were obtained. The molecular weight of PLLA-diols was measured by GPC with PS as the standard and THF as the eluent to be 3800 g/mol. The molecular weight of PLLA-diols was lower than that of PLLA due to the degradation of PLLA during the transesterification. The second stage involved copolymerization of PLLA-diol and PCL, which was carried out in dry 1,2-dichloroethane under argon atmosphere using an equimolar amounts of IPDI as a coupling agent and dibutyltin dilaurate as a catalyst by the method described previously(25,26). The temperature of the reaction was kept constant at 80°C. After 3 h, the resulting polymer was precipitated by excess ether. The precipitated copolymer was filtered and dried in a vacuum oven at 30°C. The polymerization reaction was carried out using different ratios to obtain PLLA/PCL copolymers of varying PLLA/PCL weight ratios of 90/10, 75/25, and 50/50, respectively.

2.3 The Electrospun Fibrous Scaffolds Preparation

The PLLA/PCL block copolymer was dissolved in a mixture of chloroform and methanol (3/1 by volume ratio). The mixtures were stirred at room temperature with magnetic stirring for 4 h to obtain homogeneous solutions. The concentration of the solution was varied from 4 to 10 wt%. For the process of electrospinning, the polymer solution was placed into a 2 ml syringe with a needle having an inner diameter of 0.46 mm. The electrical field was provided by a DW-P353-3ACCD high voltage power supply (Tianjin High Voltage Technology Factory, China), which could provide voltages from 0 to 30 kV. A copper wire connected to the positive electrode was inserted into the polymer solution, a grounded aluminum foil as collector was positioned opposite and perpendicular to the needle tip. The polymer jets generated from the needle by the high voltage field formed the fibers and fibrous membrane at the grounded collector. Mass flow rate of solutions was 1.5 ml/h. The ground collection plate of aluminum foil was located at a fixed distance 15 cm from the needle tip. The electrospinning experiments were performed at room temperature. As-spun fibrous membranes were dried under vacuum at room temperature over night.

2.4 Characterization

The average molecular weights and polydispersity of PLLA-diols and three PLLA/PCL copolymers with different weight ratios were measured by Agilent 1100 gel permeation chromatography (GPC) with PS as the standard and THF as the eluent.

Fourier transform infrared (FTIR) spectra were recorded on a Bruker Equinox 55 spectrometer on solvent cast polymer films on KBr plate. Chloroform was used as the solvent for film casting.

A X'Pert Pro X-ray diffractometer (Phillips, Netherlands) with Cu Kα radiation ($\lambda = 1.5406$ Å) at a generator voltage of 40 kV and a current of 40 mA was used to analyze the crystallinity properties of the copolymers. All experiments were conducted in the 2θ range of 5–30° at ambient temperature with a scanning speed of 5°C/min and step size of 0.02°.

Differential scanning calorimetry (DSC) was carried out with a Perkin-Elmer7 thermoanalyzer under a nitrogen atmosphere. DSC traces were recorded between 50°C and 200°C at a heating rate of 10°C/min.

The surface tension of the PLLA-b-PCL solutions was tested using a K99B tensiometer (Schmidt, Germany) at room temperature. The solution electrical conductivity was determined by Cond730 conductivity instrument (Shanghai, China) and the solution viscosities determined at 20°C and 80 rpm with a Brookfield R/S Rheometer (Brookfield, USA).

The morphology of the electrospun fiber was observed by a Quanta 400 scanning electron microscope (SEM, Phillips, Netherlands). The specimen was coated with a thin layer of gold prior to SEM observations. The average fiber diameter (AFD) was statistically calculated by analyzing 20 fibers at random. The average value was reported with standard deviation.

Mechanical properties of electrospun fibrous membranes of PLLA and three copolymers with different weight ratios including PLLA/PCL(90/10), PLLA/PCL(75/25), PLLA/PCL(50/50) were tested in a CMT-4104 universal testing machine (Shenzhen, China) equipped with a 10 N load cell. These electrospun fibrous membranes were obtained under a solution concentration of 10 wt%. All samples were cut in the form of rectangular shape with dimensions of 80×20 mm^2 from the electrospun fibrous membranes. Each tensile test was operated under a crosshead speed of 10 mm/min at ambient conditions. At least five samples were tested for each type of electrospun fibrous membrane.

3 Results and Discussion

3.1 Characterization of PLLA-diols and PLLA/PCL Multi-block Copolymers

The M_n of the PLLA - diols and the three PLLA/PCL multi-block copolymers with different ratios are listed in Table 1. That the molecular weight of PLLA-diols was 3800 g/mol is due to degradation of the purchased PLLA upon functionalization. The molecular weight (M_W) of the copolymers synthesized ranged between 21600 and 52500, with a polydispersity between 1.56 and 1.72.

Table 1. Molecular weight data (in g/mol) of the PLLA - diols and the PLLA/PCL block copolymers

Composition	M_w (10^3)	M_n (10^3)	M_w/M_n
PLLA-diols	4.72	3.81	1.24
PLLA/PCL(90/10)	52.5	33.7	1.56
PLLA/PCL(75/25)	24.8	15.2	1.63
PLLA/PCL(50/50)	21.6	12.6	1.72

A set of representative FTIR spectra of the PLLA, PLLA-diols and the PLLA/PCL(90/10) block copolymers are shown in Figure 1. Compared with PLLA, the OH stretching band at 3500 cm^{-1} were observed in the PLLA-diols. It can be seen that after the reaction with IPDI and PCL, the broad OH stretching band characteristic of the PLLA-diols almost disappears, while a new band at 3350 cm^{-1} (NH stretching) is observed. In the C=O stretching region, the 1760 cm^{-1} band for the PLLA carbonyl shifts to 1750 cm^{-1}, and widening of carbonyl stretch was observed in the copolymer. This may be due to merging of two peaks (PCL block and PLLA block) into one as a result of copolymers (14). Meanwhile, two new bands appear at 1680 cm^{-1} (amide I) and 1535 cm^{-1}(amide II), respectively. All these spectral changes provide convincing evidence for the formation of the copolymer.

Figure 2 presents the DSC results of the three copolymers synthesized. All three had one melting peak from the PLLA block because the PCL block could not crystallize due to its short length (12), In other word, the crystalline phase is mainly PLLA phase in these copolymers. It is apparent that their crystalline regions gradually changed, as the weight ratio of the PLLA blocks decreased. PLLA/PCL (90/10) block copolymers exhibited a cold crystallization peak at 80.1°C with crystallization enthalpy ($\triangle H_c = -19.4$ J/g),

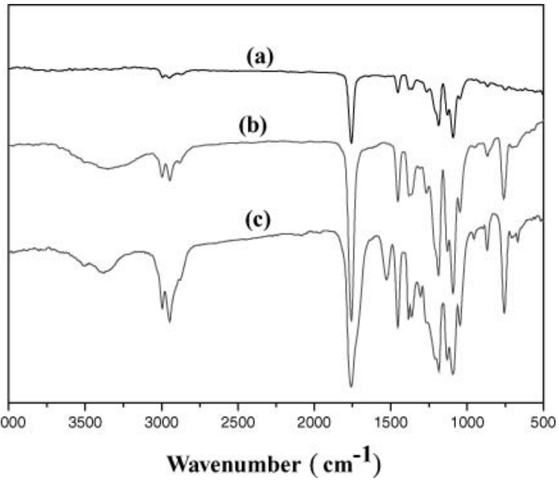

Fig. 1. FTIR spectra of (a) PLLA, (b) PLLA-diols, and (c) PLLA-b-PCL(90/10).

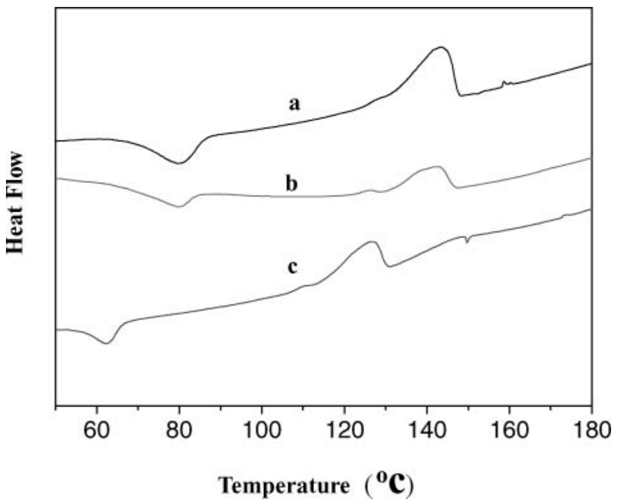

Fig. 2. DSC curves of PLLA-b-PCL (a) PLLA/PCL (90/10), (b) PLLA/PCL (75/25), and (c) PLLA/PCL (50/50).

and a relatively sharp melting peak at 145.0°C with melting enthalpy ($\triangle H_m = 37.5$ J/g). For PLLA/PCL (75/25) block copolymer, there exist the cold crystallization peak of PLLA near 79.2°C with crystallization enthalpy ($\triangle H_c = -16.1$ J/g), and melting peak of PLLA at 143.4°C with melting enthalpy ($\triangle H_m = 31.8$ J/g). As the weight ratio of the PLLA/PCL blocks decreased further (50/50), a small cold crystallization peak of PLLA near 63.1°C with crystallization enthalpy ($\triangle H_c = -15.6$ J/g), and melting peak of PLLA at 128.4°C with melting enthalpy ($\triangle H_m = 24.8$ J/g). The higher the weight ratio of PLLA, the higher the T_m and $\triangle H_m$ were. This was caused by some degree of phase separation between the two domains. The PLLA domain had a higher T_m and crystallized earlier. PLLA is a much stiffer aliphatic polyester and is chosen to create the hard blocks along the copolymeric backbone. The amorphous phase of PCL displays high mobility at room temperature. Since short PCL chains are amorphous, they were selected to perform as the flexible segments present along the copolymeric backbone. This is necessary for the PLLA/PCL block copolymer to be clinically used as a scaffolds for tissue engineering.

Figure 3 shows the WAXD patterns of the three PLLA/PCL block copolymers. Obviously, there are two main diffraction peaks at 2θ of 16.9 and 19.2°, which are attributed to PLLA crystals (14). Furthermore, the copolymers have a very weak diffraction peak near 22.3°, which is assigned to the characteristic peak of PCL (27). However, compared with PLLA, the diffraction peaks of PCL are relatively weak. All the copolymers showed an intense peak at 2θ of 16.9°, suggesting high crystallinity in all copolymers with the higher PLLA ratios. This indicates that the crystalline phase is mainly PLLA phase in these block copolymers. These results are consistent with the above DSC analysis.

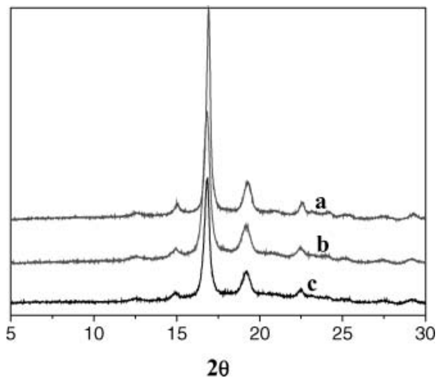

Fig. 3. XRD spectra of the PLLA/PCL copolymers (a) PLLA/PCL(90/10), (b) PLLA/PCL (75/25), and (c) PLLA/PCL (50/50).

3.2 Morphology of PLLA-b-PCL Electrospun Fibrous Scaffolds

In the electrospinning system, there are a number of parameters affecting fiber morphology and fiber diameter, such as polymer concentration, viscosity, conductivity and surface tension. Figure 4 shows SEM images of PLLA, PLLA/PCL(90/10), PLLA/PCL(75/25) and PLLA/PCL(50/50) electrospun fibers under solution concentration of 10 wt%, voltage 20 kV and tip-to-collector distance (TCD) 15 cm. In the SEM images, the higher weight ratio of PCL produced the smaller fiber diameters and fiber diameters calculated ranged from 300 nm to 1.5 μm. It can be seen that the electrospun PLLA fibers are smooth fibers with an average diameter (AD) of ~1.2 μm (Fig. 4(a)). With increasing PCL content in the PLLA-b-PCL, the AD decreases significantly. The observed AD were 850 ± 230 nm for PLLA/PCL(90/10) (Fig. 4(b)), 640 ± 160 nm for PLLA/PCL (75/25) (Fig. 4(c)), and 390 ± 180 nm for PLLA/PCL (50/50) (Fig. 4(d)). From Table 2 (Samples 1–4), the conductivity, surface tension and viscosity of the

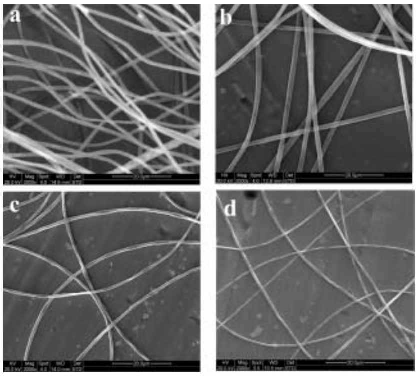

Fig. 4. SEM micrographs of electrospun PLLA-b-PCL fibers at solution concentration of 10 wt%, voltage 20 kV and TCD 15 cm. (a) PLLA/PCL (100/0), (b) PLLA/PCL (90/10), (c) PLLA/PCL (75/25), and (d) PLLA/PCL (50/50).

Table 2. Solution properties of PLLA-b-PCL

Sample number	*PLLA/PCL ratio*	*Concentration (wt%)*	*Conductivity (µs/cm)*	*Surface tension (mN/m)*	*Viscosity (Pa·s)*
1	100/0	10	0.95	26.12	0.245
2	90/10	10	0.81	25.15	0.168
3	75/25	10	0.69	22.41	0.094
4	50/50	10	0.66	21.95	0.067
5	75/25	4	0.89	12.59	0.011
6	75/25	6	0.81	16.78	0.034
7	75/25	8	0.75	20.61	0.079

copolymer solution decrease with increasing weight ratio of PCL. Especially, the decrement of solution viscosity is the largest. For example, the solution viscosity of the PLLA-b-PCL with weight ratio 50/50 decreases by 72.7%, i.e., its solution viscosity decreases to 0.067 Pa·s from 0.245 Pa·s of the pure PLLA. Obviously, the morphology and diameter of the above electrospun fibers are critically affected by the physical parameters of PLLA-b-PCL solution. (5,28,29).

Figure 5 shows the SEM micrographs of PLLA/PCL (75/25) fibers electrospun at different solution concentration. It can be seen with increasing solution concentration, fiber diameter increases and the number of bead defects is reduced. When the solution concentration was less than 8 wt%, beads (Fig. 5(a)) and beaded fibers (Fig. 5(b)) were formed for the lower viscous solutions. Meanwhile, the shape of the beads gradually changes from spherical to spindle-like as the viscosity increases. With increasing concentration to 8 wt%, the beads almost disappeared in the electrospun fibers with AD values of 450 ± 180 nm (Figs. 5(c) and (d)). When the solution concentration is further increased to 10 wt%, the bead-free smooth fibers with AD 640 ± 160 nm are obtained (Fig. 5(e) and (f)). These indicate that there is a critical concentration (~8 wt%) in the electrospinning process of PLLA-b-PCL solutions. From Table 2 (Samples 5–7 and 3), as the solution concentration increases, both the surface tension and viscosity increase but the conductivity decreases. At solution concentrations below the critical 8 wt%, there are fewer chain entanglements due to the low surface tension and viscosity. Also, the high conductivity enables the occurrence of dramatic fiber jet instability (6), which leads to unstable electrospinning. However, at solution concentrations more than 8 wt%, the improvement in electrospinability is related to the increase in solution viscosity due to the enhanced chain entanglements (28) and reduced conductivity (6).

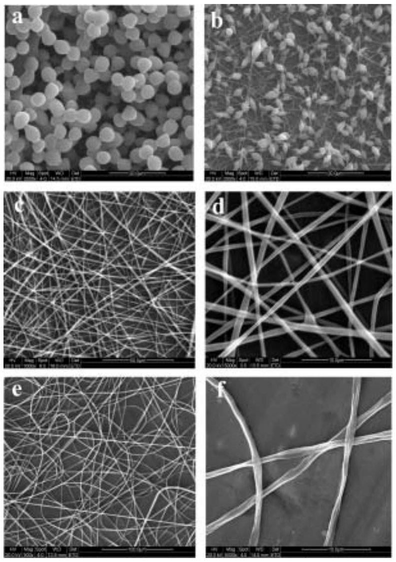

Fig. 5. SEM micrographs of fibers electrospun by different solution concentration for PLLA/PCL (75/25) at voltage 20 kV and TCD 15 cm: 4 wt% (a, ×2000), 6 wt% (b, ×2000), 8 wt% (c, ×1000; d, ×5000), and 10 wt% (e, ×500; f, ×5000).

3.3 Mechanical Properties of the Electrospun Fibrous Scaffolds

Mechanical integrity is an important property of the tissue engineering scaffolds since a scaffold must act as a temporary support to withstand the external and internal stresses (30). According to the references, such as (5, 6) and (23), it is generally considered that scaffolds morphology should be defect-free and uniform diameter to allow cell adhesion, migration, proliferation, differentiation and tissue

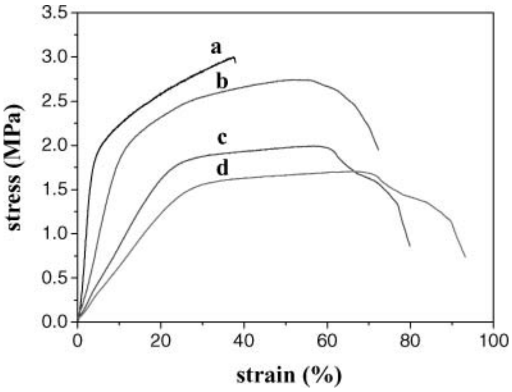

Fig. 6. Tensile stress–strain curves of the electrospun fibrous membrane (a) PLLA/PCL (100/0), (b) PLLA/PCL (90/10), (c) PLLA/PCL (75/25), and (d) PLLA/PCL (50/50).

Table 3. Mechanical properties of the electrospun PLLA and PLLA-b-PCL fibrous membranes

Mechanical Properties	*PLLA*	*PLLA/PCL (90/10)*	*PLLA/PCL (75/25)*	*PLLA/PCL (50/50)*
Young's modulus (MPa)	55.93 ± 2.11	18.11 ± 0.94	8.31 ± 0.45	6.21 ± 0.64
Tensile strength (MPa)	3.05 ± 0.21	2.75 ± 0.09	1.87 ± 0.14	1.58 ± 0.16
Elongation at break (%)	37.3 ± 3.9	66.5 ± 8.6	79.5 ± 9.3	94.6 ± 7.5

regeneration in three dimensions. Thus the solution concentration of 10 wt% was used in electrospinning and the bead-free smooth fibers are obtained and used in tissue engineering. The stress–strain curves of the electrospun fibrous scaffolds of PLLA and three copolymers with different weight ratios are shown in Figure 6. Corresponding tensile strength, Young's modulus, and elongation-at-break are all listed in Table 3. The PLLA fiber sheet showed a very rigid and brittle property with the high Young's modulus of 55.93 ± 2.11MPa and the low elongation at break of 37.3 ± 3.9%. In comparison with the electrospun PLLA membrane, PLLA-b-PCL caused a reduction in tensile strength and Young's modulus, and an increase in the elongation -at-break. It is suggested that the PCL amorphous chains performed as a molecular coil, while the crystalline PLLA blocks functioned as strong non-covalent crosslinking domains (12). For the PLLA-b-PCL fiber sheets, as the PCL content increased, the modulus decreased and the elongation at break increased gradually. For example, the elongation at break of the PLLA-b-PCL with weight ratio 75/25 increases by 114%, i.e., its elongation at break increases from 37.3 ± 3.9 % of the pure PLLA to 79.5 ± 9.3 %. Furthermore, the PLLA-b-PCL fiber membranes still retained a relatively high tensile strength and Young's modulus, thus having balanced strength and flexibility. In general, the copolymer fibrous membrane has good flexibility and deformability and provides a good fibrous scaffold in tissue engineering applications.

4 Conclusions

PLLA/PCL multi-block copolymers were synthesized from diol-terminated PLLA (PLLA-diols), as hard segments and PCL, as soft segments. Their structures and thermal properties were characterized via FTIR, DSC and XRD. FTIR spectra suggested the formation of the copolymer, DSC and XRD showed that the crystalline phase was mainly PLLA phase in these block copolymers and short PCL segments are amorphous and perform as the flexible segment. Furthermore, PLLA-b-PCL fibrous scaffolds were prepared by electrospinning. The effect of the weight ratio of PLLA/PCL and the electrospinning solution concentration on the morphology and the average diameter of the electrospun fibers were investigated. At a fixed electrospinning condition, the fiber diameter of PLLA-b-PCL was decreased with decreasing solution concentration and increasing PCL content. The results of mechanical properties showed that the PLLA-b-PCL fibrous scaffolds demonstrated an enhanced elongation at break with still high tensile strength and Young's modulus. Our results show potential applications of the PLLA-b-PCL fibrous membranes as biomaterial scaffolds for biomedical applications that will be further investigated.

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References

1. Kwon, K., Kidoaki, S. and Matsuda, T. (2005) *Biomaterials*, 26(18), 3929–3939.
2. Rinki, K. and Dutta, P. K. (2010) *J. Macromol. Sci. A,* 47(5), 429–434
3. Chen, J.L., Chu, B. and Hsiao, B.S. (2006) *J. Biomed. Mater. Res. A*, 79A(2), 307–317.
4. Yang, F., Xu, C.Y., Kotaki, M. and Wang, S. (2004) *J. Biomater. Sci. Polym. Ed.*, 15, 1483–1497.
5. Huang, Z.M., Zhang, Y.Z., Kotaki, M. and Ramakrishna, S. (2003) *Compos. Sci. Technol.*, 63(15), 2223–2253.
6. Sill, T.J. and von Recum, H.A. (2008) *Biomaterials*, 29(13), 1989–2006.
7. Doshi, J. and Reneker, D.H. (1995) *J. Electrostat.*, 35, 151–160
8. Reneker, D.H. and Chun, I. (1996) *Nanotechnology*, 7(3), 216–223.
9. Ma, P.X., Mooney, D. and Langer, R. (1995) *J. Biomed. Mater. Res.*, 29(12), 1587–1595.
10. Venugopal, J. and Ramakrishna, S. (2005) *Tissue Eng.*, 11, 847–853.
11. Stitzel, J.D., Pawlowski, K.J., Bowlin, G.L., Wnek, G.E., Simpson, D.G., and Bowlin, G.L. (2001) *J. Biomater. Appl.*, 16, 22–33.
12. Cohn, D. and Salomon, A.H. (2005) *Biomaterials*, 26, 2297–2305.
13. Huang, M.H., Li, S.M. and Vert, M. (2004) *Polymer*, 45(26), 8675–8681.
14. Garkhal, K., Verma, S., Jonnalagadda, S. and Kumar, N. (2007) *J. Polym. Sci. A*, 45, 2755–2764.
15. Yang, F., Murugan, R., Wang, S. and Ramakrishna, S. (2005) *Biomaterials*, 26, 2603–2610.
16. Na, Y.H., He, Y., Shuai, X., Kikkawa, Y., Doi, Y. and Inoue, Y. (2002) *Biomacromolecules*, 3(6), 1179–1186.
17. López-Rodríguez, N., López-Arraiza, A., Meaurio, E. and Sarasua, J.R. (2006) *Polym. Eng. Sci.*, 46(9), 1299–1380.
18. Aslan, S., Calandrelli, L., Laurienzo, P., Malinconico, M. and Migliaresi, C. (2000) *J. Mater. Sci.* 35, 1615–1622.
19. Lee, K.H., Kim, H.Y., Khil, M.S., Ra, Y.M. and Lee, D.R. (2003) *Polymer*, 44, 1287–1294.
20. Jeong, S.I., Kim, B.S., Lee, Y.M., Ihn, K.J., Kim, S.H. and Kim, Y.H. (2004) *Biomacromolecules*, 5, 1303–1309.

21. Ye, W.P., Du, F.S., Jin, W.H., Yan, J.Y. and Xu, Y. (1997) *React. Funct. Polym.*, 32, 161–168.
22. Mo, X.M., Xu, C.Y., Kotaki, M. andRamakrishna, S. (2004) *Biomaterials*, 25, 1883–1890.
23. Vaz, C.M., Tuijl S. van, Bouten, C.V.C. and Baaijens, F.P.T. (2005) *Acta Biomaterialia*, 1(5), 575–582.
24. Li, J., Li, X., Ni, X. and Leong, K.W. (2003) *Macromolecules*, 36(8), 2661–2667.
25. Hirt, D.T., Neuenschwander, P. and Suter, U.W. (1996) *Macromol. Chem. Phys.*, 197(5), 1609–1614.
26. Wang, W., Ping, P., Chen, X. and Jing, X. (2006) *Eur. Polym. J.*, 42(6), 1240–1249.
27. Rezgui, F., Swistek, M., Hiver, J.M., G'Sell, C. and Sadoun, T. (2005) *Polymer*, 46, 7370–7385.
28. Chen, H., Snyder, J.D. and Elabd, Y.A. (2008) *Macromolecules*, 41, 128–135.
29. Fong, H., Chun, I. and Reneker, D.H. (1999) *Polymer*, 40, 4585–4592.
30. Ozkoc, G., Kemaloglu, S. and Quaedflieg, M. (2010) *Polym. Compos.*, 31, 674–683.