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ORIGINAL CONTRIBUTION

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Synthesis, characterization, and thermal properties of biodegradable polyetheresteramide copolymers based on 11-aminoundecanoic acid

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Abstract In this work, new aliphatic polyetheresteramide copolymers based on ε-caprolactone, 11-aminoundecanoic acid, and poly(ethylene glycol) (PEG) were synthesized by the melt polycondensation method. The copolymers obtained were characterized by ^{1}H NMR, differential scanning calorimetry, thermogravimetric analysis/differential thermogravimetry, and wide-angle X-ray diffraction. Water absorption and hydrolytic degradation behavior was also studied. With the increase in PEG content, water absorption and the hydrolytic degradation rate increased accordingly.

Keywords Polyetheresteramide · Biodegradable copolymer · Thermal property · Hydrolytic degradation · Polycaprolactone

Introduction

Aliphatic polyesteramide copolymer is a new type of biodegradable polymer, and was developed recently [1, 2, 3, 4, 5, 6 7, 8, 9]. This copolymer combines the good degradability of polyesters and great mechanical properties of polyamides, so it has a promising future in biomedical material fields. Several kinds of polyesteramide copolymers have been studied in our laboratory [7, 8, 9]. This work is an extension of our previous work [8, 9]. In this work, hydrophilic poly(ethylene glycol) (PEG) was incorporated into the polyesteramide macromolecular main chain; as a result the hydrophilicity and degradability were enhanced compared with the polyesteramide copolymers.

Experimental

Materials

11-Aminoundecanoic acid (AU) was of chemically pure grade, and all the other materials were analytical reagent grade. The materials were used without purification.

Synthesis of polyetheresteramide copolymers

Polyetheresteramide (PEEA) copolymers were synthesized from ε-caprolactone (ε-CL), AU, and PEG1000 ($M_n = 1{,}000$) by the melt polycondensation method according to Scheme 1. The typical PEEA5 copolymer was prepared as follows. ε-CL (17.1 g, 0.15 mol), AU (21 g, 0.104 mol), PEG1000 (2 g, 0.002 mol), titanium dioxide (0.1 g), Irganox1010 (0.1 g), and tetrabutyl titanate (0.05 g) were added into the reaction vessel under a nitrogen atmosphere. The mixture was kept at 110 °C for 1 h. Later, the temperature was gradually elevated to 160 °C over 30 min. Then, the mixture was rapidly heated to 240 °C under vacuum for another 1 h. At the end, the resultant melt was poured out onto a steel plate; thus, PEEA5 copolymer was obtained. The copolymer chips were prepared by pouring the hot melt into a steel mold (100×100×1 mm). The samples for wide-angle X-ray diffraction (WAXD), water absorption, and hydrolytic degradation were cut from the chips and kept in a desiccator before use. The fibers were drawn from the hot melt kept at 150 °C by a glass stick. The fibers with a diameter of about 0.2 mm were used to study the hydrolytic degradation behavior. PEEA0 and PEEA10 copolymers were synthesized by the same method as for PEEA5 except the mass of PEG1000 was 0 and 4 g, respectively. All the PEEA copolymers synthesized in this work are listed in Table 1.

Purification of PEEA copolymers

The PEEA copolymers were first dissolved in AR grade trichloromethane, and reprecipitated from the filtrate using AR grade

Scheme 1 Synthesis of polyetheresteramide copolymers

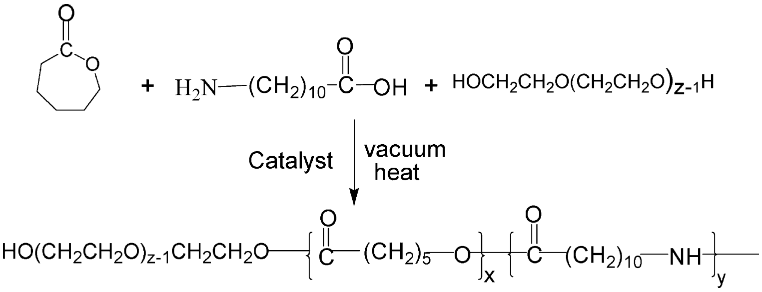


Table 1 Chemical composition and inherent viscosity of the samples used. Polyetheresteramide (*PEEA*), poly(ethylene glycol) (*PEG*), ε-caprolactone (*ε-CL*), 11-aminoundecanoic acid (*AU*)

PEEAs	PEG (% W_t)		ε-CL (% W_t)		ε-CL/AU/PEG1000 (%mol)		M_n	$[\eta]$ (dl/g)[b]
	Feed	Exp[a]	Feed	Exp[a]	Feed	Exp[a]		
PEEA0	0	0	47.3	47.1	59.1/40.9/0	58.8/41.2/0	18,738	0.69
PEEA5	5.0	6.6	44.8	42.9	58.6/40.6/0.8	57.1/41.9/1.0	14,837	0.66
PEEA10	10.0	11.9	42.6	40.5	58.1/40.3/1.6	56.6/41.5/1.9	13,459	0.66

[a] Determined by ^{1}H NMR
[b] Measured at 30 °C in *m*-cresol at a concentration of 0.5 g/dl

n-hexane. Then this mixture was filtered and vacuum-dried to constant weight. The purified materials were kept in desiccators before use.

Intrinsic viscosity measurement

The intrinsic viscosity, $[\eta]$, was measured by using an Ubbelohde viscometer at 30 ± 0.1 °C. All the copolymers were dissolved in *m*-cresol to prepare solutions of 0.5 g/dl. $[\eta]$ was calculated using Eq. (1) according to the Solomon–Ciuta method [10]:

$$[\eta]=\frac{\sqrt{2\left(\frac{t}{t_0}-1-\ln\frac{t}{t_0}\right)}}{c}, \qquad (1)$$

where *c* is the concentration of the solution, *t* is flow time of the solution, and t_0 is flow time of pure solvent.

Differential scanning calorimetry

The nonisothermal crystallization behavior of these copolymers was characterized using a differential scanning calorimeter (PerkinElmer DSC7). The samples purified by the dissolution/reprecipitation method were used for the differential scanning calorimetry (DSC) test. The specimens were first heated from 30 to 120 °C under a nitrogen atmosphere at a heating rate of 10 °C/min, and reheated to 120 °C at the same rate after being quenched to 25 °C, at last the specimen was cooled to 25 °C again at a rate of 10 °C/min.

The crystallinity of the copolymers (X_c %) was determined by dividing the observed heat of fusion of the second heating run by the theoretical value for 100% crystalline polymer according to Eq. (2). The theoretical ΔH_m^0 values for polycaprolactone (PCL) and poly(aminoundecanoic acid) (nylon11, PAU) are 135.4 J/g [11] and 196.6 J/g [12], respectively. The theoretical ΔH_m^0 values for the copolymers were calculated from the heat of fusion of the homopolymers taking into account the composition of the copolymer according to Eq. (3) [13].

$$X_c(\%)=\frac{\Delta H_m}{\Delta H_m^0}\times 100, \qquad (2)$$

$$\Delta H_m^0 = 135.4X_{PCL}+196.6X_{PAU}, \qquad (3)$$

where X_{PCL} and X_{PAU} are the molar fractions of ε-CL and AU in PEEA0 copolymer, respectively.

Fourier transform IR spectroscopy

Fourier transform (FT) IR (KBr) spectra of the copolymers were taken with a NICOLET 200SXV IR spectrophotometer.

^{1}H nuclear magnetic resonance

^{1}H NMR spectra (in $CDCl_3$) were recorded using a Bruker 300 spectrometer (Bruker, Germany) at 300 MHz using trimethylsilane as an internal reference standard.

Wide-angle X-ray diffraction

WAXD was performed at room temperature using a Rigaku DMAX1400 diffractometer (DMAX1400, Rigaku, Japan; λ = 0.154 nm) with Cu Kα radiation operated at 40 kV and 100 mA. The specimens were fixed on the equipment and the data were collected with a step interval of 0.02° at a rate of 4°/min.

Thermogravimetric analysis of PEEA copolymers

Thermogravimetric measurements (thermogravimetric analysis/differential thermal analysis) were obtained with a thermogravimetric analyzer (PerkinElmer, TGA7) coupled with a PerkinElmer computerized data station under a steady flow of air or nitrogen at a heating rate of 10 °C/min in the range from room temperature to 600 °C.

Water absorption behavior of PEEA copolymers

The water absorption experiment was carried out as follows. The copolymer chips were immersed in distilled water at 30 °C for different periods; then they were taken out and the surplus surface water was removed using filter paper. The value was calculated according to Eq. (4):

$$\mathrm{Waterabsorption}(\%) = \frac{W_{\mathrm{ht}} - W_{\mathrm{d}}}{W_{\mathrm{d}}} \times 100, \qquad (4)$$

where W_{d} is the initial weight of the dry sample, and W_{ht} is the weight of the humid sample at time t.

Hydrolytic degradation behavior

In vitro degradation tests were carried out as follows. The chips (with a thickness of about 1 mm, 100–300 mg) and fibers (with a diameter of about 0.2 mm, 100–300 mg) were placed in phosphate buffer saline (PBS, pH 7.2) at 37 °C containing sodium azide as an antibacterial agent (0.05% w/v). The PBS saline was refreshed every 2 weeks. The samples were removed from the bottles at a predetermined time, rinsed thoroughly with distilled water, and dried in vacuum at 65 °C for 12 h. The degree of degradation was calculated from the weight loss:

$$\mathrm{Weightloss}(\%) = \frac{W_0 - W_{\mathrm{t}}}{W_0} \times 100, \qquad (5)$$

where W_0 is the dry weight before degradation, and W_{t} is the dry weight at time t.

Results and discussion

Synthesis of PEEA copolymers

FTIR and ^{1}H NMR spectroscopies were used to characterize the chemical structure of such PEEA copolymers. Because the weight fraction of PEG is lower than 10 wt%, the peak due to PEG could not be observed in the FTIR spectra (data not shown). ^{1}H NMR spectra of PEEA copolymers are shown in Fig. 1. The characteristic absorption peaks are also indicated in this figure. With the increase in PEG content, the integral area of

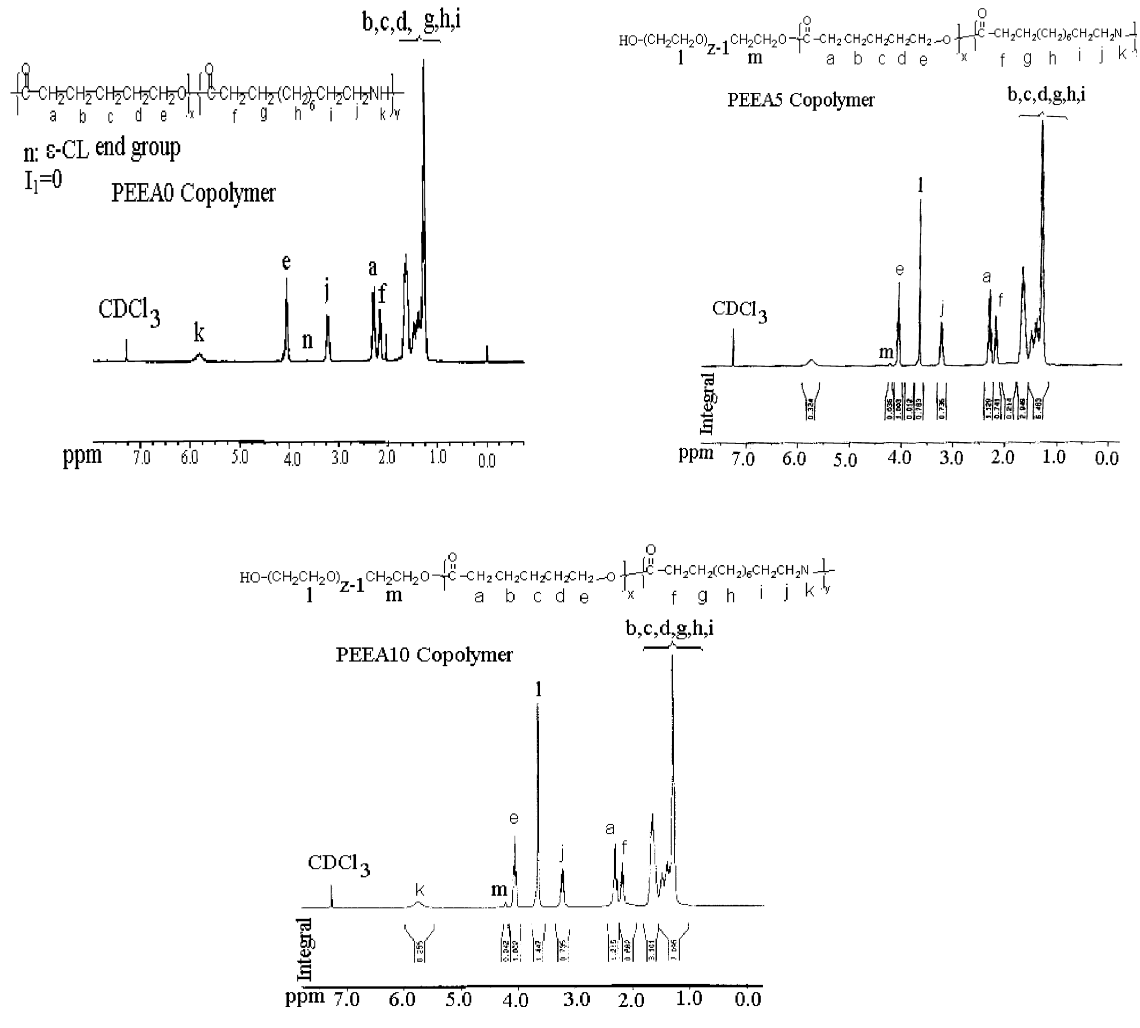


Fig. 1 ^{1}H NMR spectra of polyetheresteramide (*PEEA*) copolymers (in $CDCl_3$)

the peak at about 3.7 ppm ($-C\underline{H}_2C\underline{H}_2O-$ of the PEG main chain) increased accordingly. The chemical compositions were determined from the ^{1}H NMR spectra according to Eqs. (6), (7), and (8):

$$X_{PCL}=\frac{I_e}{I_e+I_j+I_l}, \tag{6}$$

$$X_{PAU}=\frac{I_j}{I_e+I_j+I_l}, \tag{7}$$

$$X_{PEG}=\frac{I_l}{I_e+I_j+I_l}, \tag{8}$$

where I_e, I_j, and I_l are the integral intensities of the methylene hydrogen of PCL blocks at about 4.05 ppm, the methylene hydrogen of PAU blocks at about 3.23 ppm, and the methylene hydrogen of PEG blocks at about 3.7 ppm, respectively, shown in Fig. 1.

The macromolecular weight of PEEA0 was calculated according to Eq. (9):

$$M_n = 114 \times \frac{I_e}{I_n} + 183 \times \frac{I_j}{I_n}. \tag{9}$$

The macromolecular weight of PEEA5 and PEEA10 was calculated according to Eq. (10):

$$M_n=M_{PEG}+114 \times \frac{I_e}{I_m}+183 \times \frac{I_j}{I_m}. \tag{10}$$

The chemical composition and macromolecular weight of the copolymers are listed in Table 1.

Thermal property and crystallization behavior

For these PEEA triblock copolymers, the PEG weight content is less than 12%. According to Gan and Li [14, 15], this PEG block could not crystallize at such a low content. The WAXD patterns of these copolymers crystallized from the melt are presented in Fig. 2. All the samples exhibited two strong reflections at the diffraction angle 2θ of 20° and 23°. This diffraction pattern was very similar to the α-form crystal of nylon11 homopolymer and the orthorhombic system of PCL homopolymer [14]. There is no diffraction peak of PEG block in the WAXD patterns. The WAXD data of the PEEA copolymers are listed in Table 2 [16, 17, 18, 19, 20, 21].

Further information on the crystallization behavior of these PEEA copolymers was obtained from DSC analysis. The results are summarized in Table 3 and Fig. 3. When PEG was incorporated into the polyesteramide main chain, the thermal properties of the PEEA copolymers changed accordingly. The first heating run of the PEEA copolymers is shown in Fig. 3a. Each DSC curve of the three copolymers seemed to be a sum of two peaks. And with the increase in PEG content, the melting peaks became wider. When the weight fraction of PEG1000 is lower than 5% of W_t, the

Fig. 2 Wide-angle X-ray diffraction patterns of PEEA copolymers crystallized from the melt

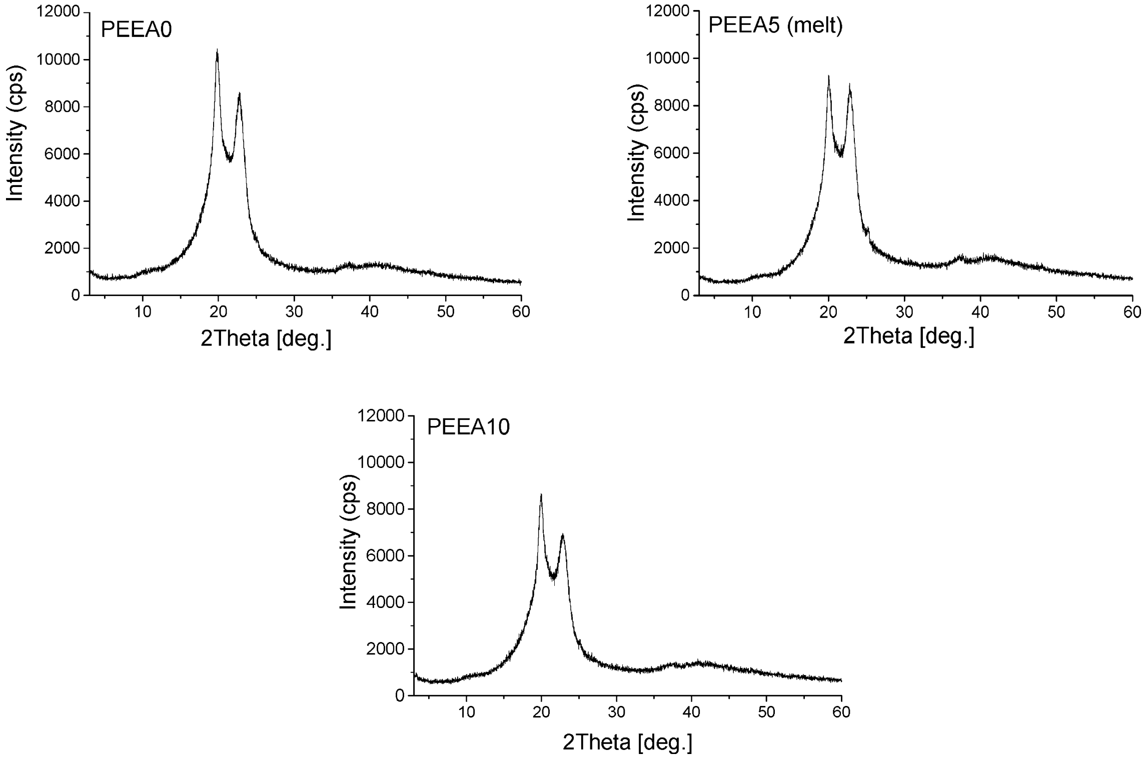


Table 2 Assignment of the PCL and nylon11 peaks in the PEEA copolymers. *d* is the d spacing

Peak	Experimental data						Reference data		
	PEEA0		PEEA5		PEEA10		PEEA copolymers		
	2θ (°)	d_{exp} (nm)	2θ (°)	d_{exp} (nm)	2θ (°)	d_{exp} (nm)	2θ (°)	d_{ref} (nm)	Crystal system
1	19.82	0.448	20.04	0.443	19.94	0.449	20.1	0.44	PAU, α form, (100)
							21.5	0.41	PCL, (110)
2	22.78	0.390	22.84	0.389	22.78	0.390	23.5	0.38	PAU, α form, (010,110)
							23.8	0.37	PCL, (200)

Table 3 Thermal properties of PEEA copolymers

Polymer code	1st heat run		2nd heat run		2nd cooling run		ΔH_m^0 (J/g)	X_c (%)
	T_m (°C)	ΔH_m (J/g)	T_m (°C)	ΔH_m (J/g)	T_c (°C)	ΔH_c (J/g)		
PEEA0	72.10	40.74	71.98	22.60	39.36	−43.42	159.9	14.1
PEEA5	64.79, 78.74	35.88	67.91	23.95	38.83	−37.27	159.2	15.0
PEEA10	52.63, 61.22	28.36	65.38	15.04	39.23	−26.02	157.9	9.5

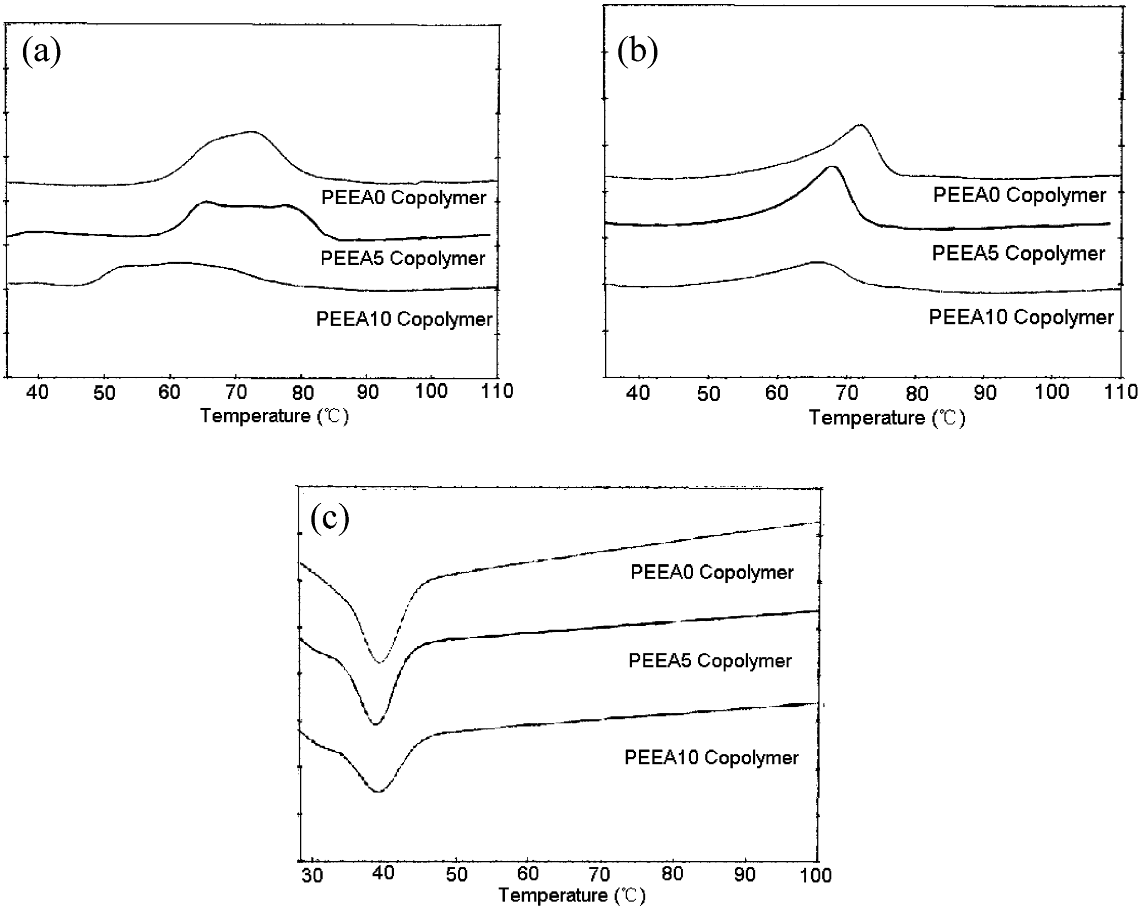


Fig. 3a–c Differential scanning calorimetry curves of PEEA copolymers under a nitrogen atmosphere. **a**) 1st heating scan ; **b**) 2nd heating scan; **c**) 2nd cooling run

Table 4 Thermogravimetric analysis data of P(CL/AU)$_{x/y}$ copolymers at a heating rate of 10 °C/min under nitrogen atmosphere

		Sample		
		PEEA0	PEEA5	PEEA10
ε-CL (% W_t) (Exp value)		47.1	42.9	40.5
PEG (% W_t) (Exp value)		0	6.6	11.9
$T_{d,5\%}$ (°C) [a]		364.1	361.1	357.3
Stage 1	$T_{d,1max}$ (°C)[b]	420.3	432.4	429.4
	Weight loss at stage 1 (%)	34.8	76.2	55.4
Stage 2	$T_{d,2max}$ (°C)[b]	428.6	484.8	475.7
	Weight loss at stage 2 (%)	20.6	22.6	36.1
Stage 3	$T_{d,3max}$ (°C)[b]	457.5	–	–
	Weight loss at stage 3 (%)	10.8	–	–
Stage 4	$T_{d,4max}$ (°C)[b]	473.4	–	–
	Weight loss at stage 4 (%)	9.9	–	–
Stage 5	$T_{d,5max}$ (°C)[b]	484.0	–	–
	Weight loss at stage 5 (%)	15.6	–	–
$T_{d,\ 50\%}$ (°C) [c]		442.3	441.5	439.2
Residue at 520 °C (%)		6.2	5.3	5.6

[a] Temperature at which the weight loss was 5%

[b] Temperature of the largest decomposition rate during the stage

[c] Temperature at which the weight loss was 50%

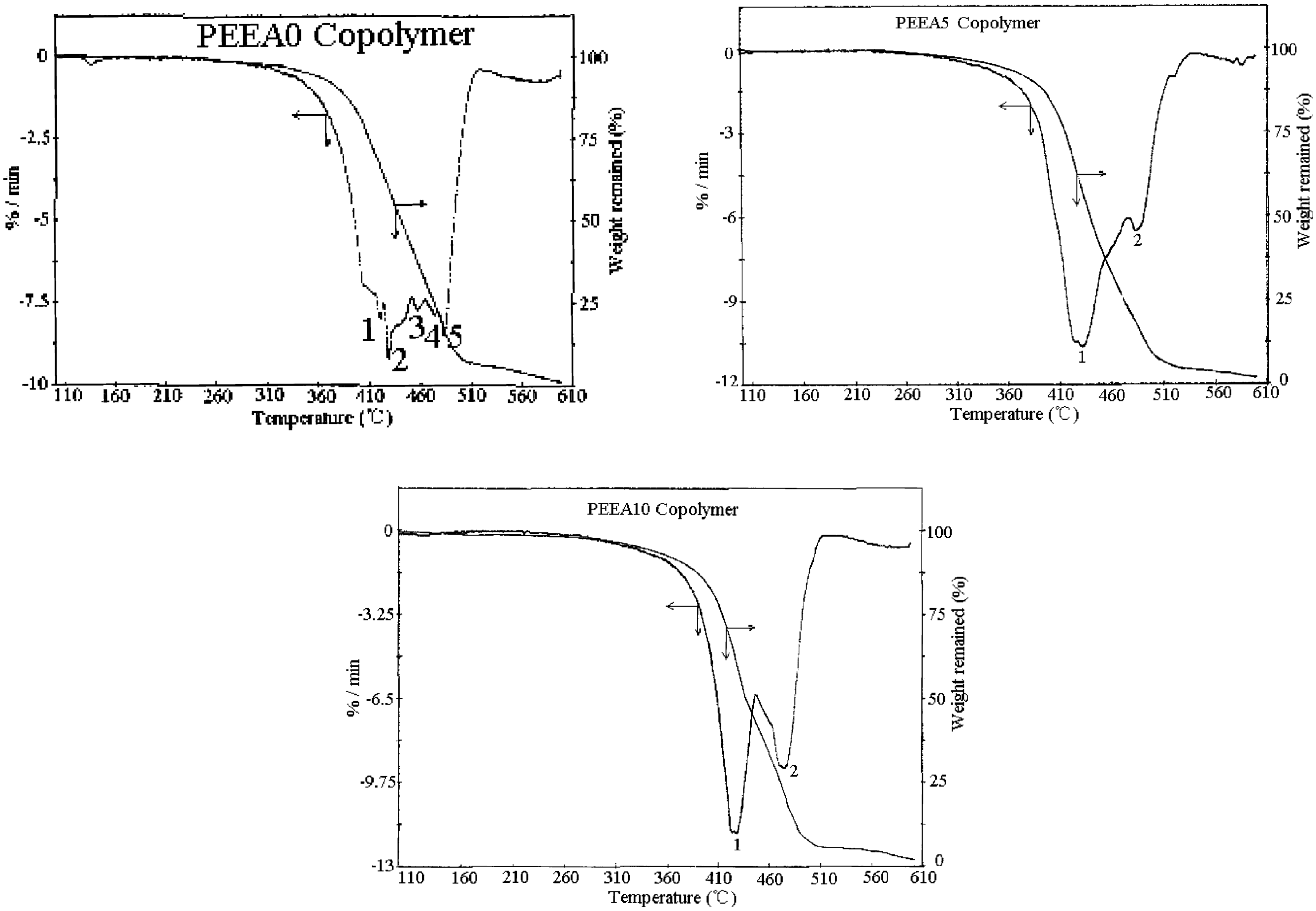


Fig. 4 Thermogravimetric analysis/differential thermogravimetry curves of PEEA copolymers in a nitrogen atmosphere

melting temperature increased, which might be due to the increase in flexibility of the macromolecule main chain when small amounts of PEG are present. But when the weight fraction of PEG1000 is up to 10% of W_t, both the melting temperature and crystallinity decreased. This phenomenon is similar to thermal property of poly(ethylene terephthalate) (PET)/PEG copolymers [22]. The second heating run of the PEEA copolymers is shown in Fig. 3b. And there is just one melting peak in the three copolymers, which is quite different from the first heating run shown in Fig. 3a. The second cooling run of the PEEA copolymers is shown in Fig. 3c. Only one crystallization peak was found for these three PEEA copolymers, which indicated that PAU and PCL blocks crystallized simultaneously.

Thermogravimetric analysis

Thermogravimetric analysis curves of PEEA copolymers under a nitrogen atmosphere are shown in Table 4 and Fig. 4. All these copolymers showed a stage-decomposition pattern, which suggested that the structure of these copolymers might be somewhat blocky. The degradation of the PCL/PEG block proceeds at a temperature lower than that of the PAU block. The peak at about 420 °C could be mainly due to the degradation of PCL/PEG blocks, while the last degradation peak at about 480 °C should be essentially due to that of PAU blocks. The degradation peaks at the middle temperature are very complicated. They might be due to the degradation of PEG/PCL/PAU blocks. With the increase in PEG content, $T_{d,5\%}$ decreased but $T_{d,1max}$ increased to some extent. And the weight loss at higher temperature (T >480 °C) increased from 15.6% for PEEA0 copolymer to 36.1% for PEEA10 copolymer. This increase in weight loss at higher temperature might be due to the microphase separation of these PEEA copolymers.

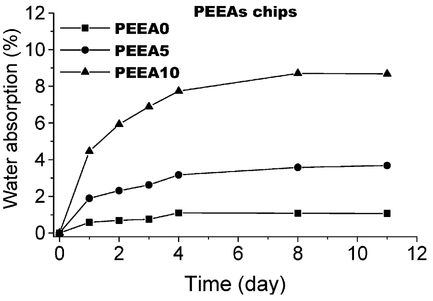


Fig. 5 Water absorption behavior of PEEA copolymers in distilled water at 30 °C

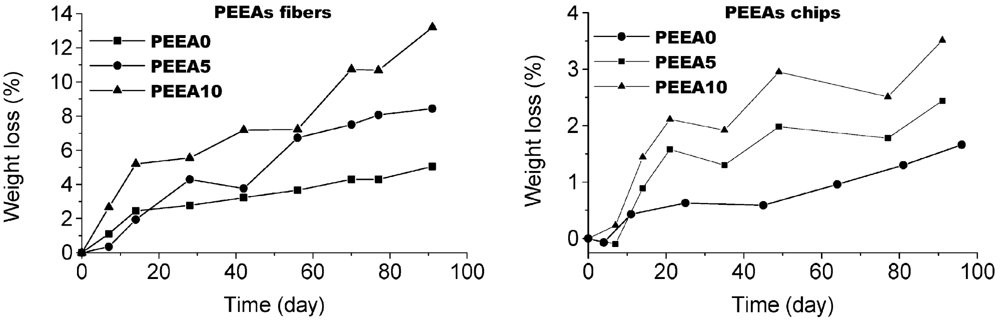
Water absorption

These PEEA copolymers are semicrystalline; when the PEG macromonomer was incorporated into the polyesteramide main chain, the hydrophilicity increased. For these PEEA copolymers, water absorption increased with the increase in PEG content; this is shown in Fig. 5. This increase in water absorption with PEG content might be due to the decrease in crystallinity of the overall copolymers shown in Table 3. The results are in good agreement with water absorption behavior of PET/PEG [22], poly(butylene terephthalate) (PBT)/PEG [23], and PCL/PEG copolymers [15].

Hydrolytic degradation

The PEEA samples with a thickness of about 1 mm and the fibers with the diameter of about 0.2 mm were incubated in PBS (pH 7.2, 37 °C). The degradation results are shown in Fig. 6. According to Malin et al. [24], the hydrolytic degradation behavior of semicrystalline polymers is determined by the chemical composition, degree of crystallinity, hydrophilicity, and molecular weight. These amphiphilic PEEA copolymers are semicrystalline; with an increase in PEG content, the hydrophilicity and water absorption increased accordingly, and as a result, the degradation rate increased. The degradation behavior of PEEA copolymers is similar to PET/PEG copolymers [14] and PBT/PEG copolymers [20]. The degradation rate of PEEA fibers is greater than that of PEEA chips owing to the different thicknesses of the test samples.

Fig. 6 In vitro degradation behavior of PEEA copolymer fibers and chips in phosphate buffer saline (pH 7.2, 37 °C)



Conclusion

In this work, amphiphilic PEEA copolymers were synthesized by the melt polycondensation method. The thermal property was greatly affected by the PEG incorporated into the main chain. Water absorption and hydrolytic degradation behavior were studied by gravimetry. With the increase in PEG content, water absorption and the degradation rate increased.

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