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One-pot synthesis of biodegradable and linear poly(ester amide)s based on renewable resources

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ABSTRACT: Poly(ester amide) has attracted much attention because they demonstrate satisfactory mechanical performance, yet are biodegradable. Owing to the increasing depletion of fossil resources, we chose 1,4-butanediol, 1,10-decanediamine (DD), 1,10-sebacic acid, and itaconic acid (IA), which can be produced in large scale by fermentation of renewable resources, to synthesize a series of biobased poly(ester amide)s (BPEAs) by condensation polymerization. We used multiple monomers to suppress crystallization. The pyrrolidone rings formed between DD and IA increases the molecular spacing and the chain irregularity of BPEAs. The properties of BPEAs were tunable by adjusting the monomer ratio. The effect of DD content on the molecular weight, thermal stability, mechanical properties, and *in vitro* degradation of BPEAs was investigated. © 2016 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2016**, *133*, 43446.

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INTRODUCTION

Poly(ester amide)s are novel polymers that have commodity and specialty applications. Some of the aliphatic poly(ester-amide)s are degradable, but aromatic poly(ester-amide)s are generally nondegradable.[1,2] A variety of poly(ester amide)s have been prepared by the polycondensation of ester-containing diamines with dicarboxylic acids or their derivatives, or by the ring-opening polymerization of depsipeptides.[3–5] Katayama *et al.* synthesized alternating polyamide esters by melt polymerization of dimethyl adipate and terephthalate or by solution polymerization of adipoyl and terephthaloyl chlorides.[6] Katsarava *et al.* prepared poly(ester amide)s by the solution polycondensation of di-*p*-toluenesulfonic acid salts of bis(α-aminoacid) α, ω-alkylene diesters, and di-p-nitrophenyl esters of diacids in chloroform or N-methyl-2-pyrrolidone at room temperature.[7] Nagata prepared poly(ester amide)s with various L-alanine contents by the interfacial polycondensation of mixtures of 1,6-hexanediol diesters of L- and L-alanine with sebacoyl chloride.[8] The ring-opening polymerization of cyclic depsipeptides (morpholine-2,5-dione derivatives) provides a convenient method to prepare a wide range of biodegradable poly(ester amide)s because various α-amino acids residues can be incorporated into morpholine-2,5-dione derivatives and these monomers can be copolymerized with other lactones.[9]

Biobased polymers from renewable resources have received considerable interests from academia and industry in recent years due to environmental concerns and the ever-declining petroleum resources.[10,11] At present, it is strategically important to construct new polymers or replace existing polymers by renewable resources. In the last decades, a variety of polymers were designed and synthesized based on biobased chemicals.[12–15] Polylactides (PLAs) and polyhydroxyalkanoates (PHAs) are the most widely known biobased plastics that have been successfully commercialized.[16,17] Polyester-typed elastomers based on biobased chemicals have been investigated and applied in the medical material field due to the excellent biocompability and biodegradability of these elastomers. Jasinska *et al.* synthesized semicrystalline biobased polyamides and co-(polyamides) from sebacic acid, diaminoisoidide, and putrescine.[18] Hablot *et al.* prepared dimer acid-based polyamides.[19] However, only a few studies on the preparation of linear poly(ester amide)s based on biobased chemicals, especially those chemicals that can be

Additional Supporting Information may be found in the online version of this article.

Table I. Recipes of BPEAs

Sample	BD/mol	DD/mol	SA/mol	IA/mol
BPEA-10	0.099	0.011	0.085	0.015
BPEA-30	0.077	0.033	0.085	0.015
BPEA-50	0.055	0.055	0.085	0.015
BPEA-70	0.033	0.077	0.085	0.015

BPEA-50 0.055 0.055 0.085 0.015
BPEA-70 0.033 0.077 0.085 0.015

produced on a large scale, have been reported in the literature. The objective of this study was to synthesize biodegradable and linear poly(ester amide)s based on biobased chemicals that can be produced on a large scale. Thus, biobased chemicals including 1,4-butanediol (BD), 1,10-decanediamine (DD), 1,10-sebacic acid (SA), and itaconic acid (IA) were chosen to synthesize biobased poly(ester amide)s (BPEAs). With the incorporation of two kinds of biobased diacids, SA and IA, the crystallization degree and degradation rate can be controlled due to their different reactivity and polarity. This route was not reported before.

MATERIALS AND METHODS

Materials

BD, SA, DD, and titanium tetrabutoxide were obtained from Sigma-Aldrich Company and used without purification. IA (purity of 99%) was obtained from Shandong Qingdao Langyatai Company and used without purification.

Preparation of BPEAs

The synthesis method consisted of three steps. Polymerizations were carried out in a 100-mL, four-neck glass flask equipped with a thermometer, a sampling device, a nitrogen inlet, and a two-bladed anchor-type impeller. According to the recipe given in Table I, 0.085 mol of SA and 0.015 mol of IA were added into the 100 mL flask, and then BD and DD were added into the flask in that order. Under the nitrogen atmosphere and stirring, the prepolymerization was allowed to proceed for 2 h at 180 °C. A large amount of water was produced in this step. Then the temperature was reduced to 150 °C, titanium tetrabutoxide (0.02 wt % of the total monomer weight) was added as catalyst, and the reaction temperature was gradually increased to 200 °C. The reaction pressure was reduced to 300 Pa, and the reaction was allowed to proceed for another 2 h to obtain poly(ester amide). The chemical reaction is shown in Scheme 1, and an image of the synthesized BPEAs is shown in Figure 1. The BPEA sheets were prepared by a vacuum tableting machine.

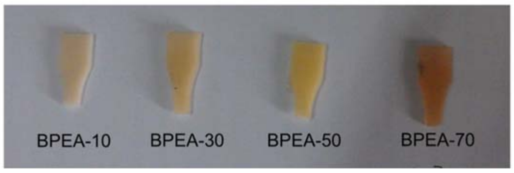
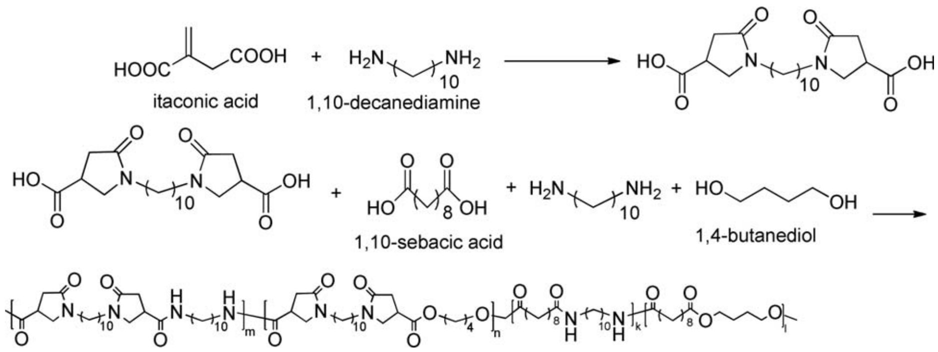


Figure 1. Image of synthesized BPEAs. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Measurements and Characterizations

The FTIR spectra of the BPEAs were recorded on a Bruker Tensor 27 spectrometer. ^{1}H NMR spectroscopy measurements were carried out on a Bruker AV400 spectrometer. $CDCl_3$ was used as the solvent for the measurements. DSC measurements were obtained on a Mettler-Toledo differential scanning calorimeter. The samples were heated to 200 °C, maintained there for 3 min, and then cooled to −80 °C. The heating or cooling rates were 10 °C/min in all cases. Thermal gravimetric analysis was carried out with 5–10 mg samples under a nitrogen atmosphere in the 50–700 °C range at a heating rate of 10 °C/min by using a Mettler-Toledo thermal gravimetric analyzer (SDAT851e). The molecular weights of the poly(ester amide)s were determined by GPC measurements on a Waters Breeze instrument equipped with three water columns (Styragel HT3_HT5_HT6E) with tetrahydrofuran (THF) as the eluent (1 mL/min) and a Waters 2410 refractive index detector. A polystyrene standard was used for calibration. Tensile tests of the poly(ester amide)s were conducted according to ASTM D412 (dumbbell-shaped) on an LRX Plus Tensile Tester made by Lloyd Instruments, Ltd., UK. For the test of *in vitro* degradation rate, weighed samples were added into phosphate buffer solution with a pH of 7.4 and stored in an incubator at 37 °C for different degradation times. The samples were weighed again after they were washed, and dried in a vacuum oven after 1, 3, 7, 14, 21, 28, 35, and 50 days.



Scheme 1. Schematic of synthesis of BPEAs.

Table II. Molecular Weight and Yield of BPEAs with Different BD/DD Molar Ratios

BD/DD	M_n (g/mol)	M_w/M_n	Yield (%)
BPEA-10	22100	1.81	75
BPEA-30	25200	2.61	83
BPEA-50	29400	2.15	87
BPEA-70	28400	2.17	90

RESULTS AND DISCUSSION

Synthesis and Structure of BPEAs

Biobased chemicals including BD, DD, SA, and IA were chosen to synthesize BPEAs. Condensation polymerization was applied to synthesis the target poly(ester amide)s because it offers several advantages including high reaction rates, simple reaction conditions, and mature formulas. Titanium tetrabutoxide was added as a catalyst. IA was used to adjust the macromolecular structures. The primary amine reacted with the double bond of IA via the Michael addition to form a pyrrolidone ring.[20,21] The pyrrolidone ring could increase the molecular spacing and the chain irregularity, thus affecting the glass transition temperature and the crystal structure of the polyamides. (FTIR and 1H NMR spectra of pyrrolidone derived monomer: Figure S1 and Figure S2 in Supporting Information). The reaction route is shown in Scheme 1. The molecular weight and yield of the polymerization are listed in Table II. The molecular weights of the BPEAs increase first and reach equilibrium with the increase of DD content. The polydispersity index of the BPEAs reaches a maximum at BPEA-30 and the yield increases with the increase of DD. The results could be explained by higher reactivity between DD and diacids than reactivity between BD and diacids.

The FTIR spectra of poly(ester amide)s with different monomer ratios are displayed in Figure 2. For a valid comparison of the different BPEA samples, the spectra were normalized on the basis of a constant strength of methylene peaks from 2800 to 3000 cm^{-1} for each sample. The absorption peaks at 2929 and 2962 cm^{-1} are attributed to the stretching vibrations of —CH$_3$, —CH$_2$, and —CH of poly(ester amide). Characteristic peaks are found at 3305 cm^{-1} (νN—H, H-bonded), ~1730 cm^{-1} (νC=O ester), 1640 cm^{-1} (amide I, νC=O), and 1540 cm^{-1} (amide II, νC—N + δN—H). Peaks at 1218 and 1172 cm^{-1} are attributed to the C(=O)—O vibration of poly(ester amide). With the increase of DD content, the intensity of the peak at 1640 cm^{-1} increases, and the intensity of the peak at 1218 cm^{-1} and that at 1172 cm^{-1} decrease significantly. The ^{1}H NMR spectrum of the BPEA with 50% of DD is shown in Figure 3. The sharp signal at 1.32 ppm corresponds to the —CH$_2$ of the decanediamine and sebacic acid segments in the BPEA. The signals in the 3.50–4.00 ppm region and at 2.58 ppm stand for the protons of the pyrrolidone ring and the methylene adjacent to the pyrrolidone ring, confirming the formation of pyrrolidone ring. The signals at 4.12 and 1.72 ppm are attributed to the protons of —O=C—O—C**H**$_2$ (i) and —O—CH$_2$—C**H**$_2$—O (j), respectively. These signals indicate the formation of ester groups.

Thermal Properties of BPEAs

The crystallization and melting temperatures and the corresponding enthalpies of the BPEAs were obtained from the first cooling and second heating DSC scan. Figure 4 shows the heating curves of the BPEAs. The increase of T_m is due to the increase of molecular weight of BPEAs. The relatively low melting enthalpy (7.4–76.8 J/g) indicates that the molecular regularity of BPEA is decreased by the introduction of various chemical units. The crystalline region of BPEA-10 consists mainly of polyester segments and the crystalline regions of BPEA-30 and BPEA-70 consist mainly of polyamide segments. The crystalline region of BPEA-30 consists of both polyester and polyamide segments, as verified by the dual melting peaks of BPEA-30. To identify if it is segregation phase, ethanol which can dissolve polyester but not polyamide and poly(ester amide) was applied to dissolve PBEA-30 at room temperature for 48 h. There is no obvious weight loss of BPEA-30. Thus, it is not

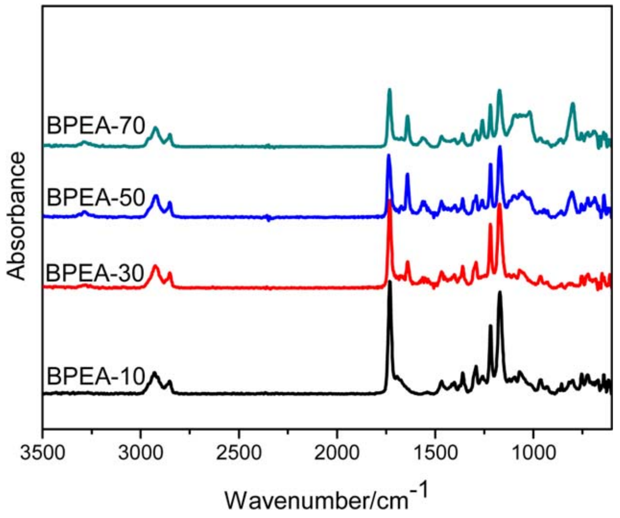


Figure 2. FTIR spectra of BPEAs. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

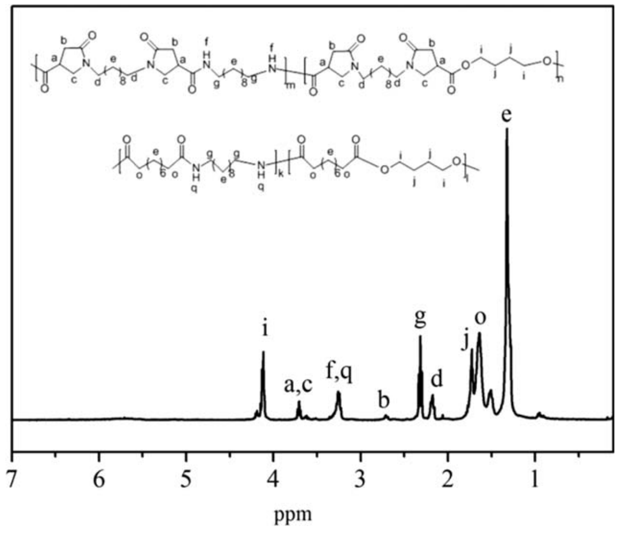


Figure 3. ^{1}H NMR spectrum of BPEA-50.

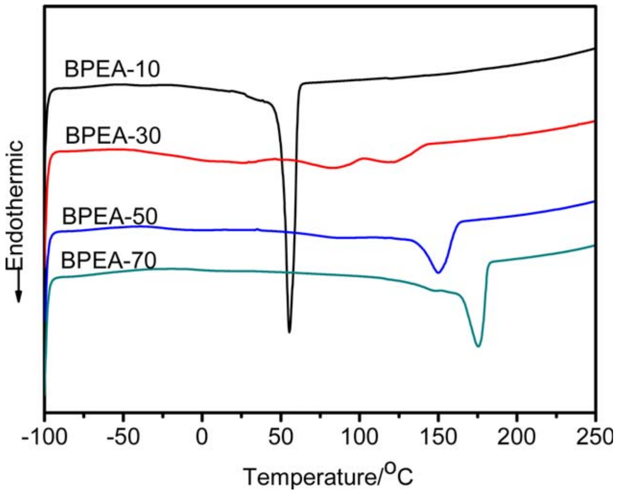


Figure 4. DSC heating curves of BPEAs with different DD contents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table III. DSC Parameters of BPEAs with Different DD Contents

DD content	BPEA-10	BPEA-30	BPEA-50	BPEA-70
T_g (°C)	−44.1	−32.5	14.5	17.8
T_m (°C)	50.8	58.6, 100.2	135.2	161.2
DH (J/g)	76.8	7.6, 7.4	32.0	60.6

Table IV. TGA Parameters of Poly(ester amide)s

Items	T_{onset} (°C)	T_{peak} (°C)	T_{offset} (°C)
BPEA-10	350.0	425.0	510.0
BPEA-30	340.0	431.5	510.5
BPEA-50	340.5	450.5	520.0
BPEA-70	350.5	462.5	520.0

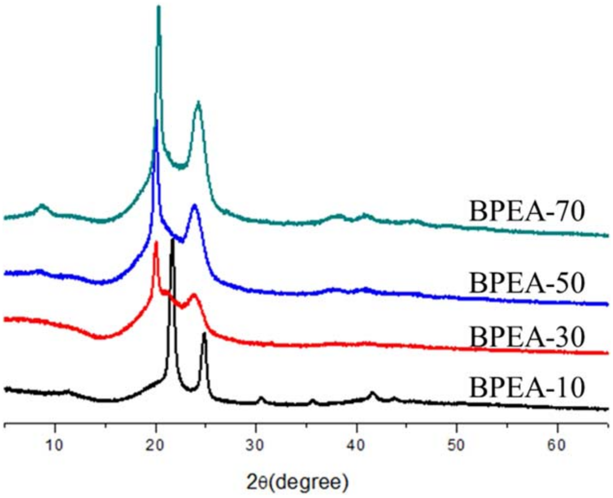


Figure 6. XRD patterns of BPEAs. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

segregation phase. It is difficult to identify the glass transition temperature (T_g) of the BPEAs because poly(ester amide) is semicrystalline and the crystalline region affects the movement of the molecular chains and the determination of glass transition temperature. We therefore determined T_g by quenching. The temperature was first increased to 200 °C, decreased at a rate of 40 °C/min to −50 °C, and then increased at a rate of 10 °C/min to 200 °C. The values of T_g are shown in Table III. With the increase of DD content, the content of amide groups increases and the content of ester groups decreases, and the T_g of the prepared BPEAs increases significantly. The T_g of BPEA-50 and BPEA-70 is obviously higher than BPEA-10 and BPEA-30, which make BPEA-50 and BPEA-70 more rigid and less elastic.

The TGA curves in Figure 5 show that the decomposition temperature of the BPEA is above 340 °C and the thermal weight loss reaches a maximum between 510 and 520 °C. For all BPEAs, the decomposition temperatures are considerably

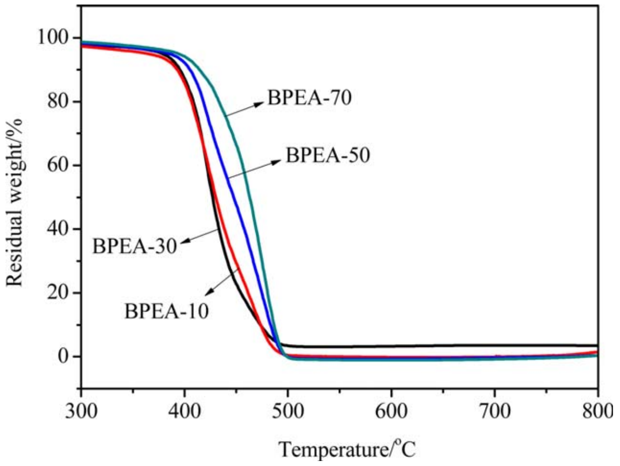


Figure 5. TGA curves of poly(ester amide)s. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

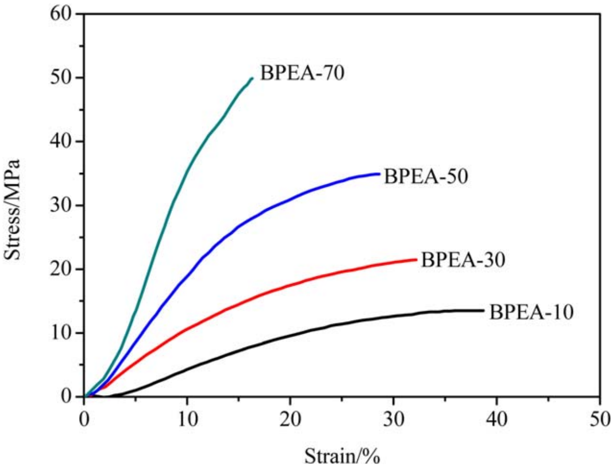


Figure 7. Stress–strain curves of BPEAs. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table V. Mechanical Properties of BPEAs

Items	Tensile strength (MPa)	Elongation at break (%)	Permanent set (%)	Hardness Shore A
BPEA-10	13.5	38.7	0	90
BPEA-30	21.5	32.3	0	93
BPEA-50	28.0	30.0	0	95
BPEA-70	49.2	16.9	0	96

higher than the melting temperatures, which is important for the processing of these materials. From the TGA results, the thermal stability of poly(ester amide) is superior to that of polyester and comparable to previous poly(ester amide)s.[22] As shown in Table IV, the thermal stability improves with the increase of DD content because of the increase of the number of amide units of BPEAs. The thermal decomposition of BPEAs can be divided into three steps: first, the loss of the combined water; second, the breakup of the macromolecular chains into small molecules; and third, the fracture of the ester groups and amide groups leading to the accelerated fracture of the macromolecular chains.

Crystallization and Mechanical Properties of BPEAs

The crystallization behavior of the BPEAs was further confirmed by XRD (Figure 6). For BPEA-10, two strong diffraction peaks at 22.1° and 25.1° reflect the crystallinity of the polyester segments. Polyamide has a variety of crystal structures, of which the α-crystalline phase and the γ-crystalline phase are most common.[23] The α-crystalline phase consists predominantly of two characteristic diffraction peaks (the reflections at 20.2° and 23.9°), while the γ-crystalline phase consists predominantly of one characteristic diffraction peak (the shoulders at 21.3°). By the XRD spectra of BPEAs, we can see two strong diffraction peaks at 20.4° and 24.1°, which were in accordance to the characteristics of the nylon α-crystalline form. Thus, the crystallinity of BPEA-30, BPEA-50, and BPEA-70 are mainly α-crystallinity of polyamide.

Typical stress–strain curves for the BPEAs are presented in Figure 7 and the parameters are listed in Table V. The tensile strength of the BPEAs increases and elongation at break decreases with the increase of DD content. To understand the physical properties of each segment, the contrast samples were synthesized and tested (Table VI). By the comparison of BPEAs and contrast samples, it showed amide groups contribute to the increase of tensile strength and polyester groups contribute to the increase of elongation at break. The tensile strengths of BPEA-30 and BPEA-50 are about 20 and 30 MPa, respectively, which are higher than those of most polyesters. The elongations at break of BPEA-30 and BPEA-50 are about 30%, which are superior to those of most polyamides. The tensile strength of BPEAs is much higher than reported poly(ester amide)s, but elongation at break of BPEAs is lower than some reported poly(ester amide)s.[24] Thus, the obtained BPEAs have the advantages of both polyesters and polyamides, as we hypothesized. There is no permanent set of BPEAs and the hardness increased with the increase of DD content which could be explained by the increase of amide groups.

Table VI. Molecular Weight and Mechanical Properties of Contrast Samples

Sample	M_n (g/mol)	M_w/M_n	Tensile strength (MPa)	Yield point (%)
PDDSA	34,200	1.8	48	12
PDDPY	31,600	2.2	42	8
PBDSA	27,200	1.8	34	15
PBDPY	19,800	1.9	29	20

1,4-butanediol (BD), 1,10-decanediamine (DD), 1,10-sebacic acid (SA), and itaconic acid (IA), pyrrolidone derived monomer (PY).

In Vitro Degradation of BPEAs

The *in vitro* degradation of BPEA was investigated, and the results are shown in Figure 8. The degradation rate decreases with the increase of DD content. For BPEA-10 and BPEA-30, the weight loss reaches 38% and 30%, respectively, after 50 days, indicating excellent degradation properties. The degradation rate of BPEAs are similar to previous reported poly(ester amide)s.[24] For poly(ester amide)s, the ester groups provide most of the degradation points. Thus, the degradation rate is low for BPEAs with high amide contents. The intermolecular

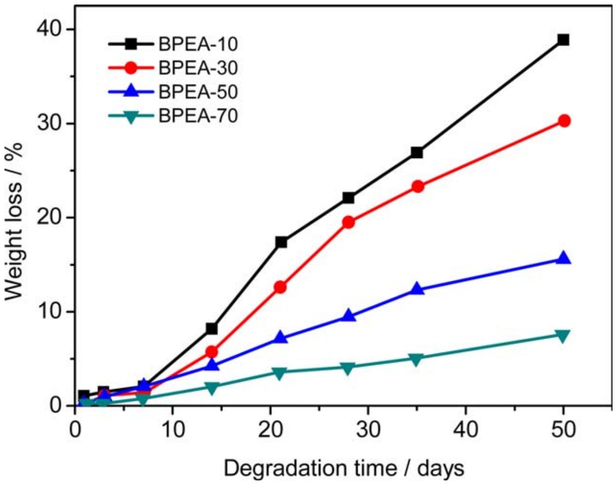


Figure 8. *In vitro* degradation of poly(ester amide)s. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

hydrogen bonding between main chains is increased with the increase of amide contents, preventing the diffusion of water and its eventual degradation. Another important factor of degradation rate is the crystallizability. At the starting period, crystallizability affect greatly on the degradation process. For example, high crystallizability of BPEA-10 delays the degradation process, which makes BPEA-10 have comparable degradation rate to BPEA-30 and BPEA-50 even though it contains low content of amide groups. For BPEA-50 and BPEA-70, the weight loss reaches 15% and 8%, respectively, after 50 days.

CONCLUSIONS

Novel BPEAs were designed and synthesized from renewable chemicals consisting of BD, DD, SA, and IA. The obtained BPEAs have high molecular weights and excellent thermal stability. Glass transition temperature, tensile strength, and thermal decomposition temperature of BPEAs increase but elongation at break and degradation rate decrease with the increase of proportion of amide groups. The amide groups in the BPEAs contribute to the increase of mechanical properties and polyester groups in the BPEAs contribute to the increase of degradation properties. With high tensile strengths and excellent degradation properties, BPEAs with a DD content of 30% and 50% are good candidates of biodegradable poly(ester amide) materials. The prepared BPEAs could be a good candidate for drug delivery and package materials.

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