In Vitro Degradation Behavior of Polyesteramide Copolymer Fiber Based on 6-Aminocaproic Acid, Adipic Acid, and 1,6-Hexane Diol

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Abstract

In this work, a kind of aliphatic biodegradable polyesteramide (PEA) copolymer based on 6-aminocaproic acid, adipic acid, and 1,6-hexane diol was synthesized by melt polycondensation method, and was characterized by ^{1}H-NMR, FTIR and DSC. The PEA fiber was prepared by melt-spinning method. Tensile properties of the as-spun and hot-drawn fibers were also investigated. Hydrolytic degradation behavior of PEA copolymer chips and fibers were evaluated by weight loss in PBS solution with different pH value. The alkaline degradation behavior of fiber was also studied on change of diameter and surface morphology. During alkaline degradation, the PEA fiber underwent surface erosion.

Introduction

Aliphatic polyesteramide (PEA) copolymer is a new type of degradable materials, which was developed recently [1–10]. This copolymer has great thermal and mechanical properties even at relatively low molecular weight. On the other side, the hydrolytic degradable ester bond in the main chain imparted this copolymer with good degradability. In our previous research, several kinds of polyesteramide copolymers based on ε-caprolactone or lactic acid have been prepared [7–10], but the cost was somewhat high. In this work, we prepared the polyesteramide copolymers P(AC/AAH)70/30 based on 6-aminocaproic acid, adipic acid, and 1,6-hexanediol by melt polycondensation method, and the cost was reduced to some extent. The PEA fiber was prepared by melt-spinning method. Tensile properties of the as-spun and hot-drawn fibers were also investigated. *In vitro* hydrolytic and alkaline degradation behavior of PEA copolymer chips and fibers were studied in detail.
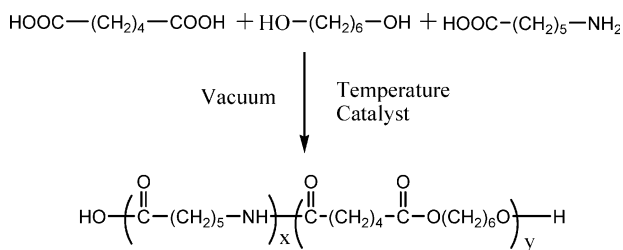
Experimental

Materials and methods

6-Aminocaproic acid (AC, purchased from Alfa Aesar), adipic acid (AA), and 1,6-hexane diol (HD) are all analytic reagent grade. All these materials were used as received.

Synthesis of P (AC/AAH) 70/30 copolymer

In this article, the copolymer was denoted as P(AC/AAH)70/30, where 70/30 represented the molar ratio of AC/AA, H represented 1,6-hexane diol.

The copolymer was synthesized from 6-aminocaproic acid, adipic acid, and 1,6-hexanediol by melt polycondensation method according to Scheme 1, which was shown as follows: AC (0.231 mol, 30.3 g), AA (0.10 mol, 14.6 g), HD (0.10 mol, 11.8 g), and tetrabutyl titanate (0.05 g) were added into the reaction vessel under nitrogen atmosphere. The mixture was kept at 120–160 °C for 1.5 h. Then, the mixture was rapidly heated to 240 °C under vacuum for about 1.5 h. At the end, the resultant hot melt was poured out onto a steel plate, thus P(AC/AAH)70/30 copolymer was obtained. The chemical composition and viscosity of the obtained sample were listed in Table 1.

$$HOOC-(CH_2)_4-COOH + HO-(CH_2)_6-OH + HOOC-(CH_2)_5-NH_2$$

Vacuum | Temperature Catalyst

$$HO-\left(\overset{O}{\overset{\|}{C}}-(CH_2)_5-NH\right)_x\left(\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-O(CH_2)_6O\right)_y-H$$

Scheme 1. Synthesis scheme of P(AC/AAH)70/30 copolymer.

Fourier transform infrared spectroscopy (FTIR)

FTIR (KBr) spectra of copolymer were taken on NICOLET 200SXV Infrared Spectrophotometer.

^{1}H-nuclear magnetic resonance (^{1}H-NMR)

^{1}H-NMR spectra (in d-DMSO) were recorded using Varian 400 spectrometer (Varian, USA) at 400 MHz using tetramethylsilane (TMS) as internal reference standard.

Differential scanning calorimetry (DSC)

Thermal property of PEA copolymer was characterized on differential scanning calorimeter (NETSCZ 204, Germany). The specimen was heated from 30 °C to 180 °C under nitrogen atmosphere at a heating rate of 10 °C/min, and a cooling rate of 10 °C/min.

Melt index of P(AC/AAH)70/30 copolymer at different temperature

The vacuum-dried polyesteramide particles were used for melt index test. The instrument is XNR-400 melt flow rate instrument (XNR-400, Changchun, China). Each sample was tested for four times, and the average value was taken as the melt index.

Intrinsic viscosity measurement

Intrinsic viscosity [η] was measured at 30±0.1 °C by using Ubbelohde viscometer. All the PEA samples were dissolved in *m*-cresol to prepare solutions at a concentration of ca. 0.5 g/dl. [η] was calculated using Equation (1) according to Solomon–Ciuta method [11].

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

Where C is concentration of solution, t is flow time of solution, and t_0 is flow time of pure solvent.

Preparation of P(AC/AAH)70/30 fibers [13]

Melt spinning of the vacuum-dried P(AC/AAH)70/30 copolymer particles was carried out using a melt flow rate instrument equipped with a single-nozzle circular spinnerette (1.5 mm in diameter). Polyesteramide was extruded at predetermined temperature. The extrudate was taken up on a glass drum at ca. 4 m/min [13]. The as-spun fibers were drawn to various ratios at 70 °C.

Tensile property of polyesteramide fibers

The tensile properties of polyesteramide fibers were evaluated on tensile testing machine (PC/YG061F, Laizhou, Shangdong province, PR China). A specimen gauge length of 100 mm was used. The tests were carried out at a crosshead speed of 300 mm/min at room temperature. The results obtained were averaged over four to five samples for each condition. Diameters of the fibers were measured with an optical microscope. The ultimate strength (σ) was calculated using Equation (2):

$$\sigma = \frac{P}{A}(MPa) \qquad (2)$$

Where P is absolute tensile breaking strength (N), A is the fiber's transverse area (mm^2) before tensile testing.

Water uptake of polyesteramide copolymer chips and fibers

The copolymer chips and fibers were immersed in distilled water at 37 °C for predetermined time, and then they were taken out at predetermined time, and the surplus surface water was removed by filter paper. The water uptake was calculated according to Equation (3):

$$\text{Water absorption}\% = \frac{W_{ht} - W_d}{W_d} \times 100 \qquad (3)$$

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

Hydrolytic degradation behavior of polyesteramide copolymer chips and fibers

In vitro degradation tests were carried out as follows: the copolymer chips (100–200 mg) and fibers were placed in 10 ml of PBS saline with pH=4.02, 6.84, and 9.10 respectively at 37 °C. The degradation media were refreshed every two weeks. The samples were removed at predetermined time, rinsed thoroughly with distilled water and vacuum-dried at 35 °C for 12 h. The degree of degradation was calculated by weight loss:

$$\text{Weight loss}(\%) = \frac{W_0 - W_t}{W_0} \times 100 \qquad (4)$$

Where W_0 is the dry weight before degradation, W_t is the dry weight at time t.

Table 1. The P(AC/AAH)70/30 copolymer prepared in this work.

Sample	AC/AA (in feed)	AC/AA (in exp)[a]	[η] (dl/g)
P(AC/AAPH)70/30	70/30	69.1/30.9	0.64

[a]Calculated from ^{1}H-NMR results.
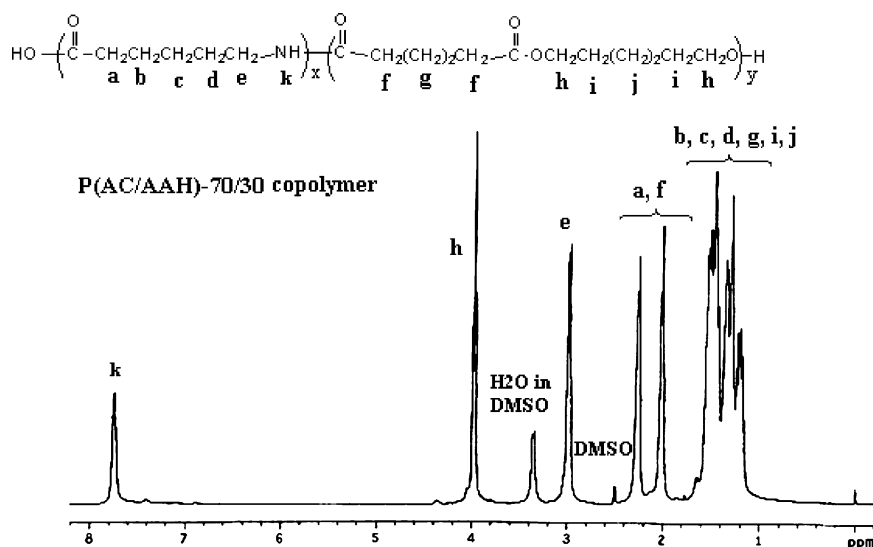
Figure 1. ¹H-NMR spectrum of P(AC/AAH)70/30 copolymer.

Alkaline degradation behavior of polyesteramide copolymer chips and fibers

Alkaline hydrolysis of PEA chips and fibers was conducted in 0.1 mol/l sodium hydroxide (NaOH) aqueous solution respectively at 37 °C. Degradation behavior was characterized by weight loss, diameter change, and surface morphology change.

Surface morphology study of fibers

Scanning electron micrographs (SEM) were observed on JSEM microscope (JSEM-5900LV, JEOL, Japan) at an electron voltage of 20 kV after sputtered with gold.

Results and discussion

Synthesis of PEA copolymer

FTIR and ¹H-NMR were used to characterize P(AC/AAH)70/30 copolymer. For this sample, its FTIR spectrum (data not shown) included bands at 3,303 (N–H), 1,732 (C=O), 1,640, 1,543 (amide I and amide II), and 1,172 cm⁻¹ (C–O). The ¹H-NMR spectrum was shown in Figure 1. The characteristic absorption peaks were also indicated. The

chemical compositions were determined from ¹H-NMR spectra according to Equation (5) and Equation (6):

$$X_{amide} = I_e/(0.5I_h + I_e) \tag{5}$$

$$X_{ester} = 1 - X_{amide} \tag{6}$$

Where I_e and I_h were integral intensities of methylene hydrogen of P(AC) blocks at about 3.04 ppm, and methylene hydrogen of P(AAH) blocks at about 3.98 ppm, respectively. For this sample, AC/AA ratio (mol%)=69.1/30.9, which was consistent with the feed ratio of AC/AA (mol%)=70/30.

Preparation of PEA fiber

For the PEA copolymers, apparent viscosity of the melt was mainly determined by processing temperature, which followed Arrhenius equation in Equation (7).

$$\eta = \frac{A \cdot \exp E_\eta}{RT} \tag{7}$$

Where A is constant, E_η is the active energy, and T is the absolute temperature (K).

With increase in processing temperature, the apparent viscosity of the copolymer decreased then, but the intrinsic viscosity didn't change obviously, which could be seen from Table 2. Due to the thermal stability of polyesteramide fiber and continuity of melt-spinning, the spinning

Table 2. Melt index of P(AC/AAH)70/30 copolymer at different temperature.

Sample	Temperature (°C)	MI (g/10 min)	[η] (dl/g)	The optimal spinning temperature (°C)
P(AC/AAH) 70/30	125	1.952	0.68	130
	130	9.892	0.66	
	135	16.895	0.67	

Table 3. Thermal properties of P(AC/AAH)70/30 copolymer.

Sample	ΔH_c (J/g)	T_c (°C)	ΔH_m (J/g)	T_m (°C)
P(AC/AAH)70/30	−5.5	51.9	22.3	117.9

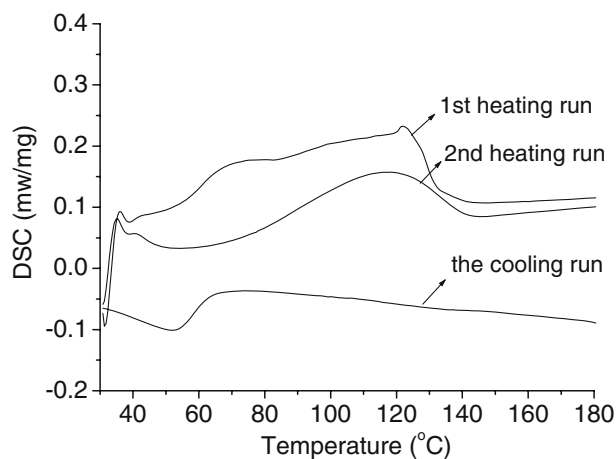The data of heating run was obtained according to the second heating scan.

Figure 2. DSC curves of P(AC/AAH)70/30 copolymer.

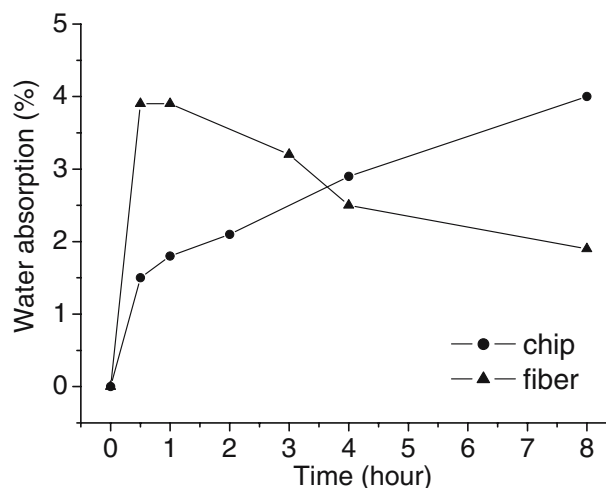

Figure 3. The water absorption of P(AC/AAH)70/30 copolymer chips and fibers at 37 °C in distilled water.

temperature must be chosen carefully. For P(AC/AAH)70/30 copolymer, we found that the melt index (MI) changed greatly with temperature increasing from 125 °C to 135 °C. Furthermore, according to Table 3 and Figure 2, we could find that melting temperature(T_m) of this copolymer was 117.9 °C. So we chose 130 °C as the practical spinning temperature.

Tensile properties of PEA fibers

Tensile properties of polyesteramide fibers were mainly determined by chemical composition and the drawn ratio of the fibers. Effect of drawn ratio was discussed as follows:

When the as-spun fiber was drawn, the crystallinity and molecular orientation increased then [12]. For this P(AC/AAH)70/30 fiber, the tensile strength increased from 54.3 MPa to 186.3 MPa, and the elongation at break decreased from 228.7% to 41.1% with increase in drawn ratio from 0 to 2, which could be seen from Table 4. This phenomenon is similar to previous study on P(CL/AU) fibers [13].

Water absorption of PEA copolymer

The water absorption behavior of P(AC/AAH)70/30 fibers and chips in distilled water at 37 °C was illustrated in Figure 3. The results showed that the maximum value of water uptake for the chip or fiber was both about 4%, and achieved after 0.5 h or 8 h respectively. For the chip, after 8 h, the water uptake kept constant within 24 h due to the water was absorbed to a large extent. However, for the

fiber, after 0.5 h the water uptake decreased gradually, which might be attributed to the combined effect of water absorption and hydrolytic degradation of the biodegradable fiber [14]. P(AC/AAH)70/30 copolymer was semicrystalline. When it was incubated in aqueous medium, water could permeate into the amorphous region. At the same time, the hydrolytic degradation occurred; as a result, the weight of the samples would decrease then. However, in the early days, the weight of these samples would increase because water absorption rate was greater than hydrolytic degradation rate before water was absorbed to the maximum. These could be also confirmed by the hydrolytic degradation behavior shown in Figure 4. In detail, during hydrolytic degradation in PBS (initial pH=6.84, 37 °C), weight loss of the fiber was up to about 4% within 24 h, but for copolymer chips, the weight of the chip increased instead due to water absorption before absorbed to the maximum.

Hydrolytic degradation behavior of PEA copolymer

P(AC/AAH)70/30 copolymer chips and fibers were incubated in PBS solution with pH=4.02, 6.84 and 9.10 respectively at 37 °C, and the degradation behavior was shown in Figure 4. For copolymer chips and fibers, the degradation ratio both increased with increasing on pH value of degradation media, which was consistent with our previous study [15, 16].

According to Figure 4, in addition, the weight loss of fibers was about two times as much as that of chips in the same degradation medium, which might be due to the greater specific surface area of fibers compared with chips.

Alkaline degradation behavior of PEA copolymer

Weight loss of the copolymer chips and fibers
When P(AC/AAH)70/30 copolymer chips and fibers were incubated in 0.1 mol/l sodium hydroxide (NaOH) solution

Table 4. Effect of drawn ratio on tensile properties of P(AC/AAH)70/30 fibers.

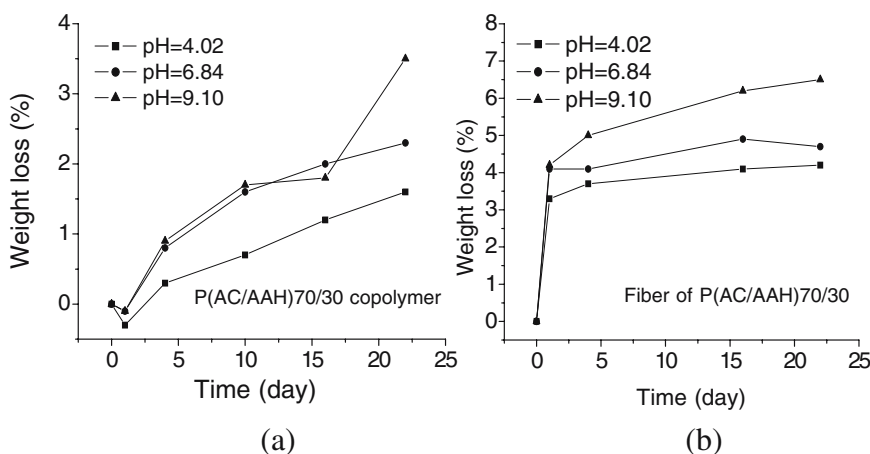| Sample	Drawn ratio	Tensile strength (MPa)	Elongation at break (%)
P(AC/AAH)70/30	R=0	54.3	228.7
	R=1	101.5	115.6
	R=2	186.3	41.1

Figure 4. The hydrolytic degradation behavior of P(AC/AAH)70/30 copolymer chips (a) and fibers (b) at 37 °C respectively.
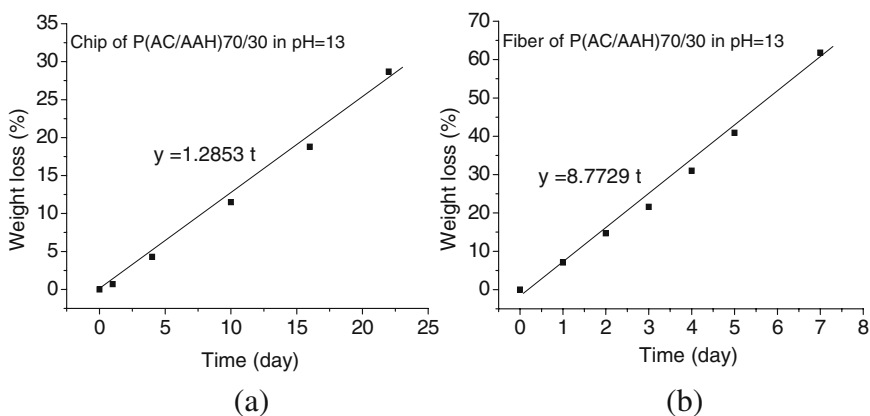

Figure 5. The degradation behavior of P(AC/AAH)70/30 copolymer chips (a) and fibers (b) in 0.1 M NaOH solution at 37 °C respectively.

at 37 °C, the degradation rate increased quickly compared with that in aqueous environment with pH=4.02, 6.84, and 9.10 respectively. Figure 5 showed the degradation profile of P(AC/AAH)70/30 chips and fibers. After seven days, the fibers' mass decreased by ca. 60%, whereas the chips' mass

decreased by ca. 30% after 22 days. It could be confirmed that the fiber exhibited faster degradation rate than did the chip in alkaline solution according to Figure 5. This was similar to hydrolytic degradation profile of PEA copolymer in phosphate buffer solution shown in Figure 4. These P(AC/AAH)70/30 copolymer chips and fibers underwent linear degradation profile, which was a typical characteristic of surface-eroding polymers [15, 17]. Additionally, during degradation of P(AC/AAH)70/30 copolymer chips in the concentrated alkaline solution with pH=13 at 37 °C, the intrinsic viscosity of copolymer chip after different times hardly changed within 15 days, which was shown in Figure 6. In other words, the corresponding viscosity-average molecular weight of copolymers should not exhibit change during degradation, which indicated that bulk erosion hadn't occurred, as the degradation of PEA fiber [11] and PLA fiber [18] in concentrated alkaline solution.
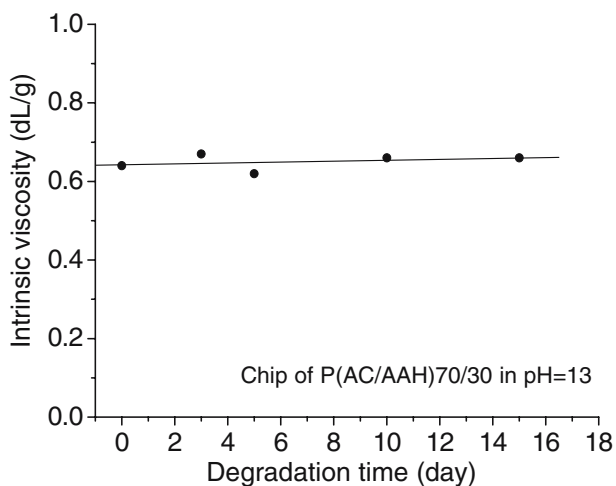
Diameter and surface morphology change of PEA fibers

Figure 7 presented the changes in diameter and surface morphology of P(AC/AAH)70/30 fibers during degradation in 0.1 mol/l sodium hydroxide solution at 37 °C. As was shown on left in Figure 7, compared to primary diameter of
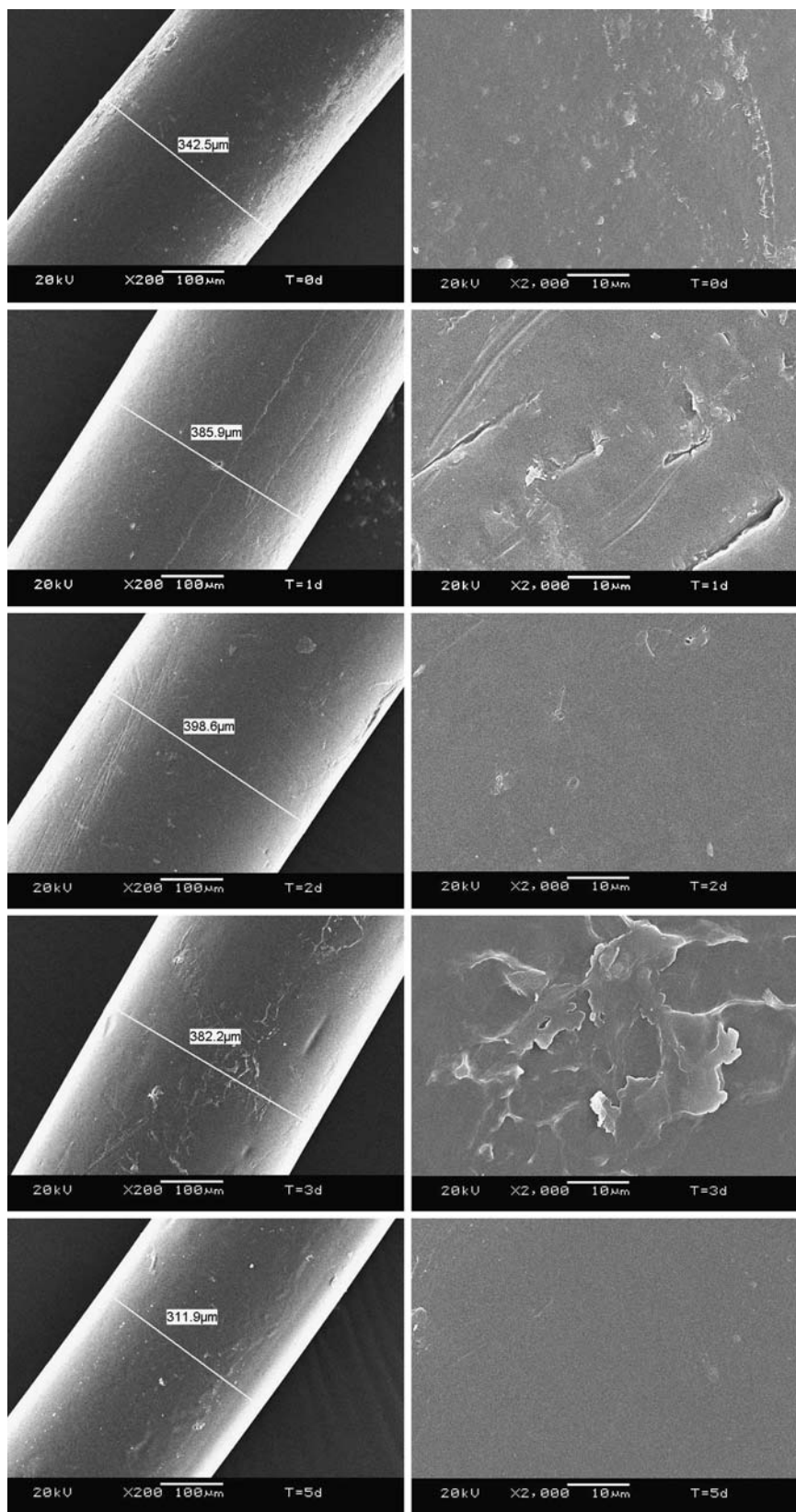

Figure 6. Change in intrinsic viscosity of P(AC/AAH)70/30 copolymer chips after degraded in concentrated alkaline solution for different period.

Figure 7. SEM micrographs of P(AC/AAH)70/30 fibers during degradation in 0.1 M NaOH (*Left*: ×200, *right*: ×2,000).

fiber, the diameter of degraded fibers increased firstly and then decreased. In detail, when immersed in alkaline solution at first day, the surface layer of fibers swelled and thickened, so the diameter of fibers increased from 342.5 μm to 385.9 μm. The fibers continued to swell and

the diameter reached 398.6 μm after degraded for two days. At the third day, the loose surface layer shed due to degradation, and the diameter decreased to 382.2 μm, which was still more than the original diameter. And then fibers underwent the same degradation progress from the

third day to the fifth day, and the diameter became smaller and smaller, which was finally smaller than the original diameter of PEA fibers before degradation.

Similarly, from the right part in Figure 7, the changes of fibers surface morphology during alkaline degradation could also confirm the above degradation progress. In another words, before degradation, the fibers had a relatively smooth surface. When they were incubated in alkaline solution, small clefts along fibers came into being and the surface became some rough and loose at the first stage of degradation, then the loose surface layer gradually dropped off, which made new smooth surface appear. In the following degradation progress, the above change of fibers surface was observed again. From Figure 7, a conclusion could be made that this PEA fiber underwent surface erosion when incubated in concentrated alkaline solution, which was consistent with the results studied previously [12, 15].

Conclusion

In this paper, degradable aliphatic polyesteramide (PEA) copolymer was synthesized successfully and the fiber was prepared by melt-spinning method. With increase in drawn ratio, tensile strength of the fiber increased, and the elongation at break decreased. When the polyesteramide copolymer chips and fibers were immersed in PBS solution, the degradation rate of chips and fibers both increased with pH value. And the degradation rate of fibers was greater than that of chips. From the alkaline degradation behavior of P(AC/AAH)70/30 copolymer chips and fibers studied by change of weight loss, diameter and surface morphology. In conclusion, this PEA copolymer underwent surface erosion in concentrated alkaline solution.

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