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Synthesis, characterization and biodegradation of butanediamine-grafted poly(DL-lactic acid)

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Abstract

Novel butanediamine-grafted poly(DL-lactic acid) polymers (BDPLAs) were synthesized via a series of chemical bulk modifications in this study. Briefly, maleic anhydride (MAH) was first grafted onto the side chain of poly(DL-lactic acid) (PDLLA) molecules via melt free radical copolymerization using benzoyl peroxide (BPO) as initiator to get maleic anhydride-grafted PDLLA polymers (MPLAs); thereafter butanediamine (BDA) was immobilized onto grafted anhydride groups in MPLAs via *N*-acylation reaction to obtain the desired BDPLAs. Gel permeation chromatography with multi-angle laser light scattering (GPC-MALLS), FT-IR, ^{13}C NMR and XPS were employed to qualitatively characterize these synthesized polymers. Rhodamine–carboxyl interaction method and ninhydrin reaction were further used to quantitatively determine the graft ratio of MAH (MAH%) in MPLAs and the graft ratio of BDA (BDA%) in BDPLAs, respectively. The degradations of BDPLAs, PDLLA and MPLAs were investigated by observation of the changes of the pH value of incubation medium, molecular weight and weight loss ratio for a time interval of 12 weeks *in vitro*, respectively. The results revealed that grafting butanediamine onto PDLLA has weakened or neutralized the acidity of PDLLA degradation products. A uniform degradation of BDPLAs was observed in comparison with an acidity-induced auto-accelerating degradation featured by PDLLA and MPLAs. The biodegradation behaviors of BDPLAs are tunable by controlling the content of BDA. BDPLAs might be a new derivative of PDLLA-based biodegradable materials for medical applications without acidity-caused irritations and acidity-induced auto-accelerating degradation behavior as that of PDLLA.

Keywords: Poly(DL-lactic acid); Maleic anhydride; Butanediamine; Biodegradation

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1. Introduction

Poly(lactic acid) (PLA) is a well-known biodegradable polymer. It was widely used in pharmaceutical and tissue engineering fields due to its good biocompatibility and biodegradability through natural pathways [1–5]. However, it has some disadvantages as follows: (i) strong hydrophobicity due to lack of hydrophilic groups in its molecular chain, which leads to poor cell affinity; (ii) absence of suitable functional groups for covalently coupling with bioactive molecules, which restricts its specific application in tissue engineering; (iii) increased local acidity during PLA degradation, which results in

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negative effects at the site of polymer employed [6,7]. In order to overcome these problems, many research groups focused on the chemical modifications of PLA. Common approaches involve introducing various kinds of reactive groups by copolymerization of lactide with chemicals containing functional groups in its side chain (e.g., amino group [8], carboxyl group [9,10], or hydroxyl group [11]). Another approach is coupling chemicals such as poly(ethylene glycol) and its derivatives [12,13] with the end groups of PLA. Plasma or radiation is an alternative to surface modify the chemistry of PLA [14]. But the copolymerization would change the main chain structure of PLA, which may change its biodegradability or biodegradable behavior. The amount of coupled reactive groups on PLA ends may be limited. The reactive groups introduced by plasma or radiation are only located in the surface of PLA, which may be lost after a period of degradation [15–17]. Moreover, these approaches did not eventually solve the problem of increased acidity during PLA degradation.

In this study, a novel butanediamine-grafted poly(lactic acid) (BDPLA) was synthesized through chemical bulk modifications: firstly, maleic anhydride (MAH) was grafted onto the side chain of Poly(DL-lactic acid) (PDLLA) via melt free radical copolymerization using benzoyl peroxide (BPO) as the initiator to get maleic anhydride-grafted PDLLA (MPLA); thereafter butanediamine (BDA) was added to react with the grafted anhydride groups in MPLA by *N*-acylation to give the desired butanediamine-grafted PDLLA polymer (BDPLA). MAH is employed in this study due to its highly reactive anhydride groups. We hypothesized that the introduction of BDA would be helpful for neutralizing the acidic degrading products of PLA. We have previously reported the synthesis and characterization of ethylenediamine- and hexanediamine-grafted PDLLAs [18,19]. However, only simple and qualitative characterizations based on NMR and FT-IR were reported. The objective of this study was to synthesize and qualitatively and quantitatively characterize BDPLA, and to investigate the biodegradation behaviors of BDPLA, MPLA and PLA *in vitro*.

2. Experimental

2.1. Materials

Poly(DL-lactic acid) (PDLLA) was prepared by melt ring-opening polymerization of DL-lactide in our laboratory initiated by stannous octoate at 140 °C for 24 h in vacuum, with $\overline{M}_w = 132,800$ and polydispersity = 1.44. Butanediamine (BDA) and rhodamine 6G were used as received from Sigma–Aldrich Corporation. Maleic anhydride (MAH) and benzoyl peroxide (BPO) (Chongqing Oriental Chemical Factory) were dried at room temperature in vacuum before used. Succinic acid, ninhydrin and all solvents used in this study were analytical grade and obtained from Chongqing Drug Stock Limited Company.

2.2. Preparation of butanediamine-grafted poly(DL-lactic acid)

The synthesis route of BDPLA is shown in Fig. 1. MPLA was synthesized and characterized as described in our previous study [20]. Briefly, MAH was grafted onto the backbone of PLA by melt free radical copolymerization using BPO as initiator. Different ratios of PDLLA/MAH were mixed evenly in dichloromethane, and 5 wt% of BPO on a MAH weight basis was then added. The mixture was vacuum dried at room temperature and then reacted at 100 °C for 10 h under nitrogen protection. The

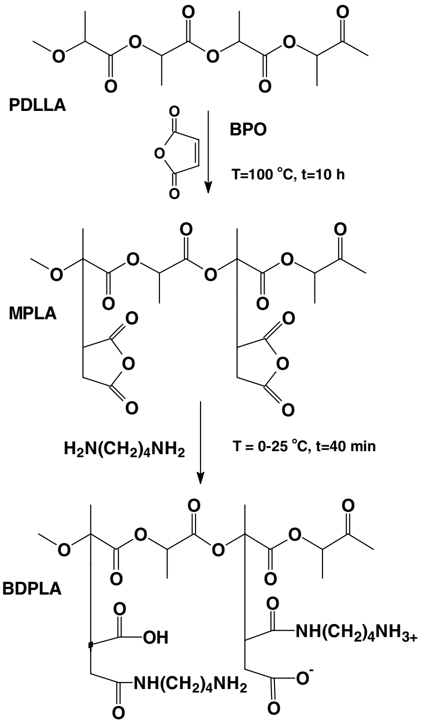

Fig. 1. The synthesis route of BDPLA from PDLLA.

obtained crude product was purified through coprecipitation in a chloroform–methanol system. Purified polymer was then vacuum dried at room temperature for 48 h. [FT-IR (CaF_2) (cm^{-1}): 1734 and 1773 ($\nu_{C=O}$ in O=C–O–C=O); ^{13}C NMR (300 MHz, $CDCl_3$): δ (ppm) = 25.557 (methylene carbons), 72.311 (quarternary carbons), 167.788 (anhydride carbons)].

Anhydride groups in MPLA were *N*-acylated by $-NH_2$ in BDA to obtain BDPLA (see Fig. 1). It was carried out in a three-necked flask with mechanical stirring. A predetermined amount of MPLA and BDA (120–200 wt% of its stoichiometric amount) were dissolved in 50 mL and 5 mL tetrahydrofuran (THF), respectively. Then, the MPLA solution was dropped into the BDA solution with stirring at a temperature below 20 °C. The reaction lasted for 10 min below 20 °C and 30 min at room temperature. After reaction, the crude BDPLA was dissolved into THF and subsequently precipitated into excessively distilled water. The filtered fibrous solids were precipitated till the pH value of the mother liquid was 7–8. Finally, the fibrous solids were vacuum dried at room temperature to constant weight. [FT-IR (CaF_2) (cm^{-1}): 1680 ($\nu_{C=O}$ in –CONH–); 1540 (δ_{N-H} in –CONH–); ^{13}C NMR (300 MHz, $CDCl_3$): δ (ppm) = 66.677 and 67.906 (methylene carbons from BDA)].

2.3. Characterization

The number-average molecular weights ($\overline{M}_n$), the weight-average molecular weights ($\overline{M}_w$), and the polydispersity (PD) were determined from gel permeation chromatography with multi-angle laser light scattering (laser photometer Dawn EOSTM, Wyatt Technology Corporation, USA) (GPC-MALLS). Three Agilent 1100 HPLC columns (300×8.0 mm) were used in series with THF as the eluent at a flow rate of 1 mL/min.

Fourier transform infrared spectrometry (FT-IR) spectra were recorded on a Perkin–Elmer Spectrum GX model by using thin films, which were cast onto the surface of a CaF_2 plate with THF as solvent. ^{13}C NMR spectra were recorded at 300 MHz on a Bruker AV-300 nuclear magnetic resonance spectrometer with Bruker software. Samples of about 40 mg were dissolved in $CDCl_3$ (Fluka chemica, deuteration degree not less than 99.8%) in 5 mm o.d. sample tubes.

X-ray photoelectron spectroscopy (XPS), also known as ESCA, was performed on a Microlab MK II X-ray Photoelectron Spectrometer (Vacuum Generators Incorporation, UK) with a monochromatic Mg Kα (1253.6 eV) X-ray source.

The content of the anhydride groups grafted in the MPLA samples was determined by a modified rhodamine–carboxyl interaction method [21]. Before detecting, the samples were firstly immersed in distilled water for 2 h to make anhydride groups totally hydrolyze into carboxyl groups, followed by vacuum dried. Ninhydrin method was used to determine the content of the amino groups in the BDPLA samples [22].

2.4. Sample preparation for pH value change and biodegradation tests

Solutions of PDLLA, MPLAs and BDPLAs in THF were added into glass vials (2.0 cm in diameter, 3.0 cm in height) with lids (0.1 g polymer/vial). The solvent was allowed to evaporate for 72 h to form films. These films were then dried in vacuum for 12 h. All experiments were performed at room temperature. The obtained circular films (2.0 cm in diameter and 250 ± 10 μm in thickness) were UV sterilized for 30 min before use for pH value change test and biodegradation study.

2.5. pH Value change test during degradation

To test pH value change of the polymers and their degradation products, about 4 mL sterile distilled water was added to the glass vials containing films. The distilled water was not refreshed in the whole 12 weeks. All the vials were lidded and kept in a shaking incubator of 37 ± 0.5 °C (50 strokes per min). The pH values of suspension liquor were measured once a week for 12 weeks using Model PHS-3C pH meter. Three samples were prepared for every polymer, and the reported pH value was the average of three samples.

2.6. Study of biodegradation

In the study of biodegradation of the polymers, sterile PBS solution (0.1 M, pH 7.4) was used as a medium, and 48 samples were prepared for each polymer film. About 4 mL PBS solution was added to the glass vials containing films. The PBS solution was not refreshed in the whole 12 weeks. All the vials were lidded and kept in a shaking incubator of 37 ± 0.5 °C (50 strokes per min). Four vials of each polymer film were taken out every week to discharge the PBS solution. Then the polymer films were rinsed with distilled water and dried to a constant weight in vacuum for molecular weight and weight loss ratio measurements.

GPC-MALLS was used to determine the molecular weight of the original and degraded polymer samples. The weight loss ratio was calculated according to the equation:

$$\text{Weight loss ratio} = \frac{W_0 - W_1}{W_0} \times 100\%$$

where W_0 and W_1 are weights of the sample before and after the hydrolytic degradation, respectively. The reported molecular weight and weight loss ratio were the average of four samples.

3. Results and discussions

3.1. Immobilization of MAH

The influence of monomer (MAH) concentration on the properties of MPLA and on the MAH graft ratio (MAH%) is shown in Table 1. In this study, the MAH concentration was ranged from 5 to 20 wt% (based on PLA weight) while the initiator concentration (5 wt% to MAH), temperature (100 °C), and reacting time (10 h) were kept constant. The MAH graft ratio increased from 1.61% to 3.16% as MAH monomer concentration increased from 5% to 20%. This indicates that an increasing amount of MAH monomer concentration leads to an increase of the MAH graft ratio. However, the molecular weight ($\overline{M}_w$) of the obtained MPLAs decreased from less than 3% in MPLA-1 to more than 28% in MPLA-3 compared to the pure polymer. This is due to more chain scission at a higher concentration of maleic anhydride [23]. Therefore, in following experiments, we only chose MPLA-1 and MPLA-2 materials for the further modification.

3.2. Immobilization of BDA

XPS is a technique to characterize the outermost layers of a material, providing with surface chemistry information. Fig. 2 shows the XPS spectra of MPLA (Fig. 2a) and BDPLA (Fig. 2b) films. MPLA film displayed two peaks corresponding to C1s (binding energy, 285 eV) and O1s (binding energy, 533 eV), as expected. However, BDPLA film showed an additional peak contributing to N1s (binding energy, 397 eV), which was attributed to the amine groups ($-NH_2$) and amide bonds (–CONH–). This result suggests that BDA has covalently bound to the backbone of PLA.

Compounds with amino groups could react with ninhydrin to give a blue-purple condensate, which could be used to quantitatively determine the amount of amino groups in polymer. Table 2 shows the BDA content and the BDA graft ratio (BDA%) in BDPLA. With the increase of MAH%, the content of amino groups in BDPLA and the BDA% are also increased. In this study, BDA was used in stoichiometric excess about 20–100% in order to ensure all anhydride groups in MPLA could react with BDA. The contents of anhydride groups in MPLA-1 and MPLA-2 (Table 1) are almost equal to the contents of amino groups in BDPLA-1 and BDPLA-2 (Table 2), respectively, indicating the full conversion of anhydride groups in MPLA.

3.3. pH Value change during degradation of PDLLA, MPLAs and BDPLAs

The main purpose of grafting BDA to PLA in the present study is to overcome the acidity of PLA degradation products and to eliminate the acidity-caused auto-accelerating degradation behavior possessed by PLA. Investigations of the pH value change and degradation profile of BDPLA using PLA as a control could well demonstrate the effects

Table 1
The influence of MAH concentration on the properties of MPLA and on the MAH graft ratio (MAH%)

Sample	MAH (wt%)	$\overline{M}_w$[a] (g/mol)	$\overline{M}_n$[a] (g/mol)	PD[a]	Anhydride groups content[b] (mmol/100 g)	MAH%[c] (wt%)
Pure PLA	–	132,800	92,100	1.44	–	–
MPLA-1	5	129,000	87,200	1.48	17.05	1.61
MPLA-2	10	118,500	76,500	1.55	26.95	2.58
MPLA-3	20	95,300	55,100	1.73	32.85	3.16

[a] Measured by GPC-MALLS.

[b] Determined by rhodamine–carboxyl interaction method.

[c] Amount of MAH after purification on total amount of MPLA.

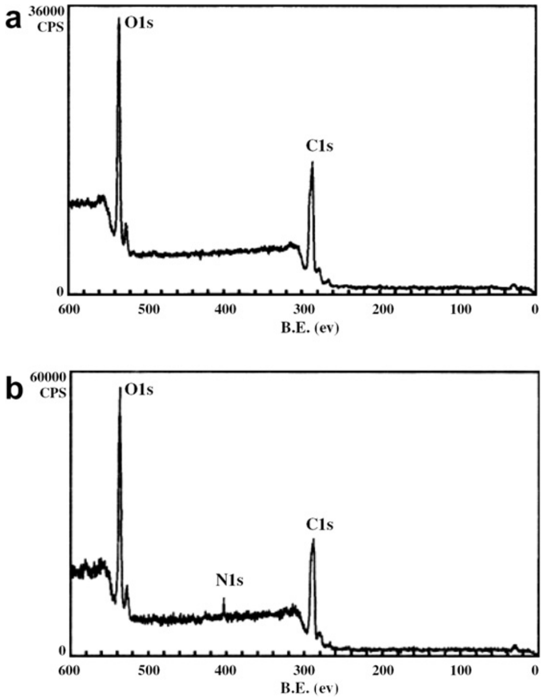

Fig. 2. XPS spectra of MPLA (a) and BDPLA (b).

of the grafted BDA. In order to more clearly clarify the acidity of the degradation products of PLA and BDPLAs, distilled water, instead of a buffered solution such as phosphate buffer solution (PBS) which is a commonly employed medium [24,25] and has also been ever used as a medium by our research group [19], was used in the pH value change test. Furthermore, in order to investigate the effect of the accumulated degradation products on the pH value and the degradation profile of the polymers, no media were refreshed within the whole degradation period.

PDLLA, MPLA-1, MPLA-2, BDPLA-1 and BDPLA-2 were used in this study. When PDLLA, MPLAs and BDPLAs are incubated in distilled water, the polymer molecules degrade as usual, leading to pH value changes of the media, as shown in Fig. 3. The degradation of PLA is believed to occur through four consecutive steps: hydration, initial degradation, further degradation, and solubilization [25]. The similar four steps are expected for the grafted PLA such as MPLAs and BDPLAs because their backbones are still PLA.

In Fig. 3, three phases can be observed for PDLLA. In the first phase (before forth week), the pH value of the incubating media gradually decreases from 6.45 to 5.00. This corresponds to the hydration stage and the initial degradation of PDLLA. For PDLLA, in the hydration stage, the aqueous medium penetrates the polymer matrix, which results in polymer relaxation and T_g decrease [26] but does not cleave its chemical structure. As a result, the pH value of the incubation media for PDLLA keeps stable. After the hydration stage, the initial degradation starts in the hydrated region of the polymer through ester bond hydrolysis. The hydrolysis cleaves the polymer backbone and releases oligomers or monomers with end carboxyl groups, leading to pH value decrease of the incubation media. However, since the hydrated regions and the hydrolysis sites are limited at this stage, the released oligomers or monomers with carboxyl groups are few so that only slow pH value decrease is observed. In the second phase (between forth week and sixth week), with the increasing of hydration regions and hydrolysis sites, the rate to release oligomers or monomers with carboxyl groups increases. The accumulated hydrogen ions in the incubation media further accelerates the ester bond hydrolysis, resulting in a dramatic and sharp drop of the pH value of the incubation media from 5.00 to 2.45. This stage is called further degradation, i.e. the period from forth week to sixth week for PDLLA in Fig. 3. In the third phase, i.e. after sixth week, the pH value declines at a very low rate and reaches a plateau (from 2.45 to 1.93). This result regarding PDLLA degradation is consistent with a previous study [25].

Table 2
The properties of BDPLA and the graft ratio of BDA in BDPLA (BDA%)

Sample	MPLA Sample	$\overline{M}_w$[a] (g/mol)	$\overline{M}_n$[a] (g/mol)	PD[a]	Content of Amino groups[b] (mmol/100 g)	BDA%[c] (wt%)
BDPLA-1	MPLA-1	120,800	80,500	1.50	15.6	1.37
BDPLA-2	MPLA-2	115,400	73,000	1.58	25.0	2.20

[a] Measured by GPC-MALLS.

[b] Determined by ninhydrin reaction.

[c] Amount of BDA after purification on total amount of BDPLA.

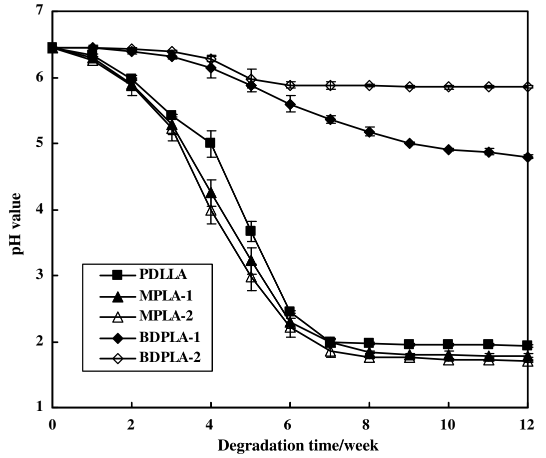

Fig. 3. pH Value change of the incubating media as a function of time during degradation of PDLLA, MPLAs and BDPLAs within 12 weeks. Medium: sterile, distilled water; $T = 37 \pm 0.5$ °C. No medium was refreshed.

MPLA-1 and MPLA-2 exhibit similar three-phase pH value changes to that of PDLLA. However, the pH value of the incubation media for MPLAs is lower than that of PDLLA at the same degradation time. The dramatic pH value drop for MPLAs starts from the third week, one week earlier than PDLLA. Moreover, the media for MPLA-2 with MAH% of 2.58% shows smaller pH value than that for MPLA-1 with MAH% of 1.61%. Regarding the pH value change for BDPLAs, no dramatic and sharp drop of pH value is observed. BDPLA-1 and BDPLA-2 demonstrate mild and stable pH value decrease within the whole 12 weeks from 6.45 to 4.80 and from 6.45 to 5.85, respectively. In the further degradation stage, hydration region increase and acidity-caused auto-acceleration play important roles in PDLLA's degradation. Any factors favoring hydration and acidity-increase may speed up PDLLA's degradation. The grafted maleic anhydride groups in MPLAs hydrolyze to form carboxyl groups, leading to improved hydrophilicity as well as lowered pH value of the incubation media compared with PDLLA. This is why MPLAs show faster degradation and stronger auto-catalytic degradation than PDLLA. On the other hand, the grafted strong basic BDA neutralizes or absorbs the hydrogen ions partially ionized from PDLLA degradation products, thus the acidity-induced auto-catalytic degradation is overcome and no dramatic and sharp drop of pH value is observed (Fig. 3). BDPLA-2 with BDA% of 2.20% can neutralize or absorb more acidic degradation products than BDPLA-1 with BDA% of 1.37%, so that BDPLA-2 exhibited a smaller pH value drop from 6.45 to 5.85 than BDPLA-1 from 6.45 to 4.80.

3.4. Molecular weight changes of PDLLA, MPLAs and BDPLAs during degradation

The $\overline{M}_w$ of PDLLA, MPLAs and BDPLAs as a function of time during a degradation in PBS solution is plotted in Fig. 4. As shown in this figure, PDLLA, MPLAs and BDPLAs degraded at different rates, and the same kind of polymers such as MPLAs with various MAH% or BDPLAs with various BDA% hydrolyzed differently either.

In order to more clearly investigate the degradation rate of these polymers, the natural logarithm of $\overline{M}_w$ vs. degradation time is depicted in Fig. 5. Three phases can be observed from Fig. 5. The first phase ends at about week 1 for all polymers, where the degradation rates are very slow since all polymers are mainly in the hydration stage and negligible chemical structure change takes place.

The second phase starts from the second week, and all polymers degrade almost linearly in this phase. However, for the second phase, the phase duration and degradation rate begin to differentiate for various polymers. The second phase of PDLLA terminates at the end of the seventh week, MPLA-1 and MPLA-2 at the end of the sixth week, and BDPLA-1 and BDPLA-2 even at the end of the

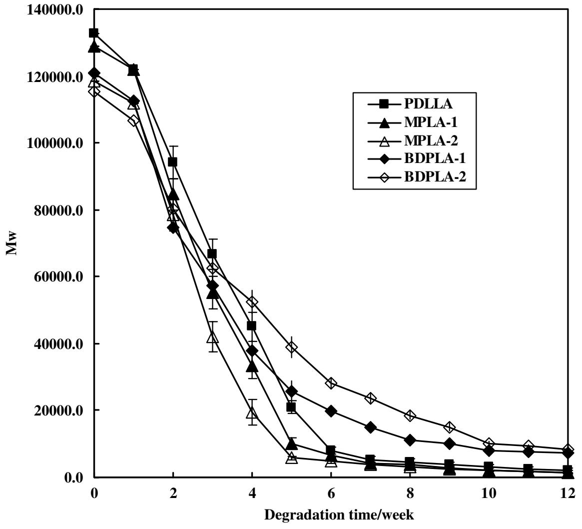

Fig. 4. Weight-average molecular weights as a function of time during degradation of PDLLA, MPLAs and BDPLAs within 12 weeks. Medium: sterile, 0.1 M pH 7.4 PBS; $T = 37 \pm 0.5$ °C. No medium was refreshed.

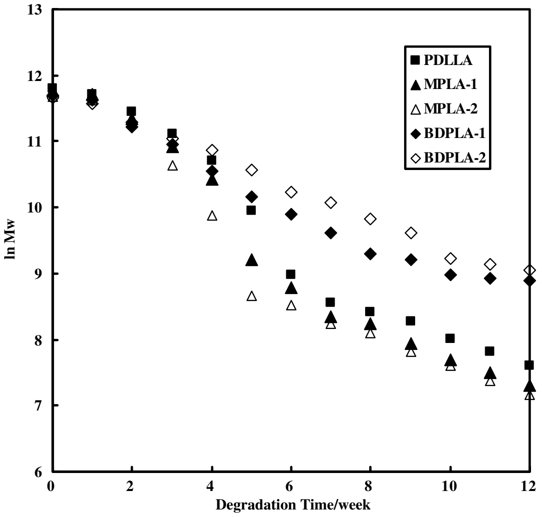

Fig. 5. Natural logarithm of weight-average molecular weights as a function of time during degradation of PDLLA, MPLAs and BDPLAs within 12 weeks. Medium: sterile, 0.1 M pH 7.4 PBS; $T = 37 \pm 0.5$ °C. No medium was refreshed.

10th week. There is a general hypothesis for PLA hydrolytic degradation [27]:

$$\ln \overline{M}_{\mathrm{n}}(t_2) = \ln \overline{M}_{\mathrm{n}}(t_1) - kt$$

where k is the hydrolysis rate constant, $\overline{M}_{\mathrm{n}}(t_2)$ and $\overline{M}_{\mathrm{n}}(t_1)$ are $\overline{M}_{\mathrm{n}}$ values at the hydrolysis times of t_2 and t_1, respectively. Based on this hypothesis, the hydrolysis rate constants (k) of the polymers in the second phase were estimated and summarized in Table 3, where $\overline{M}_{\mathrm{w}}$ was used instead. Table 3 demonstrates that MPLAs degrade faster than PDLLA and BDPLAs much slower than PDLLA. In addition, MPLA-2 with higher MAH% (2.58%) exhibits a higher k value than MPLA-1 with lower MAH% (1.61%). In contrast, BDPLA-2 with higher BDA% (2.20%) produces a lower k value than BDPLA-1 with lower BDA% (1.37%). The second phase is corresponding with both initial degradation stage and further degradation stage. In the initial degradation stage, the molecular weights of all polymers are high and thus ester bonds could be easily and quickly cleaved. In the further degradation stage, acidity-induced auto-catalysis of PDLLA and MPLAs (see Fig. 3) speeds up the polymer chain cleavage. Both the high molecular weights at the initial degradation stage and the acidity-induced auto-catalysis at the further degradation stage contribute to the fast degradation rates for PDLLA and MPLAs in the second phase. Furthermore, stronger acidity-induced auto-catalysis for MPLA-2 with higher MAH% results in its quicker degradation than MPLA-1 with lower MAH%. BDPLAs have eliminated the acidity-induced auto-catalysis (see Fig. 3), leading to slower degradation at the same degradation time interval compared with those of PDLLA and MPLAs (see Fig. 5, Table 3).

The obvious effects of acidity-induced auto-catalysis on molecular weights of PDLLA and MPLAs were also observed in other PDLLA-based specimens, especially in those specimens of larger sizes [28,29]. In order to elucidate the effects of acidity on PLA hydrolysis, Makino et al. [30] investigated the hydrolysis of PDLLA microcapsules with a mean diameter of 1.5 μm, and Tsuji and Nakahara [27] examined the hydrolysis of amorphous poly(L-lactide) (PLLA) films of 50 ± 10 μm thick in pH 2.0 HCl solution and DL-lactic acid (DLLA) solution. Unfortunately, insignificant catalytic effect of acids on both molecular weight decrease and weight loss of PLA were noticed. This discrepancy probably results from their much smaller sample size and the difference between hydrogen ions in media and those produced and entrapped inside polymer samples.

3.5. Weight loss ratio changes of PDLLA, MPLA and BDPLA during degradation

Fig. 6 shows the weight loss ratios of PDLLA, MPLAs and BDPLAs as a function of time during incubation in PBS solution. As one can see in Fig. 6, weight losses of PDLLA and MPLAs proceed slowly until the sixth week, which is corresponding to the first three degradation stages. In such stages, their molecular weights still remain too high to become soluble. Then, sharp increase of weight loss ratios of polymers was observed, mainly because the fragments of PDLLA and

Table 3
The hydrolytic degradation rate constants (k) of PDLLA, MPLAs and BDPLAs

Sample	PDLLA	MPLA-1	MPLA-2	BDPLA-1	BDPLA-2
k (week^{-1})	0.5551	0.6162	0.6888	0.2983	0.2527
k (day^{-1})	0.0793	0.0880	0.0984	0.0426	0.0361

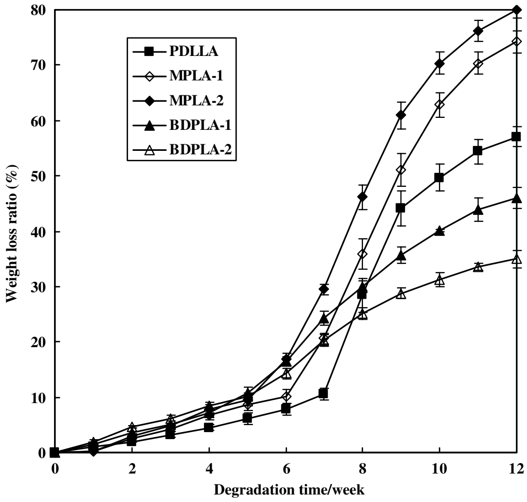

Fig. 6. Weight loss ratios as a function of time during degradation of PDLLA, MPLAs and BDPLAs within 12 weeks. Medium: sterile, 0.1 M pH 7.4 PBS; $T = 37 \pm 0.5$ °C. No medium was refreshed.

MPLAs are further cleaved to molecules that are soluble in the aqueous incubating media. This is the solubilization stage of PDLLA and MPLAs. The weight loss ratio of PDLLA is 57% after degradation time of 12 weeks, while MPLA-1 and MPLA-2 are 74.2% and 80.1%, respectively. The reason for MPLAs having higher weight loss ratio is that MPLAs degraded faster than PDLLA due to stronger acidity-induced auto-catalysis and higher hydrophilicity of the degraded products than PDLLA (see Figs. 3 and 4). However, the weight loss ratios of BDPLA-1 and BDPLA-2 are only 46% and 35% after degradation time of 12 weeks, respectively. The much lower weight loss rates of BDPLAs than PDLLA and MPLAs is attributed mainly to the slower degradation rates of BDPLAs and the higher $\overline{M}_w$ even at the end of 12 weeks' degradation (Figs. 4 and 5), which is correlated with BDPLAs' eliminated acidity-induced auto-catalysis.

4. Conclusions

In this research, maleic anhydride and butanediamine were successfully introduced into the side chain of PLA for the purpose of incorporating such reactive groups as carboxyl groups and amino groups into PLA and settling the acidity of PLA in hydrolysis. The modified substrates were qualitatively and quantitatively characterized with GPC-MALLS, FT-IR, ^{13}C NMR, XPS and classical chemical reaction, respectively. The pH value change test and the biodegradation study of various PDLLA-based films reveal that the introduction of butanediamine in PDLLA has weakened or neutralized the acidity of PLA degradation products, and has eliminated the acidity-induced auto-accelerating degradation behaviors featured by PLA. The biodegradation behaviors of BDPLAs can be controlled by adjusting the graft ratio of butanediamine. All the results above confirm that BDPLA might be a safer PDLLA-based biodegradable material without acidity-induced irritations and acidity-induced auto-accelerating degradation.

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