

This article was downloaded by:

On: 24 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Journal of Macromolecular Science, Part A

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597274>

The Preparation and Biodegradable Properties of Poly(L-lactic acid)-Poly(ϵ -caprolactone) Multiblock Copolymers

Cuiqing Teng^a; Hong Xu^a; Kai Yang^a; Muhuo Yu^a

^a College of Materials Science and Engineering, State Key Laboratory for Modification of Chemical Fibers and Polymer Materials, Donghua University, Shanghai, P. R. China

To cite this Article Teng, Cuiqing , Xu, Hong , Yang, Kai and Yu, Muhuo(2006) 'The Preparation and Biodegradable Properties of Poly(L-lactic acid)-Poly(ϵ -caprolactone) Multiblock Copolymers', Journal of Macromolecular Science, Part A, 43: 11, 1877 – 1886

To link to this Article: DOI: 10.1080/10601320600941276

URL: <http://dx.doi.org/10.1080/10601320600941276>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

The Preparation and Biodegradable Properties of Poly(L-lactic acid)-Poly(ϵ -caprolactone) Multiblock Copolymers

CUIQING TENG, HONG XU, KAI YANG, AND MUHUO YU

College of Materials Science and Engineering, State Key Laboratory for Modification of Chemical Fibers and Polymer Materials, Donghua University, Shanghai 200051, P. R. China

Multi-block copolymers of PLLA and PCL were prepared by a coupling reaction between PLLA and PCL prepolymers with –NCO end groups. FTIR proved that the products were PLLA-PCL copolymers. The weight-average molecular weight of the copolymers was up to 180,000 at a composition of 60% PLLA and 40% PCL. The degradation properties of PLLA and PLLA-PCL copolymers were studied by a soil burial test and a hydrolysis test in a phosphate-buffer solution. The degradation rate was estimated by the mass loss, molecular weight reduction, pH value changes and swelling index; the degradation rates of the copolymers were a function of the composition of PLLA and PCL. Increasing PCL content in the copolymers resulted in lower degradation rate.

Keywords poly(lactic acid), poly(ϵ -caprolactone), multiblock copolymers, degradation, soil buried test, hydrolysis test

Introduction

Poly(L-lactic acid) (PLLA) and PLLA-based copolymers are well established semi-crystalline, biodegradable materials used not only for a variety of applications in the pharmaceutical and biomedical field, but also as biodegradable plastics for disposable consumer products (1–4). Although high molecular weight PLLA is a relatively stiff polymer with good mechanical strength, it is too brittle for application as packaging films and coating materials. To improve the properties of PLLA and expand its applications, copolymerization or blending techniques have been applied (5–7). Polymer blends or copolymers of PLLA and poly(ϵ -caprolactone) (PCL) have been the subject of great interest in recent years (8–10). PCL is also one of the most widely investigated aliphatic polyesters because of its unique properties such as biodegradability, biocompatibility, and high flexibility. The syntheses of ϵ -CL/LA copolymers have been widely studied, but most effort has focused on random, diblock, and triblock copolymers by the ring opening polymerization of lactide (9); however, these synthetic methods affected the properties

Address correspondence to Muhuo Yu, College of Materials Science and Engineering, State Key Laboratory for Modification of Chemical Fibers and Polymer Materials, Donghua University, Shanghai 200051, P. R. China. Tel.: 0086-21-62373507; E-mail: yumuhuo@dhu.edu.cn

of copolymer due to phase separation and led to a high cost of production for the lactide as a monomer.

We have developed a new process to synthesize PLLA-PCL multiblock copolymers with high molecular weight and low cost using melt polycondensation of lactic acid. The multiblock copolymers are prepared by coupling reactions between PCL telechelic oligomers (OCN-PCL-NCO) and the PLLA oligomers. The advantage of this new process is that the high molecular weight of lactic acid-based polymers can be prepared directly by melt polycondensation of lactic acid, rather than ring opening polymerization using the lactide as monomer. This new synthetic method reduces the cost of production, and the PLLA is toughened by the copolymerization, which results in a compatible system compared with the blending system.

As a widely used biodegradable polymer, the biodegradation behavior of PLLA and PLLA-based copolymers is an important property determining its final application. The *in vitro* degradation and *in vivo* degradation of PLLA has been widely investigated (11–16); for PLLA-PCL copolymer, the degradation properties have also been studied by several research groups (9, 17). PCL is also a biodegradable material, but its long degradation time (3–5 years) is usually a disadvantage for application. PLA behaves in the opposite way. Their random copolymer always degrade faster than either homopolymers, but the block copolymers of PLLA-PCL have the advantages over the random copolymers that both the permeation rate of steroids and the degradation rate are between their homopolymers, and can be controlled by adjusting composition of the copolymer. However, the degradation properties of the PLLA-PCL multiblock copolymers have not been reported so far. In this paper, the degradation properties of PLLA-PCL multiblock copolymers were studied by a soil burial test and a hydrolysis test in a phosphate-buffer solution. The degradation rate was estimated by the mass loss, molecular weight reduction, pH value and swelling index.

Experimental

Materials

Poly(ϵ -caprolactone)diols with M_n of 1000 was supplied by Daicel Chemical Co. Ltd (Japan). L-Lactic acid as a 90 wt% aqueous solution was purchased from JiangXi Musashino Bio-chem. Co. Ltd (China). 1,6-Hexamethylene diisocyanate (HDI) was supplied by Nippon Polyurethane Industry Co., Ltd. Tin II chloride dihydrate ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$), tetrahydrofuran, citric acid ($\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$) and disodium hydrogen phosphate ($\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$) were purchased from Shanghai Chemical Reagent Company, China Medicine (Group). All materials above were analytical-grade and were used without further purification.

Synthesis of PLLA-PCL Multi-Block Copolymers

PLLA homopolymer (HO-PLLA-COOH) was synthesized by the melt condensation polymerization of L-lactic acid, Tin II chloride dihydrate ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$) (0.5% based the mass of L-Lactic acid) was used as a catalyst. L-Lactic acid was first dehydrolyzed at 130°C for 3 hr under vacuum and then polycondensation was carried out at 160°C for 6 h under *vacuo*. Poly(ϵ -caprolactone)diols and HDI (molar ratio of HDI/PCL = 2:1) were put into a three-necked round-bottomed flask, and the reaction was performed at 80°C for 3 h. The prepolymer of NCO-terminated PCL was obtained after deaeration. The PLLA and PCL telechelic with –NCO end groups (NCO-PCL-NCO)

were put into a flask. The mass feed ratio of PLLA and NCO-PCL-NCO was 90:10, 80:20, 70:30, 60:40, and 50:50. The reaction was carried out at 180°C for 10 min under a nitrogen atmosphere. The product was poured out and solidified naturally. Consequently, PLLA-PCL multiblock copolymers were obtained by the reaction of –NCO groups at the end of PCL with the –OH (or –COOH) groups at the end of PLLA. The multiblock copolymer codes are listed in Table 1.

Characterization of PLLA-PCL Structure

The molecular weight and the distribution of the polymers were measured by GPC (Waters 208). Tetrahydrofuran (THF) was used as the mobile phase at a flow rate of 1.0 mL/min. Calibration was performed using polystyrene standards to determine absolute weight-average and number-average molecular weights (M_w and M_n). The multi-block polymers were ground to powder for use as FTIR specimens. FTIR spectra in the range of 4000–400 cm^{-1} were recorded on KBr pellet samples, using a Nicolet NEXUS-670 Spectrometer with a resolution of 2 cm^{-1} . The viscosity measurements were conducted on an Ubblohde viscometer with an internal diameter of 0.35 mm, the solvent was THF and the measurement temperature was $30 \pm 0.1^\circ\text{C}$. The viscosity-average molecular weight of polymers was calculated by the following formula (18):

$$[\eta] = 1.25 \times 10^{-4} M_\eta^{0.717}$$

Soil Burial Test

The molded samples were cut into a rectangular shape with dimensions of $50 \times 50 \times 3 \text{ mm}^3$ for *in vitro* degradation studies. The cut specimens of PLLA and PLLA-PCL copolymers were buried in soil. After various time periods the sample was removed, gently wiped to clean the surface water, dried at 50°C for 24 h in a vacuum, and reweighed. The molecular weights of the polymers were determined by viscosity measurements. The degradation rates were estimated by the mass loss (%) and molecular weight reduction (%) calculated with the following equations:

$$\text{Mass loss } V = \frac{W_0 - W_t}{W_0} \times 100\% \quad (1)$$

Where W_0 is initial weight and W_t is weight after degradation.

$$\text{Molecular weight reduction } L = \frac{M_\eta^0 - M_\eta^t}{M_\eta^0} \times 100\% \quad (2)$$

Where M_η^0 is initial molecular weight and M_η^t is molecular weight after degradation.

Table 1
The codes of PLLA-PCL multi-block copolymers

Sample codes	PLLA	PLLA90	PLLA80	PLLA70	PLLA60	PLLA50
Composition PLLA/PCL (w/w)	100/0	90/10	80/20	70/30	60/40	50/50

The morphology of PLLA and PLLA-PCL multi-block copolymers was observed under an OLYMPUS BH-UMA optical microscope.

Hydrolysis Test

Buffer solutions of citric acid ($C_6H_8O_7 \cdot H_2O$) and disodium hydrogen phosphate ($Na_2HPO_4 \cdot 2H_2O$) were prepared according to the composition shown in Table 2. The specimens of PLLA and PLLA-PCL copolymers were placed in closed bottles containing 50 mL of phosphate buffer solution at ambient temperature for up to 84 days. At various intervals, the specimens were removed, washed with distilled water, the surface dried and reweighed. The swelling index (SI) was calculated using the following equation:

$$SI = \frac{W_t - W_0}{W_0} \times 100\% \quad (3)$$

Where W_0 is the initial weight of the specimen and W_t is the weight at time t .

Results and Discussion

Synthesis and Structure Characterization

Figure 1 shows the FTIR spectra of homopolymer and multiblock copolymer. The spectrum of PLLA homopolymer (Curve b) exhibits characteristic absorption peaks of ester at 1759 cm^{-1} for the stretching vibration of $-COO-$ and at 1090 cm^{-1} , 1131 cm^{-1} , and 1185 cm^{-1} for the stretching vibration of $C-O-C$. The other characteristic absorption peaks of PLLA correspond to $C-H$, CH_3 , and $-OH$ at 2997 cm^{-1} , 1145 cm^{-1} and 3440 cm^{-1} , respectively. As shown in Figure 1 (curve a), the spectrum of PCL prepolymer exhibits a characteristic absorption peak of the end group of $-NCO$ at 2270 cm^{-1} . However, the peak at 2270 cm^{-1} disappears for the PLLA-PCL multi-block copolymer, as shown in Figure 1 (curve c). This indicates that the groups $-NCO$ at the end of PCL have reacted with the $-OH$ (or $-COOH$) groups at the end of PLLA.

Molecular Weight of PLLA-PCL Copolymers

The data in Table 3 show the molecular weight of the copolymers. As expected, the molecular weight of copolymer increases after coupling reaction of PLLA and PCL. The molecular weight of copolymer with 40 wt% PCL is more than 14 times than that of the PLLA homopolymer. This is further evidence to prove the products of PLLA-PCL multi-block copolymers. The active functional groups $-NCO$ at the end of PCL prepolymers are easy to react with $-OH$ or $-COOH$ functional groups of PLLA, which

Table 2
The composition of phosphate-buffered solution

Buffer solution	$C_6H_8O_7 \cdot H_2O$	$Na_2HPO_4 \cdot 2H_2O$	Deionized water
pH = 7.4	1.9 g	32.3 g	to 1 L

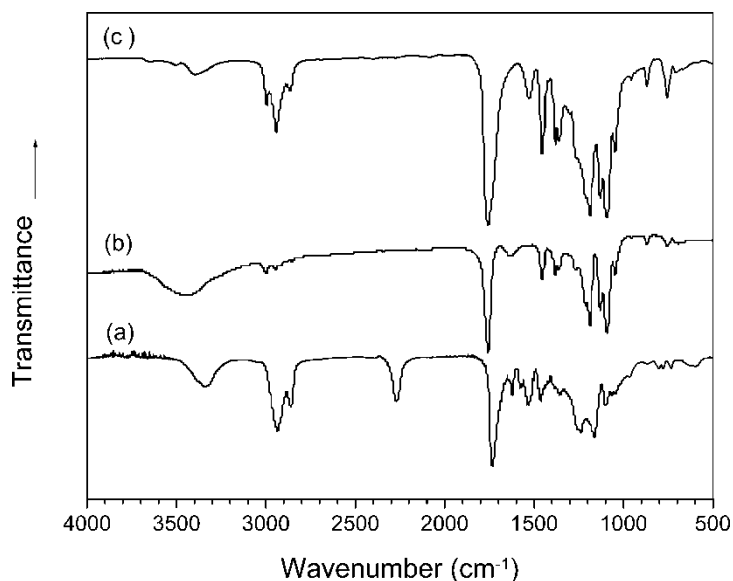


Figure 1. FTIR spectra of (a) OCN-PCL-NCO, (b) PLLA, and (c) PLLA-PCL multi-block copolymer.

results in an increase of the molecular weight. The molecular weight is maximum at the composition of PLLA/PCL = 60/40 (w/w).

Soil Burial Test

The photographs of films obtained from the PLLA before and after the degradation test are illustrated in Figure 2. Before degradation, the surface of PLLA is smooth without pores and cracks. After 7 days of burial, the polymer film shows a rough and porous surface, indicative of the ongoing erosion. After 28 days of burial, the pores and cracks at the surface are seen growing into the film, and the surface shows channel-like structures. With the prolongation of the degradation time, the channel-structure becomes larger and larger, and after about 4 months of burial the PLLA polymer had cracked into pieces.

Table 3

Molecular weight of PLLA and PLLA-PCL multi-block copolymers

Samples	M_n^a	M_n^b	M_w^b	M_w/M_n^b
PLLA	12700	6900	14100	2.04
PLLA90	18000	—	—	—
PLLA80	32800	15100	37500	2.48
PLLA70	96300	47500	100100	2.11
PLLA60	166800	99000	179900	1.82
PLLA50	115200	—	—	—

^aMeasured in THF at $30 \pm 0.1^\circ\text{C}$ using an Ubbelohde viscometer.

^bMeasured by GPC.

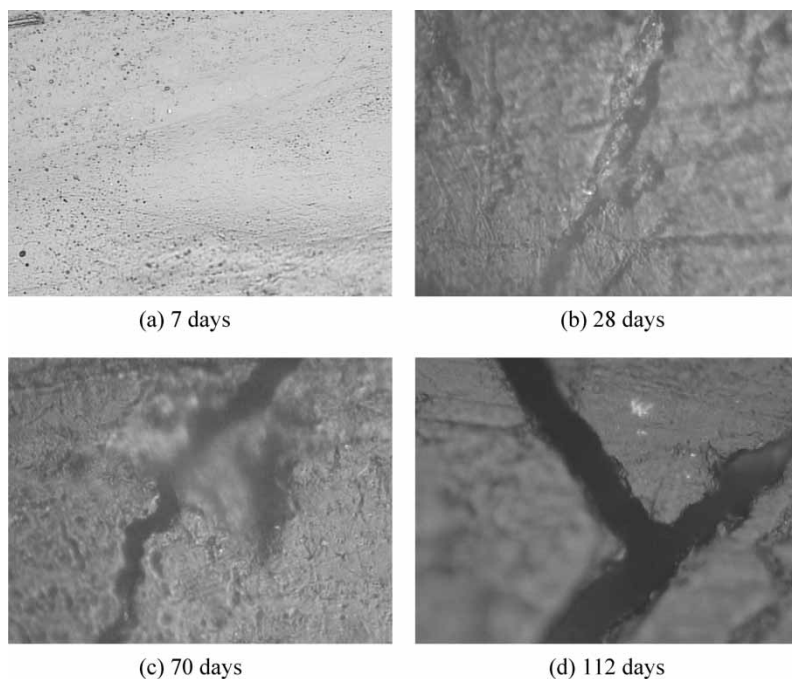


Figure 2. Surface photographs of PLLA at various time in soil buried test.

Figure 3 shows the morphology of PLLA-PCL multiblock copolymers before and after degradation. Even though the degradation trends of PLLA-PCL were similar to those of PLLA homopolymer, the change of structure is relatively slower, which indicates the degradation rate of PLLA-PCL copolymers is slower than that of PLLA. PCL is also a degradable material, but its degradation rate is slower than that of PLLA. The difference of degradation rates between the PLLA and PLLA-PCL copolymer are attributed to the introduction of PCL segments in the copolymer and the high molecular weight of PLLA-PCL.

Figure 4 shows the weight changes of the PLLA homopolymer and PLLA-PCL multi-block copolymers during the soil burial test. At the beginning of degradation, all of the polymers show a slight weight loss. After 28 days of degradation, the changes in weight become significant. Compared with the PLLA homopolymer, the degradation rate of PLLA-PCL multi-block copolymers is slower than that of PLLA, and with the increasing of PCL content in the copolymers, the degradation rate becomes slower.

Figure 5 displays the time course of molecular weight changes of the polymers during the degradation test. It is evident that the degradation rate in the molecular weight of PLLA is also faster than those of the multi-block copolymers.

Hydrolysis Test

The PLLA and PLLA-PCL multi-block copolymers samples were immersed in the phosphate-buffer solution, and the effect of time on the hydrolysis rate were examined by pH value changes of the solution and degree of swelling of the samples. Figure 6 shows the pH value changes of the buffer solution with degradation time. There are no

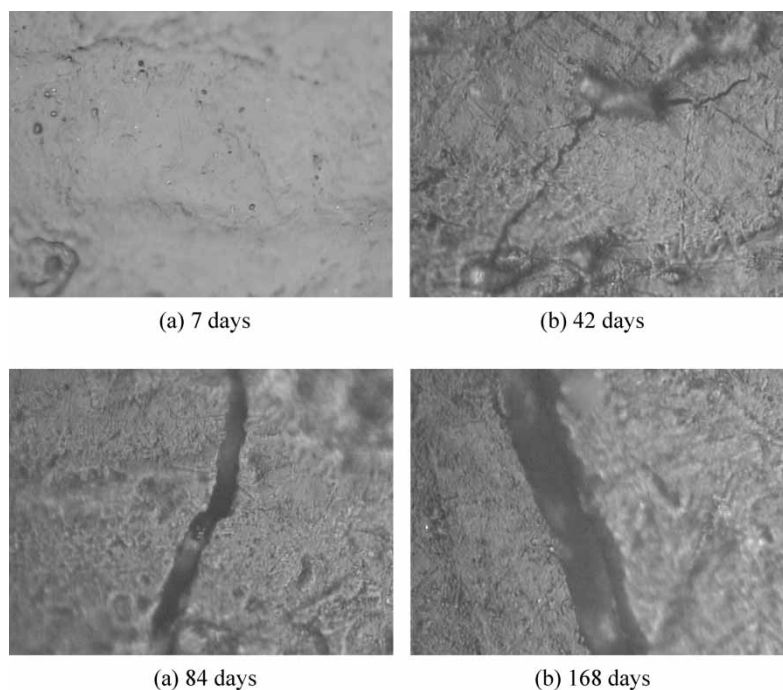


Figure 3. Surface photographs of PLLA70 at various time in soil buried test.

significant changes in pH value at the beginning of degradation, and a slight decrease of pH value can be observed after 14 days of degradation. However, with the prolongation of the degradation time, especially after 28 days of degradation, the decrease rate of pH value becomes faster. At 84 days of degradation, the pH of the solution decreases to 5.6.

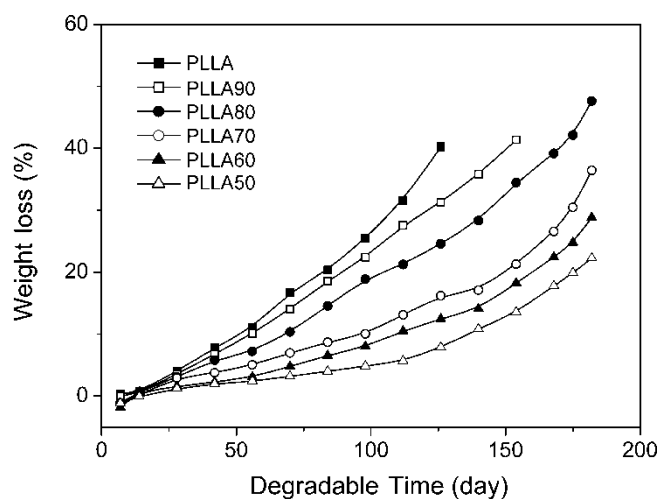


Figure 4. Weight loss of PLLA and PLLA-PCL copolymers in soil buried test.

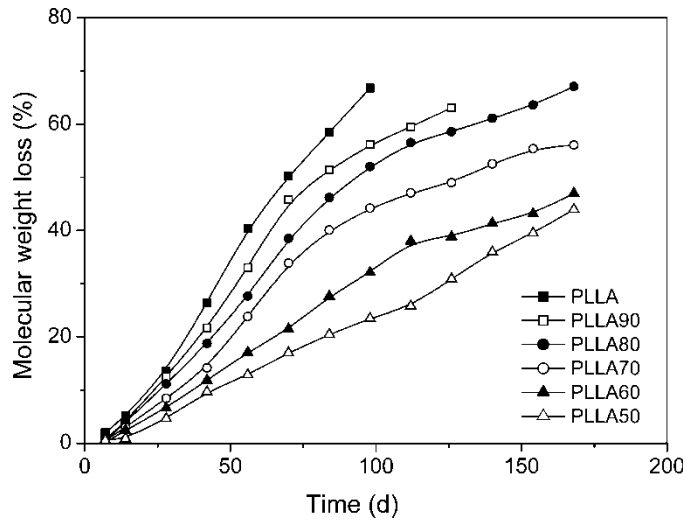


Figure 5. Molecular weight changes of PLLA and PLLA-PCL copolymers in soil buried test.

PLLA is a hydrolytically biodegradable polymer that followed a bulk degradation mechanism when it is immersed in a neutral aqueous medium, such as phosphate-buffer solution (pH 7.4) (19). The ester bonds in the backbone chain of the polymer break randomly to generate carboxyl groups, which autocatalytically accelerates the degradation reaction and results in a decrease of the pH value of the solution with degradation time. But the bulk degradation of the PLLA is a slow process and the changes in the associated properties can rarely be detected in a short time of several days at ambient temperature, so at the beginning of degradation, there were no significant changes in pH value.

For the PLLA-PCL multi-block copolymer, the trend of pH value changes with the degradation time is similar to that of PLLA homopolymer, but the rate of pH values changes of PLLA-PCL is relatively slower. The fact further indicates the hydrolysis

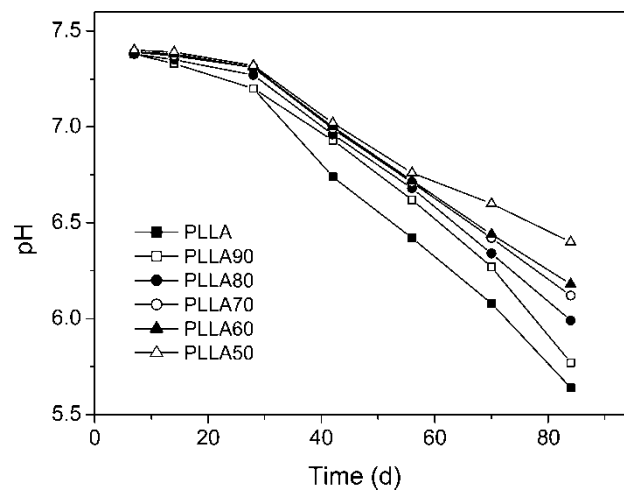


Figure 6. Changes of pH value in buffer solution with immersing time.

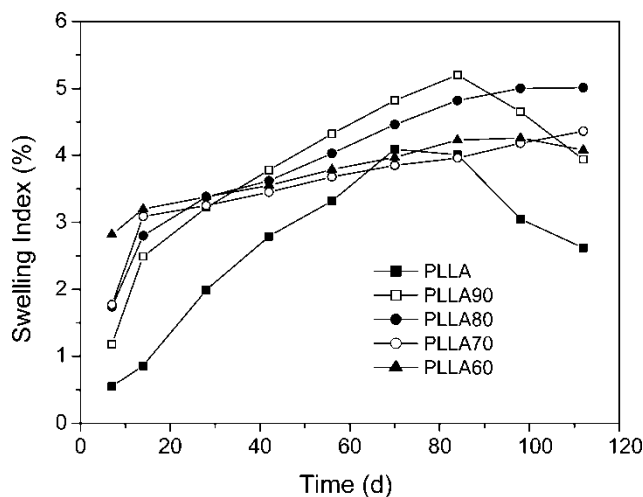


Figure 7. The swelling index of PLLA and PLLA-PCL copolymers with emerging time.

rate in the phosphate-buffer solution of the copolymer is slower than that of PLLA homopolymer, which is consistent with the results got from the soil buried test.

The swelling index of PLLA and PLLA-PCL copolymers immersed into the buffer solution is shown in Figure 7. From the curve, it is clear that sorption reaches a maximum and then a weight decrease can be recorded. When the PLLA polymers are immersed into the buffer solution, there is a balance between sorption and hydrolysis. In the early days of immersion, sorption is the main interaction, so the weight of samples increased greatly. After about 14 days, when the hydrolysis becomes obvious, the rate of increased samples weight becomes slower. When the immersion time was 84 days, the hydrolysis predominates the interaction, and consequently the degree of swelling of samples decreased.

Conclusions

Multi-block copolymers of PLLA and PCL can be prepared by the following process: the PLLA homopolymer was first prepared by melt polymerization and then the copolymer was synthesized by a coupling reaction between PLLA and PCL prepolymers with –NCO end groups. FTIR proved that the products were PLLA-PCL copolymers, and the weight-average molecular weight of the copolymers was up to 180,000 at a composition of 60% PLLA and 40% PCL. The degradation properties of PLLA and PLLA-PCL copolymers were studied by a soil burial test and a hydrolysis test in a phosphate-buffer solution (pH = 7.4). The degradation rate was estimated by the mass loss, molecular weight reduction, pH value changes and swelling index. As a result, the degradation rates of the copolymers were a function of the composition of PLLA and PCL. Increasing PCL content in the copolymers resulted in lower degradation rate.

Acknowledgement

This work was financially supported by the National Natural Science Foundation of China (Grant No. 50573010 and No. 20504006).

References

1. Sodergard, A. and Stolt, M. (2002) *Prog. Polym. Sci.*, 27: 1123–63.
2. Sahoo, S.K., Panda, A.K., and Labhasetwar, V. (2005) *Biomacromolecules*, 6: 1132–39.
3. Kohler, W.H., Shrikhande, P., and McHugh, A.J. (2005) *J. Macromol. Sci., Phys.*, 44: 185–202.
4. Jacobsen, S., Degee, Ph., Fritz, H., Dubois, Ph., and Jerome, R. (1999) *Polym. Eng. Sci.*, 39: 1311–19.
5. Ljungberg, N. and Wessle'n, B. (2005) *Biomacromolecules*, 6: 1789–96.
6. Zhang, D., Xu, J., Alcazar-Roman, Ls., Greenman, L., Cramer, C.J., Hillmyer, M.A., and Tolman, W.B. (2004) *Macromolecules*, 37: 5274–81.
7. Bechtold, K., Hillmyer, M.A., and Tolman, W.B. (2001) *Macromolecules*, 25: 8641–48.
8. Zhang, L., Shen, Z., Yu, C., and Fan, L. (2004) *J. Macromol. Sci., Pure and Applied Chemistry*, 41: 927–935.
9. Jeon, O., Lee, S.H., Kim, S.H., Lee, Y.M., and Kim, Y.H. (2003) *Macromolecules*, 36: 5585–92.
10. Liu, Y.-C., Ko, B.T., and Lin, C.C. (2001) *Macromolecules* 34: 6196–6201.
11. Li, S. and McCarthy, S. (1999) *Biomaterials*, 20: 35–44.
12. Gorrasi, G., Tamaro, L., Vittoria, V., Paul, M.-A., Alexandre, M., and Dubois, P. (2004) *J. Macromol. Sci., Phys.*, 43: 565–575.
13. Li, S. and McCarthy, S. (1999) *Macromolecules*, 32: 4454–56.
14. Nagata, M., Yamazaki, A., and Hayashi (2004) *J. Macromol. Sci. Pure and Applied Chem.*, 41: 345–355.
15. Tsuji, H. and Ishida, T. (2003) *J. Appl. Polym. Sci.*, 87: 1628–33.
16. Tsuji, H., Nakahara, K., and Ikarashi, K. (2001) *Macromol. Mater. Eng.*, 286: 398–406.
17. Ye, W., Du, F., Jin, W., Yang, J., and Xu, Y. (1997) *React. Funct. Polym.*, 32: 161–168.
18. Kricheldorf, H.R., Lee, S.R., and Bush, S. (1996) *Macromolecules*, 29: 1375–81.
19. Yuan, X., Mak, A.F.T., and Yao, K. (2003) *Polym. Degrad. Stabil.*, 79: 45–52.