

生物可降解聚(5-羟基乙酰丙酸-co-L-乳酸)的合成与表征^{*}

张 艳¹ 郭正虹¹ 程 捷¹ 方征平^{1,2**}

(¹浙江大学宁波理工学院高分子材料与工程研究所 宁波 315100)

(²浙江大学高分子复合材料研究所 高分子合成与功能构造教育部重点实验室 杭州 310027)

摘 要 通过 5-羟基乙酰丙酸(5-HLA)与 L-乳酸(LLA)的熔融缩聚合成了聚(5-羟基乙酰丙酸-co-L-乳酸)(PHLL),并用凝胶渗透色谱法、X 射线衍射法、核磁共振、红外光谱和差示量热扫描法对其进行表征.结果表明,由于 5-HLA 的羰基与 LLA 的羟基发生醚化反应,使得共聚产物中存在烯醚键支化结构.在较宽的共聚组成范围内共聚物呈无定形态.同时由于共聚物中 5-HLA 链节中的氢键作用,使得 5-HLA 含量的增加可将 PHLL 的玻璃化温度由 54.6℃ 提高到 91.4℃.PHLL 在去离子水中的降解行为表明,PHLL 在水性溶液中容易发生降解,其降解速度与微观结构有关.无定形的 LLA 链节比 5-HLA 链节降解速度快.

关键词 可降解,可再生资源,乙酰丙酸,缩聚,生物质

SYNTHESIS AND CHARACTERIZATION OF BIODEGRADABLE POLY(5-HYDROXYLEVULINIC ACID-co-L-LACTIC ACID)^{*}

ZHANG Yan¹, GUO Zhenghong¹, CHENG Jie¹, FANG Zhengping^{1,2**}

(¹ Lab of Polymer Materials and Engineering, Ningbo Institute of Technology, Zhejiang University, Ningbo 315100)

(² Institute of Polymer Composites, Zhejiang University, Key Laboratory of Macromolecular Synthesis and Functionalization, Ministry of Education, Hangzhou 310027)

Abstract Synthesis of biobased and biodegradable polymers from renewable biomass has attracted much attention in recent years. Levulinic acid has been deemed as a platform chemical from non-food stuff biomass, and some of its derivatives are starting materials for new polymers. In this paper, poly(5-hydroxylevulinic acid-co-L-lactic acid) (PHLL) was synthesized *via* melt copolycondensation of 5-hydroxylevulinic acid (5-HLA) and L-lactic acid (LLA) and characterized with GPC, X-ray, ¹H-NMR, FTIR and DSC. The results showed that the copolymers had interesting olefinic ether branch structures formed *via* etherification between carbonyl of 5-HLA and hydroxyl in LLA. The copolymer was amorphous in a broad composition range and had high glass transition temperature (T_g) ranging from 54.6℃ to 91.4℃, which increased with the increase of 5-HLA content due to the existence of hydrogen bonds in the 5-HLA moiety of the copolymer. The hydrolytic degradation behavior in deionized water showed that PHLL readily degraded hydrolytically in aqueous medium, and the degradation rate depended on its microstructure. The amorphous LLA moiety degraded faster than the 5-HLA counterpart.

Keywords Biodegradable, Renewable resources, Levulinic acid, Polycondensation, Biomass

1 INTRODUCTION

Biobased and biodegradable polymers are becoming increasingly attractive in last decades as compared with

traditional nondegradable polymers because they can be produced from renewable biomass resources and biodegraded in composts and therefore, offer great opportunities in current challenges of resources lack

^{*} Received July 14, 2008; Revised September 7, 2008; This work was supported in part by the National Natural Science Foundation of China (Nos. 20304012, 20674067, 20406018) and the Natural Science Foundation of Ningbo (No. 2007A610030); ^{**} Corresponding authors: FANG Zhengping (方征平), E-mail: zpfang@zju.edu.cn

and environment concern in polymer industries^[1~4]. Some biodegradable polyesters, such as poly(L-lactic acid), are produced from foodstuff such as corn^[5], but more attention needs to be paid to non-foodstuff biomass resources such as cellulose and lignin, not only because of their abundance and cheapness, but more important, for their non-foodstuff nature. Recent technical breakthrough in production of levulinic acid (LA) from waste cellulose or lignin on large scale and at low cost^[6] not only made it a potential platform chemical but also a starting material for biobased (and biodegradable) polymers^[7~9].

In our previous studies, we synthesized poly(5-hydroxylevulinic acid) (PHLA) using 5-hydroxylevulinic acid (5-HLA) as monomer^[10], which was synthesized from LA^[11]. The homopolymer PHLA has unordinarily high glass transition temperature (T_g) though its molecular weight is low. The high T_g arises from the existence of hydrogen bonds between carbonyl and enol in the polymer structure^[10]. Since the T_g s of most traditional biodegradable aliphatic polyesters are usually lower than 60°C^[12], this result may provide a new way to increase their T_g s. With this in mind, poly-(5-hydroxylevulinic acid-co-L-lactic acid) (PHLL) was synthesized *via* melt copolycondensation of 5-hydroxylevulinic acid (5-HLA) and L-lactic acid (LLA). However, in this apparent 2-2 bifunctional system, branched copolymers PHLLs were obtained. Aimed at this interesting phenomenon, polymerization mechanism, microstructure and properties of products were discussed in this paper.

2 EXPERIMENTAL

2.1 Materials

5-Hydroxylevulinic acid (5-HLA, T_m 99 ~ 100°C) was synthesized from LA as previously reported^[11]. Levulinic acid (LA, Shuangyu Co., China) was purified by distillation before use. Stannous chloride dihydrate ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$) and *p*-toluenesulfonic acid (TSA) with purity over 99% were purchased from Sinopharm Chemical Reagent Co. (China) and used as catalysts without further purification. L-Lactic acid (LLA), diethyl ether and tetrahydrofuran (THF) were

A.R. grade agents and used as received.

2.2 Melt Copolycondensation

5-HLA and LLA were charged into a flask equipped with a reflux condenser. The resulting mixture was stirred with a magnetic stirrer at 130°C under atmospheric pressure for 2 h and then dehydrated under reduced pressure (*ca.* 2000 Pa) for 8 h. Then, a given amount of catalysts with equimolar ratio ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ /TSA 1/1) was added. After the pressure was reduced to 300 Pa and the temperature was raised to 170°C, the melt copolycondensation was carried out for another 18 h. When the reaction was finished, the product was dissolved in THF and poured into diethyl ether. The resultant precipitate was filtered and dried in vacuum, giving a brown powdery copolymer. A series of copolymers with various compositions were prepared by changing the monomer molar ratio in the feed.

2.3 Characterization

The molecular weight (M_w and M_n) and its distribution (PDI) were determined at 30°C by a Waters 1525 type gel permeation chromatography (GPC) equipped with a Waters 2414 refractive index detector. Three Waters styragel columns, HR1, HR2 and HR3, were connected in series. THF was used as eluant, and its flow rate was 1.0 mL/min. The concentration of the polymer solution was 5 g/L, and the injection volume was 50 μL . Polystyrene samples with M_w in the range of 160 ~ 20000 were used as standards.

The X-ray diffraction (XRD) patterns were recorded on a diffractometer (D/max-rA, Rigaku Co. Japan) using $\text{CuK}\alpha$ radiation in the 2θ range of 5 ~ 60° with a scanning rate of 2 (°)/min.

The ^1H -NMR (500 MHz) spectrum was recorded on an Advance DMX 500 spectrometer in CDCl_3 containing 1 vol% tetramethylsilane as the internal reference.

The FTIR spectrum was recorded with Nicolet 560 infrared spectrometer using a KBr pellet of the sample.

The glass transition temperature (T_g) was determined using differential scanning calorimetry (DSC7, Perkin-Elmer Co.) The samples were heated from 20°C to 200°C in the first run at 20 K/min and

then cooled again to 20℃ at 80 K/min quickly. Before and after cooling,the temperature was kept constant for 1 and 3 min, respectively. In the second run, the samples were again heated from 20℃ to 200℃ at 20 K/min.The T_g was determined from the DSC curve of the second run.

2.4 Degradation

Powdery samples were placed in a tube containing 30 mL deionized water at 37℃. After incubation for certain time,the samples were washed with water and dried at 30℃ under vacuum oven for 48 h until constant weight (W).Normalized weight W/W_0 (W_0 is the initial weight) was calculated. The molecular weights of the degraded samples were determined with GPC.

3 RESULTS AND DISSCUSSION

3.1 Synthesis and Microstructure

The change of the molecular weight of the resultant copolymer poly(5-hydroxylevulinic acid-*co*-L-lactic acid) (PHLL) with monomer feed ratio is shown in Table 1. The molecular weight decreased with the amount of 5-HLA increasing. This can be explained by the special structure of 5-HLA. The δ -hydroxyl and γ -carbonyl are prone to form a 5-number ring *via* intramolecular hydrogen bond^[10], and the reactivity of the δ -hydroxyl in 5-HLA for nucleophilic esterification reaction was depressed. Therefore,it is hard for 5-HLA to polymerize to obtain long chain length. The introduction of more active LLA to this system will benefit for the increasing of the chain length of product as Table 1 showed. However,the more active monomer LLA was prone to homopolymerize in the 5-HLA/LLA system,and the long LLA blocks will be formed,which can be manifested in the GPC spectrum of PHLL in Fig. 1. The shoulder peak in the GPC curve of PHLL1/9 can be ascribed to the LLA block formed due to the difference of reactivity of LLA and 5-HLA. The low reactivity of 5-HLA is the reason for that the compositions of product are quite different from feed ratios. Moreover, the intermolecular cyclization of 5-HLA^[13] also contributes to these differences,which can form 1,6,9,13-tetraxadispiro[4.2.4.2]tetradecane-2,10-dione^[13] and result in the loss of 5-HLA.

Table 1 Poly(5-HLA-*co*-LLA) synthesized with various 5-HLA/LLA feed ratios^a

Copolymer	5-HLA/LLA	5-HLA /LLA ^b	M_w	M_n	PDI	Yield (%)
PHLL1/9	10:90	7:92	12470	6510	1.92	51.1
PHLL2/8	20:80	14:86	5750	3040	1.89	53.5
PHLL3/7	30:70	21:79	4700	2520	1.86	59.8
PHLL4/6	40:60	32:68	3000	1970	1.52	58.1
PHLL5/5	50:50	37:63	2380	1640	1.45	60.2
PHLL6/4	60:40	42:58	1680	1240	1.35	65.4
PHLL7/3	70:30	51:49	1290	980	1.31	68.7
PHLL8/2	80:20	58:42	1370	1050	1.30	75.3
PHLL9/1	90:10	72:28	1780	1060	1.68	86.3

^a Reaction conditions $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}/\text{TSA} = 1/1$; $\text{SnCl}_2 \cdot 2\text{H}_2\text{O} = 0.7$ wt% based on all the monomer ; 170℃ ; 300 Pa ; 18 h ; ^b 5-HLA/lactate mol ratio in final copolyester was roughly calculated based on integrate area of hydrogen proton peak by $^1\text{H-NMR}$: 5-HLA/LLA = $\frac{S_{5\text{-HLA-CH}_2\text{-CH}_2} + S_{5\text{-HLA-CH}_2}}{S_{\text{LA-CH}} + S_{\text{LA-CH}_3}} \times \frac{4}{6}$

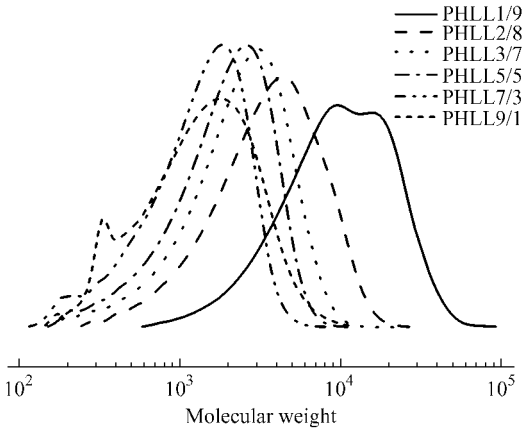


Fig. 1 GPC curves of PHLLs prepared with different monomer molar ratios
 $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}/\text{TSA} = 1, \text{SnCl}_2 \cdot 2\text{H}_2\text{O} = 0.7$ wt %, 170℃ ; 18 h ; 300 Pa

X-ray diffraction patterns (XRD, see Fig. 2) showed the same results as GPC curves showed. PHLA is an amorphous polymer with unordinary high glass transition temperature (T_g , 85 ~ 120℃, depending on molecular weight)^[10], and PLLA is a semicrystalline polymer with T_g of 30 ~ 55℃ and melting point of 160 ~ 180℃. When the LLA content reaches 90 mol%, PHLL becomes semicrystalline, indicating that long LLA blocks are formed with high LLA feed. The diffraction peaks of PHLL9/1 located at 2θ of 16.0°, 18.5° and 22.3° are in good accordance with the classical crystal structure of PLLA^[14]. PHLL with a

LLA content less than 80 mol% is amorphous. This result suggests that the chain structure of the copolymer is random, and the chain regularity is weakened as compared with PLLA.

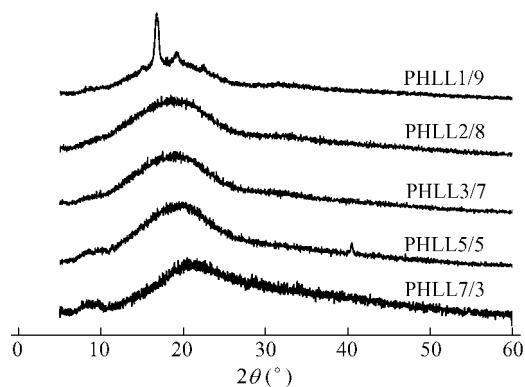


Fig. 2 XRD spectra of PHLLs

To make a clear view of the microstructure of PHLL, both $^1\text{H-NMR}$ and IR spectra of PHLLs were measured, which were shown in Fig. 3 and Fig. 4, respectively. Compared with PHLA and PLLA, the signals for $-\text{CH}_3$, $-\text{CH}_2$ and $-\text{CH}$ attributed to PHLA and PLLA all appeared in the $^1\text{H-NMR}$ spectra of PHLLs. However, it is more complicated than we expected, which means other reaction may occur besides conventional linear polycondensation. It has been reported that carbonyl of aldehyde was able to react with hydroxyl of *t*-butaneol to form olefinic ether bonds^[15]. Moreover, in our study of the 5-HLA/diols system, the crosslink phenomenon was observed in this apparent 2-2 bifunctional system, which is also due to the reaction between γ -carbonyl of 5-HLA and hydroxyl of diols^[16]. Therefore, although the reaction of carbonyl was not found in homopolymerization of 5-HLA^[10], more reactive hydroxyl groups of LLA may react with carbonyls of 5-HLA to form olefinic ethers and result in branched copolymer. This special structure of PHLL can be manifested from their different chemical shifts in $^1\text{H-NMR}$ spectrum. Seen from Fig. 3, besides the presence of $\text{C}=\text{CH}$ of the intrinsic enol ($\delta = 5.67$) of PHLA segment, we can also find the presence of $\text{C}=\text{CH}$ of the olefinic ether ($\delta = 4.72$). Because of the surrounding electronegative environment changed by formation of olefinic ether bonds, the chemical shift of $\text{C}=\text{CH}$ appeared in a

higher field. The $^1\text{H-NMR}$ spectrum showed that only partial γ -carbonyl of 5-HLA reacted with hydroxyl groups of LLA, and there still existed γ -carbonyl and its enol structure in 5-HLA segment. The ascription of chemical shifts of PHLL5/5 in detail is shown in Scheme 1.

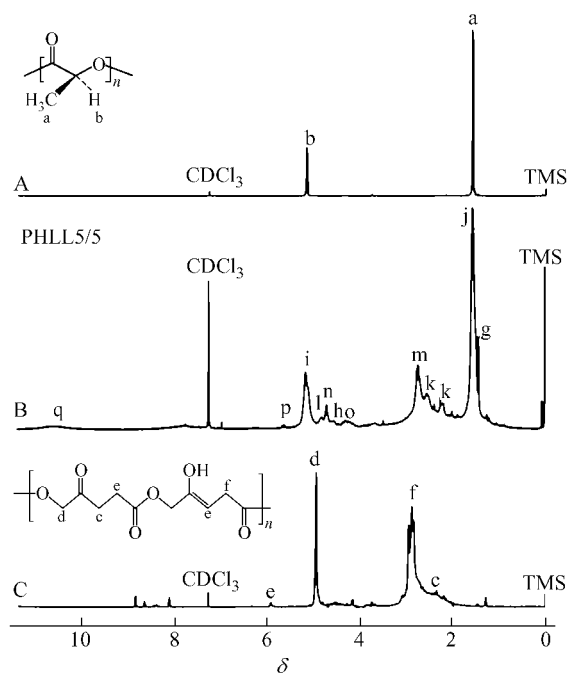


Fig. 3 $^1\text{H-NMR}$ spectra of (A) PLLA, (B) PHLL5/5, and (C) PHLA

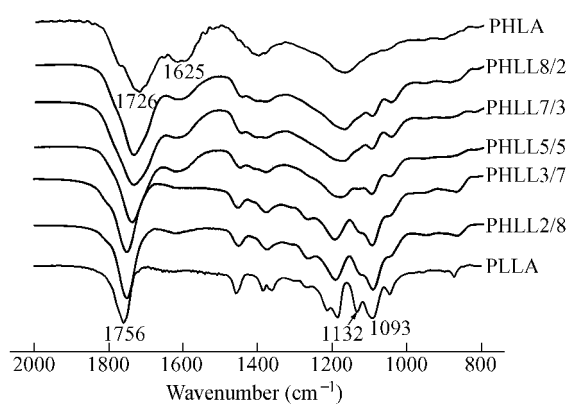


Fig. 4 FTIR spectra of PHLA, PHLLs and PLLA

Because of the formation of olefinic ether bonds, the result copolymers are branched polymers with the branch points in PHLA segments. The branching reaction also hindered the improvement of the chain length of copolymers.

According to the above analyses, there are two

main reasons for the lower molecular weight of copolymers: the low reactivity of 5-HLA and the branching reaction. When the content of 5-HLA was much higher, its low reactivity is the main reason, because the lower content LLA is hard to form more branch points to block the increasing of molecular weights of copolymers. On the other hand, although the molecular weights of copolymers were greatly improved when the content of LLA was much higher, the effect of the branching reaction was also obvious, which can limit the linear increasing of polymer chain to a higher extent as the homopolymerization of LLA. When the difference of the content of the two monomers was little, both reasons can't be neglected. These analyses are in accord with the results in Table 1.

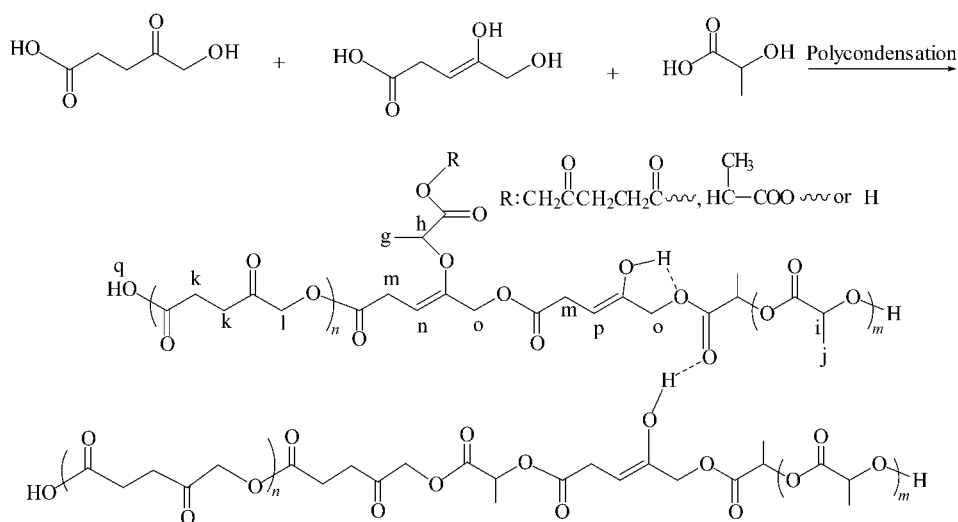
Figure 4 shows the FTIR spectra of PHLLs with various compositions. Strong absorption of ester carbonyls at $1726 \sim 1756 \text{ cm}^{-1}$ appeared for all the samples. Due to the γ -ketonic ester structure in 5-HLA moiety, the strong absorption of ester carbonyls changed from 1756 cm^{-1} to 1726 cm^{-1} when the 5-HLA content increased. As compared with PLLA, a new absorption peak appeared at 1625 cm^{-1} and was enhanced with increasing 5-HLA content. It is ascribed to stretching band of $\text{C}=\text{C}$ in olefinic ether and enol form in 5-HLA moiety. In addition, the absorption at 1093 cm^{-1}

and 1132 cm^{-1} ascribed to stretching band of $\text{C}-\text{O}$ in ester bonds was weakened with decreasing LLA content.

3.2 Thermal Properties

The DSC curves of the amorphous PHLLs are shown in Fig. 5. The T_g of PHLLs increases from 54.6°C (PHLL2/8) to 91.4°C (PHLL8/2) with the variable 5-HLA content. This result is attributed to the intermolecular hydrogen bonds formed in the copolymer. The γ -carbonyl in 5-HLA is prone to tautomerize to form an enol form to generate intra- and intermolecular hydrogen bonds between the enol hydroxyls and the carbonyls in the copolymer chain, as shown in Scheme 1. The intra- and intermolecular hydrogen bonds enhance the chain or segment rigidity and lead to high T_g . However, the partial formation of olefinic ether destroyed the formation of intra- and intermolecular hydrogen bonds between the enol hydroxyls and the carbonyls in the copolymer chain. Therefore, the T_g can be improved obviously only if the feed ratio of 5-HLA/LLA was over 7/3.

According to the above analysis, there are ester bonds, keto, enol and olefinic ether branch microstructure in the copolymer. The possible microstructure is presented in Scheme 1.



Scheme 1 Schematic diagram of the copolycondensation of 5-HLA and LLA and possible microstructure of PHLL

3.3 Hydrolytic Degradation

The degradation experiments were carried out in deionized water at 37°C , since we found that PHLA

degraded in phosphate-buffered saline (PBS) became no longer soluble in $\text{THF}^{[10]}$. As expected, PHLLs degraded in water *via* hydrolysis. Diffusion and

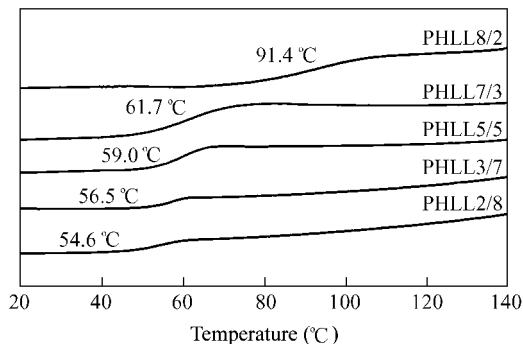


Fig. 5 DSC curves (second scan) of amorphous PHLLs

dissolution of soluble oligomer formed *via* degradation led to weight loss and the cleavage of ester bonds resulted in decrease in molecular weight, as shown in Figs. 6 and 7, respectively. Due to the low molecular weights of PHLLs, the weight loss and decrease in molecular weight happened simultaneously. Semicrystalline PHLL1/9 exhibited a relatively slow degradation rate as its crystalline phase hindered the water molecules from diffusing and attacking the ester bonds. With the increasing degradation time, the

amorphous region degraded at first and the crystalline degree was increased gradually (see Fig. 8), which is in accordance with the result of Li^[17]. In comparison, amorphous PHLL3/7 and PHLL5/5 degraded more rapidly since the ester bonds in these amorphous copolymers were easily accessible for water molecules. In addition, the hydrogen bonds in the polymer structure may also hamper the attack from water; as a result, PHLL5/5 degraded slower than PHLL3/7.

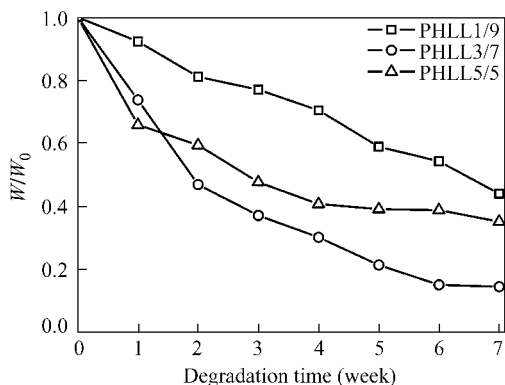


Fig. 6 Change of normalized weight (W/W_0) of PHLLs during degradation in deionized water at 37°C

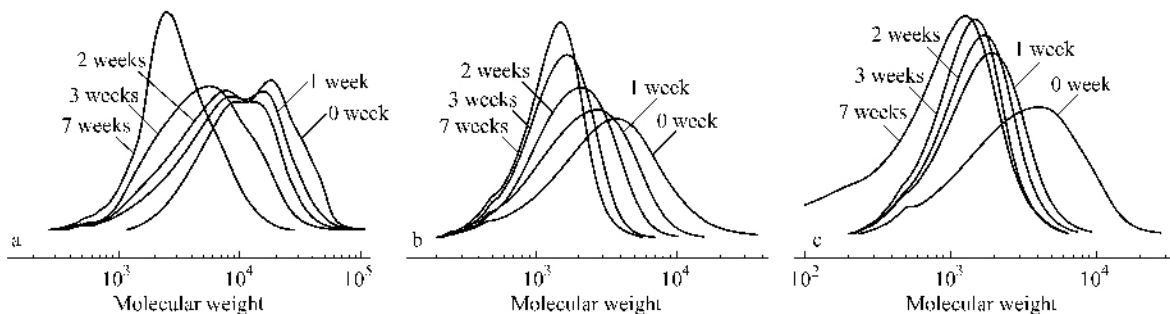


Fig. 7 GPC curves of PHLL during degradation in deionized water at 37°C
a) PHLL1/9; b) PHLL3/7; c) PHLL5/5

The FTIR spectra of PHLLs before and after degradation are compared in Fig. 9. After degradation for 7 weeks, the stretching band of the C—O in ester bonds at 1093 cm^{-1} was weakened, while the stretching absorption band of the enol C=C in 5-HLA segments at 1625 cm^{-1} were enhanced for all the samples examined. This result indicates that the 5-HLA moiety degraded slower than the LLA counterpart. The difference in degradation rate may also be arisen from the existence of hydrogen bonds in 5-HLA moiety.

4 CONCLUSIONS

A biodegradable aliphatic copolyester, poly (5-hydroxylevulinic acid-co-lactic acid) (PHLL) was synthesized *via* melt polycondensation of 5-HLA and LLA. The molecular weight increases with increasing LLA content. The interesting branched structure was formed in the copolymer chain due to the potential third functional group — γ -carbonyl of 5-HLA. The thermal properties characterized by DSC indicated that the T_g of the copolymers can be adjusted from 54.6°C to 91.4°C with different feed ratio of monomers. PHLL

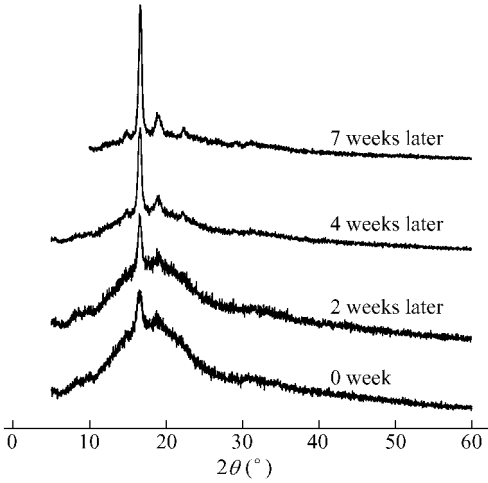


Fig. 8 XRD spectra of PHLL1/9 with different degradation time

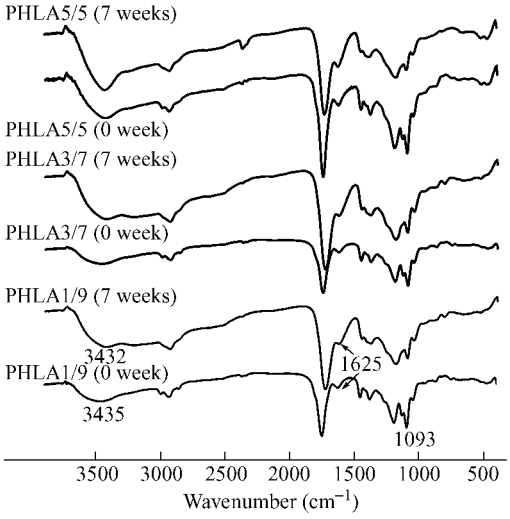


Fig. 9 FTIR spectra of PHLL1/9, PHLL3/7 and PHLL5/5 before and after degradation for 7 weeks

polymer matrix does not exhibit any crystalline phase until the PLLA chain/segment of copolyester is long enough to crystallize. The copolyesters PHLLs showed

degradation behavior in water. The amorphous PLLA segments were much easier to degrade than PHLA segments.

REFERENCES

1 Barbiroli G, Lorenzetti C, Berti C, Fiorini M, Manaresi P. *Eur Polym J*, 2003, 39 655 ~ 661

2 Scott G. *Polym Degrad Stab*, 2000, 68 1 ~ 7

3 Lindblad M S, Liu Y, Albertsson A C, Ranucci E, Karlsson S. *Adv Polym Sci*, 2002, 157 139 ~ 161

4 Hussain S, Fawcett A H, Taylor P. *Prog Org Coa*, 2002, 45 435 ~ 439

5 Drumright R E, Cruber P R, Henton D E. *Adv Mater*, 2000, 12 1841 ~ 1846

6 Bozell J J, Moens L, Elliott D C, Wang Y, Neuenschwander G G, Fitzpatrick S W, Bilski R J, Jamefeld J L. *Resour Conserv Recy*, 2000, 28 227 ~ 239

7 Chang C, Cen P, Ma X. *Bioresource Technol*, 2007, 98 1448 ~ 1453

8 Zhang P, Wu L B, Li B G. *Acta Polymerica Sinica (in Chinese)*, 2006, (3) 510 ~ 515

9 Zhang P, Wu L B, Bu Z Y, Li B G. *J Appl Polym Sci*, 2008, 108 3586 ~ 3592

10 Wu L B, Zhang Y, Fan H, Bu Z Y, Li B G. *J Polym Environ*, 2008, doi 10.1007/s10924-008-0082-y

11 Zhang Y, Wu L B, Li F, Bu Z Y, Li B G. *J Zhejiang Univ Eng Sci*, 2006, 40 1895 ~ 1899

12 Hiltunen K, Seppälö J V, Hörkönen M. *Macromolecules*, 1997, 30 373 ~ 379

13 Zhang Y, Wu L B, Li F, Li B G. *Synth Comm*, 2005, 35 2729 ~ 2733

14 Kim K W, Woo S I. *Macromol Chem Phys*, 2002, 203 2245 ~ 2250

15 van der Rest G, Chamot-Rooke J, Mourgues P, McMahon T B, Audier H E. *J Am Soc, Mass Spectrom*, 2001, 12 938 ~ 943

16 Zhang Y. *Synthesis and Characterization of Novel Biodegradable Polymers from 5-Hydroxylevulinic acid*. Doctoral Dissertation of Zhejiang University, 2006

17 Li S. *J Biomed Mater Res*, 1999, 48 342 ~ 353