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Study on the degradability of poly(ester amide)s derived from the α-amino acids glycine, and L-alanine containing a variable amide/ester ratio

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Abstract

Two series of poly(ester amide)s prepared from sebacic acid and different ratios of 1,12-dodecanediamine and a diamine that contains both α-amino acid residues and ester groups have been synthesized and characterized. In order to maintain hydrogen bonding interactions, two diamines with the same number of main chain atoms were selected. The series differ on the nature of the α-amino acid residue: glycine or L-alanine. The calorimetric analysis shows that melting temperatures increase as the amide/ester ratio does. Polymers derived from L-alanine show lower crystallinities and melting temperatures than those constituted by glycine units. Hydrolytic and enzymatic degradabilities of both series of poly(ester amide)s have also been studied. The ratio and nature of α-amino acid residues in the chemical repeat unit greatly affect the degradation rate. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Hydrolytic and enzymatic degradabilities; L-Alanine; Glycine

1. Introduction

Different works with poly(ester amide)s [1–6] have recently been carried out, since these polymers may offer an interesting combination of properties: a high degradability caused by the ester linkages and good mechanical properties due to the establishment of hydrogen bonds between amide groups. Furthermore, the inclusion of α-amino acids may enhance susceptibility to degradation with proteolytic enzymes and in general, biodegradability. Sequential poly(ester amide)s with the unit repeat $-[NHCH(R)CO-O(CH_2)_mO-COCH(R)NH-CO(CH_2)_nCO]-$ can be easily synthesized by a two-step procedure based on an interfacial polyamidation [7–9] or by a thermal polyesterification, as has recently been established [10]. This group of polymers has been a subject of our research for the last few years. Synthesis, characterization, structure and degradability have been studied for polymers derived from different amino acids, diols and diacids [11–16]. Thus, the published results indicate that amino acids without bulky side groups, such as glycine or L-alanine, are the most promising due to the melting temperature (close or higher than 100°C) and the crystallinity of the derived polymers. Moreover, sebacoyl or dodecanoyl chlorides are the most adequate monomers when polymers are prepared by interfacial polymerization due to their stability to hydrolysis.

The main purpose of this paper is to determine how the amino acid content and the proportion between amide and ester groups influences thermal properties and degradability. Two series of polymers derived from either L-alanine or glycine were prepared by interfacial polymerization using the stable sebacoyl chloride. Random polymers with a variable ester/amide ratio were obtained by using the appropriate mixtures of 1,12-dodecanediamine (DA) and the diamine with the sequence $NH_2CHRCOO(CH_2)_6O-COCH(R)NH_2$ (R: H or CH_3) containing two amino acid units and ester linkages. Note that the two amines have the same number of atoms in their main chain. Consequently, the hydrogen bond interactions between the resultant random copolymers may not be disrupted when the two kinds of diamines are interchanged.

2. Experimental

2.1. Synthesis

The series of poly(ester amide)s PDA_xGHG_y8 and PDA_x-AHA_y8 were synthesized by interfacial polymerization following the procedure outlined in Scheme 1, which is similar to that previously reported for related derivatives with a sequential composition [11–13].

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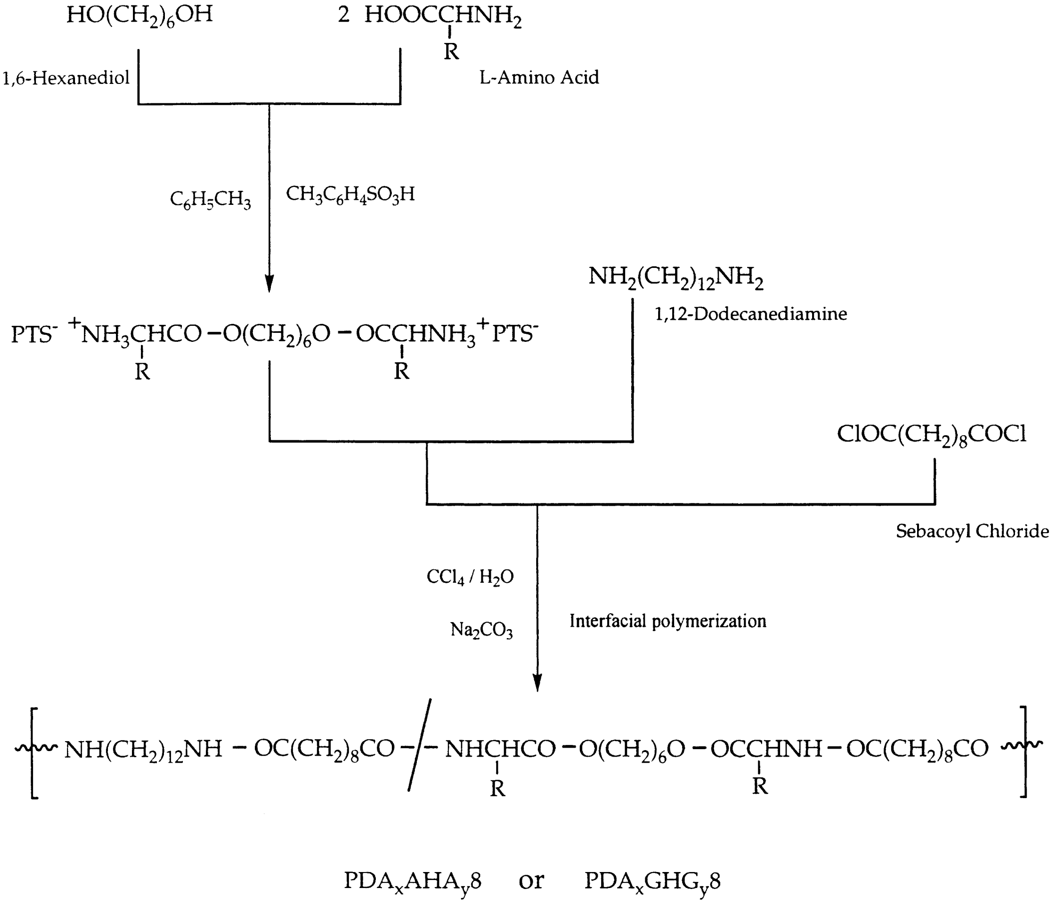

Scheme 1.

The series of poly(ester amide)s PDA_xGHG_y8 and PDA_xAHA_y8 were synthesized by interfacial polymerization following the procedure outlined in Scheme 1, which is similar to that previously reported for related derivatives with a sequential composition [11–13].

In our notation, x and y refer to the percentage of 1,12-dodecanediamine and the diamine derived from the condensation of 1,6-hexanediol with two residues of the appropriate amino acid (AHA for the alanine derivative and GHG for the glycine derivative), respectively. Following the nomenclature used in previous works, the dicarboxylic unit is described by the number of methylene groups (8 for sebacic acid). Note also that $PDA_{100}GHG_08$ and $PDA_{100}AHA_08$ correspond to the Nylon 12 10, whereas the sequential poly(ester amide)s $PDA_0GHG_{100}8$ and $PDA_0AHA_{100}8$ correspond to PGHG8 and PAHA8 (as named in previous papers), respectively.

2.1.1. Monomer synthesis

Preparation of the *p*-toluenesulfonic acid salt of *O,O′*-bis(glycyl)-hexamethyleneglycol ($PTS^{\pm}GHG^{+}PTS^{-}$) has previously been reported [11].

2.1.1.1. p-Toluenesulfonic acid salt of O,O′-bis(alanyl)-hexamethylenglycol ($PTS^{\pm}AHA^{+}PTS^{-}$). A three-neck, round bottom flask equipped with a $CaSO_4$ drying tube, a Dean–Stark apparatus, and a magnetic stirrer was charged with 1,6-hexanediol (0.1 mol), L-alanine (0.22 mol), *p*-toluenesulfonic acid monohydrate (0.22 mol), and toluene (500 ml). The reaction mixture was refluxed until no more water was distilled (for approximately 15 h). Then, it was cooled down to room temperature and the toluene was evaporated under reduced pressure to obtain a hard white solid that was twice recrystallized from ethanol.

Yield: 75%, mp: 182°C.

^{1}H-NMR ($CDCl_3$/TFA, TMS, int. ref.): δ 7.7–7.2 (m, 8H, Ar–H), 4.32 (m, 2H, $CH(CH_3)$), 4.26 (t, 4H, $COOCH_2$), 2.42 (s, 6H, Ar–CH_3), 1.70 (d, 6H, $CH(CH_3)$), 1.68 (m, 4H, OCH_2CH_2) and 1.37 (m, 4H, $OCH_2CH_2CH_2$).

^{13}C-NMR ($CDCl_3$/TFA, TMS, int. ref.): δ 170.37 (COO), 143.8–125.7 (aromatic carbons), 67.70 (OCH_2), 50.48 (CH), 27.84 (OCH_2CH_2), 24.88 ($OCH_2CH_2CH_2$), 21.24 (Ar–CH_3) and 15.58 ($CH(CH_3)$).

Anal. calcd for $C_{26}H_{40}N_2O_{10}S_2$: C, 51.66%; H, 6.62%; N, 4.64%. Found: C, 51.79; H, 6.52; N, 4.73%.

2.1.2. Interfacial polyamidation

An aqueous solution (70 ml) of 7 mmol of the appropriate mixture of diamines (1,12-dodecanediamine and $PTS^{\pm}GHG^{+}PTS^{-}$ or $PTS^{\pm}AHA^{+}PTS^{-}$ for the PDA_xGHG_y8

or PDA$_x$AHA$_y$8 series, respectively) and sodium carbonate (14 mmol) was carefully added over a solution of sebacoyl chloride (7 mmol) in carbon tetrachloride (140 ml). Then, the two phases were stirred for a period of 30 min. The polymer which precipitated was isolated by filtration and successively washed with ethanol, water, ethanol, carbon tetrachloride and ethyl ether before drying in a vacuum desiccator at 60°C. All the polymers were purified by precipitation of formic acid or trifluoroacetic acid solutions with a mixture of water/acetone (1/1, v/v).

2.2. Methods

Intrinsic viscosities were determined with a Cannon–Ubbelohde microviscometer in dichloroacetic solutions at 25 ± 0.1°C.

Infrared absorption spectra were recorded with a Perkin–Elmer 1600 FT-IR spectrometer in the 4000–500 cm^{-1} range from films obtained from evaporation of trifluoroethanol solutions. NMR spectra of poly(ester amide)s were registered from chloroform/trifluoroacetic acid solutions. Chemical shifts were calibrated using tetramethylsilane as an internal standard. A Bruker AMX-300 spectrometer operating at 300.1 and 75.5 MHz was used for ^{1}H- and ^{13}C-NMR investigations, respectively. Thermal analysis was performed by differential scanning calorimetry with a Perkin–Elmer DSC-PYRIS 1, using indium metal for calibration. Thermogravimetric analysis was carried out with a Perkin–Elmer TGA-6 thermobalance.

Plates of 1.5 cm × 1.5 cm × 200 μm were cut off from films prepared by melt pressing 200 mg of powder samples. Films of the PDA$_x$AHA$_y$8 series were obtained by applying 1 metric ton for 1 min at the fusion temperature, which increased as the 1,12-dodecanediamine content did. Films of PDA$_x$GHG$_y$8 were much more difficult to prepare, since two steps were necessary: first the sample was kept for 3 min at its melting temperature and then, 4 metric tons were applied for five additional minutes at the same temperature.

Hydrolytic degradation studies of plate samples were carried out in a pH 7.4 sodium phosphate buffer at 37°C to simulate physiological conditions. Enzymatic degradation studies were performed at 37°C by using lipases from *Candida cylindracea* (943 units/mg) and *Pseudomonas cepacia* (1500 units/mg), and proteolytic enzymes such as papain (30,000 units/mg, No. 7144) and proteinase K (*Tritirachium album*, 13 units/mg). The media consisted of a sodium phosphate buffer (pH 6.0 for papain and 7.2 for the other enzymes) containing sodium azide (0.03%) to prevent microbial growth and the appropriate enzyme. In the case of papain, the solution also contained L-cysteine (34 mM) and ethylenediaminetetraacetic disodium salt (30 mM) for activation. Solutions were renewed every 72 h because of enzymatic activity loss. In all cases, the plates were placed in glass vials containing the degradation media (30 ml hydrolytic or 10 ml enzymatic) and removed after the prescribed times. Mass loss, intrinsic viscosity, and changes in NMR and IR spectra were evaluated in all these different degradation experiments. The samples PDA$_{20}$AHA$_{80}$8 and PDA$_{20}$GHG$_{80}$8, which gave the best films, were used to test the activity of the different enzymes. Then, degradation of all samples was compared using powder samples and the papain enzymatic medium.

Surfaces of polymer films after degradation tests were also observed with a JEOL JSM-6400 scanning electron microscope.

3. Results and discussion

3.1. Synthesis

During polycondensation, the polymers derived from L-alanine showed a great tendency to form aggregates of a sticky nature that hinder the stirring. Although previous works with related polymers demonstrated that carbon tetrachloride was a suitable solvent for the organic phase, we tried to optimize conditions such as solvent and concentrations again. The best results were still obtained with carbon tetrachloride, but in order to diminish aggregation, we reduced the monomer concentration in the organic phase (up to 0.05 M) and increased the stirring speed considerably at the beginning of the polymerization process.

Polymerization yields were similar and practically independent of the nature of the amino acid and the ratio between the two kinds of diamines. Values in the 60–75% range were obtained, as summarized in Table 1. However, significant differences were observed between the intrinsic viscosities of the samples (Table 1). Thus, the increase of

Table 1
Yields, intrinsic viscosities and composition of the polymers studied in this work

Polymer	Yield (%)	Intrinsic viscosity (dl/g)[a]	Percentage of 1,12-dodecanediamine[b]
PDA$_0$GHG$_{100}$8[c]	68	0.77	0
PDA$_{10}$GHG$_{90}$8	71	0.70	12
PDA$_{20}$GHG$_{80}$8	69	0.59	15
PDA$_{50}$GHG$_{50}$8	60	0.50	49
PDA$_{70}$GHG$_{30}$8	65	0.45	68
PDA$_0$AHA$_{100}$8[d]	75	1.05	0
PDA$_{10}$AHA$_{90}$8	70	0.76	13
PDA$_{20}$AHA$_{80}$8	60	0.67	19
PDA$_{50}$AHA$_{50}$8	62	0.60	50
PDA$_{70}$AHA$_{30}$8	63	0.56	70
PDA$_{100}$AHA$_0$8[e]	72	0.60	100

[a] Measured in dichloroacetic acid at 25°C.

[b] Referred to the total diamine content and determined from ^{1}H-NMR spectra.

[c] PGHG8.

[d] PAHA8.

[e] Nylon 12 10.

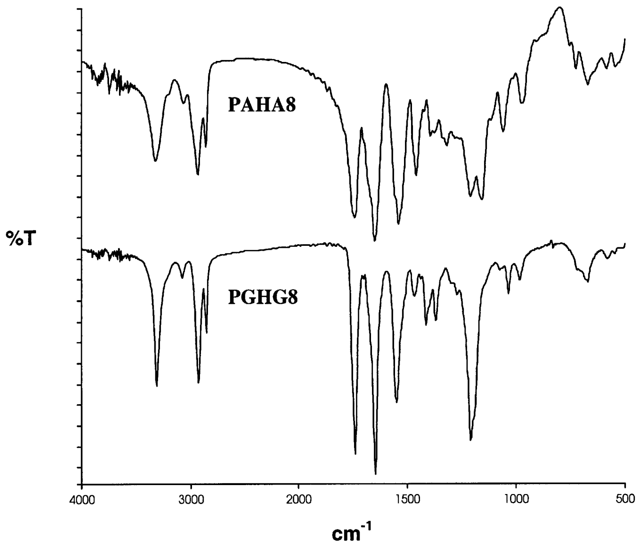

Fig. 1. Infrared spectra of the sequential poly(ester amide)s PGHG8 and PAHA8.

the 1,12-dodecanediamine ratio led to a decrease of the intrinsic viscosity of the random poly(ester amide)s. In the same way, alanine derivatives showed a higher viscosity than the equivalent polymers of the PDA$_x$GHG$_y$8 series. Both trends could be explained in terms of a decrease in polymer solubility when the ratio of 1,12-dodecanediamine or glycine residues increases.

3.2. Molecular polymer characterization

Infrared and NMR spectra of the polymers were fully consistent with the anticipated chemical constitution.

Fig. 1 shows the infrared spectra of the sequential homopolymers PGHG8 and PAHA8 poly(ester amide)s, whereas Fig. 2 compares the spectra for the whole series of PDA$_x$AHA$_y$8. Note that the main difference corresponds to the relative intensity between the carbonyl absorptions of the ester (ca. 1740 cm^{-1}) and amide (ca. 1640 cm^{-1}) groups. The wave numbers of the main infrared absorption bands, summarized in Table 2, are similar for all the polymers and indicate an important fact: strong hydrogen bonds are always established, as deduced from the single signal attributed to the NH stretching mode that appears near 3300 cm^{-1} (amide A). This behavior is consistent with our purpose of combining diamines with similar length in order to keep hydrogen bonding interactions.

Table 3 summarizes the most representative signals observed in the ^{1}H-NMR spectra of the two series of polymers. Protons of the methylene group of glycine appear at practically the same displacement as those of the CH$_2$–O group (ca. 4.30 ppm), whereas the proton of the alanine units is separated from them (Fig. 3 and Table 3). Copolymer compositions were verified from the area (I_1) of the peak at 3.52 ppm (four protons for the NHCH_2 groups of the 1,12-dodecanediamine residue) and the area (I_2) of the signal at 4.28–4.30 (four and two protons for the diamines constituted by glycine and alanine residues, respectively). Thus, the percentage of 1,12-dodecanediamine incorporated in the synthesized polymers is given by the simple relationships

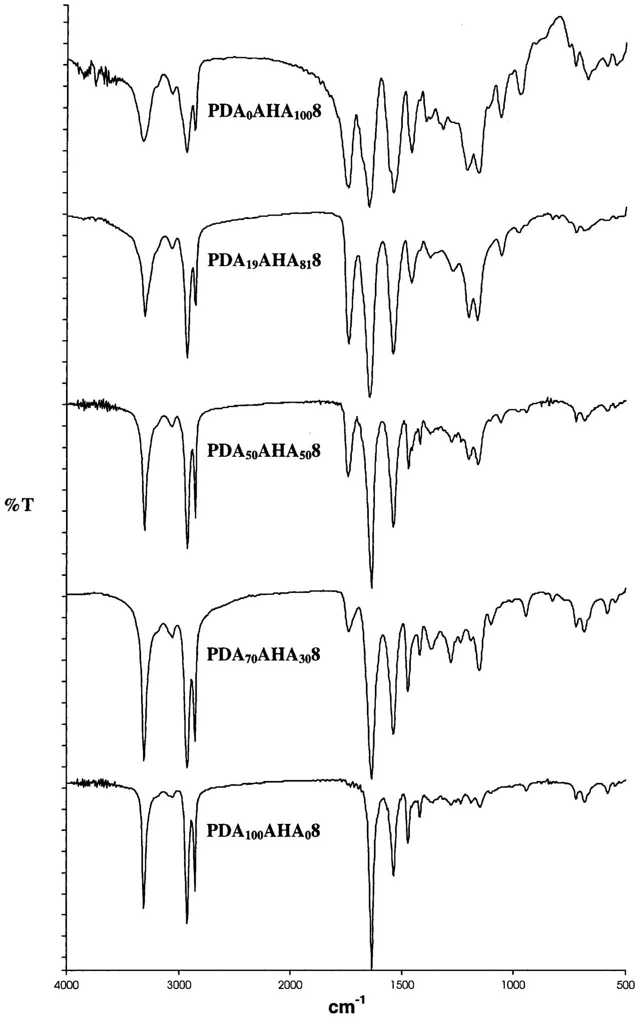

Fig. 2. Infrared spectra of the series of poly(ester amide)s derived from L-alanine.

Table 2
Main absorption bands (cm^{-1}) observed in the infrared spectra of the polymers studied in this work

Polymer	Amide A	Amide B	C=O (ester)	Amide I	Amide II
PDA$_0$GHG$_{100}$8	3310	3073	1739	1646	1548
PDA$_{10}$GHG$_{90}$8	3307	3074	1739	1647	1540
PDA$_{20}$GHG$_{80}$8	3309	3072	1738	1643	1549
PDA$_{50}$GHG$_{50}$8	3305	3071	1738	1634	1539
PDA$_{70}$GHG$_{30}$8	3302	3054	1736	1642	1539
PDA$_0$AHA$_{100}$8	3294	3063	1741	1644	1542
PDA$_{10}$AHA$_{90}$8	3303	3060	1740	1646	1540
PDA$_{20}$AHA$_{80}$8	3305	3062	1740	1645	1540
PDA$_{50}$AHA$_{50}$8	3307	3060	1740	1636	1540
PDA$_{70}$AHA$_{30}$8	3309	3070	1734	1638	1537
Nylon 12 10	3309	3052	–	1639	1536

Table 3
Chemical shifts (in ppm and referred to tetramethylsilane) of main signals observed in the ^{1}H-NMR spectra of the polymers studied in this work

	PDA_xGHG_y8	PDA_xAHA_y8
NH	7.78	7.71
$NHC\mathit{H}(CH_3)CO$	–	4.72
$NHC\mathit{H}_2CO$	4.32	–
CH_2O–	4.29	4.28
$CH_2C\mathit{H}_2NHCO$	3.52	3.52
$C\mathit{H}_2COCH_2CH_2$	2.67	2.66
$C\mathit{H}_2CONHCHRCO$	2.54	2.49
$C\mathit{H}_2CH_2O$	1.76	1.74
CH_3	–	1.53

$[(I_1/4)/(I_1/4 + I_2/4) \times 100]$ and $[(I_1/4)/(I_1/4 + I_2/2) \times 100]$ for the PDA_xGHG_y8 and PDA_xAHA_y8 series, respectively. Note that the experimental values fit well with the theoretical feed ratio (Table 1).

^{13}C-NMR spectra showed the characteristic signals observed for the homopolymers, which are summarized in Table 4. Changes in intensity for a given series were consistent with composition. It is worth noting that, in any case, a splitting of signals could be detected due to the long repeat units. Consequently, analysis of the type of sequences (block or random distribution) could not be undertaken from NMR studies.

Nylon 12 10 and polymers of the PDA_xGHG_y8 series were well-soluble only in strong acids such as formic, dichloroacetic or trifluoroacetic acid. However, PAHA8 was also soluble in chlorinated solvents such as chloroform or dichloromethane. In the same way, a partial solubility was found for polymers of the PDA_xAHA_y8 series depending on the proportion of 1,12-dodecanediamine units. For example, only 20% in weight of $PDA_{50}AHA_{50}8$ solubilizes in chloroform. This is animportant fact, since it demonstrates that the polymer does not correspond to a simple mixture of the Nylon 12 10 and PAHA8 homopolymers. Furthermore, $PDA_{10}AHA_{90}8$ is not wholly soluble in chloroform, thus suggesting a tendency to form block copolymers.

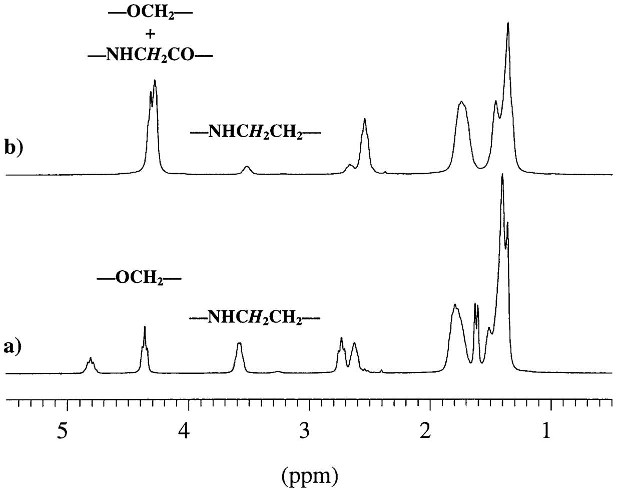

Fig. 3. ^{1}H-NMR spectra of the random poly(ester amide)s $PDA_{20}AHA_{80}8$ (a) and $PDA_{50}GHG_{50}8$ (b). Signals used for composition determination are labeled.

Table 4
Chemical shifts (in ppm and referred to tetramethylsilane) observed in the ^{13}C-NMR spectra of the sequential polymers studied in this work

	Nylon 12 10	PGHG8	PAHA8
CONH	181.45	180.42	179.56
COO	–	172.54	175.04
OCH_2	–	68.50	68.12
$NH\mathit{C}H_2CH_2$	45.13	–	–
$NH\mathit{C}H(CH_3)CO$	–	–	50.40
$NH\mathit{C}H_2CO$	–	43.05	–
$CO\mathit{C}H_2CH_2$	35.61	35.94	35.28
$OCH_2\mathit{C}H_2$	–	28.68	28.24
$COCH_2CH_2\mathit{C}H_2CH_2$	29.87	29.56	28.80
$COCH_2\mathit{C}H_2$	26.97	25.90	26.13
$OCH_2CH_2\mathit{C}H_2$	–	25.36	25.46
CH_3	–	–	17.03

3.3. Thermal behavior

The calorimetric analysis of each polymer consisted of four DSC runs, as shown in Fig. 4 for $PDA_{70}AHA_{30}8$. In the first run, the samples, coming directly from polymerization, were heated at 20°C/min through fusion and left in the melt state for 2 min. Subsequent cooling was performed at 10°C/min to observe crystallization from the melt. A second heating was performed at 20°C/min to check the reproducibility of the transitions and to obtain data for the melt crystallized samples. In order to determine glass transition temperatures, a third heating run at 20°C/min was also performed with samples quenched from the melt state.

In general, the poly(ester amide)s derived from glycine showed a T_g close to 0°C, whereas this temperature increased towards 10–25°C for the alanine derivatives. Chain mobility appeared consequently reduced by the presence of the CH_3 side groups. Heats of fusion were used to evaluate the crystallinity of the polymers (solution- and melt-crystallized samples) taking into account the heats of fusion for 100% crystalline materials. These values (ΔH_f^{eq}) were estimated from the reported [17] group contributions of ester (−2.5 kJ/mol), amide (2.0 kJ/mol), $CH(CH_3)$ (4.7 kJ/mol) and methylene (4.0 kJ/mol). Note that these values are only approximate due in part to the base-line shift observed in some cases before and after melting. The main calorimetric parameters of the studied polymers are summarized in Table 5. Some points can be emphasized:

(a) Melting temperature is higher for Nylon 12 10 than for PGHG8 (Fig. 5). This fact indicates that the substitution of methylene units by ester groups

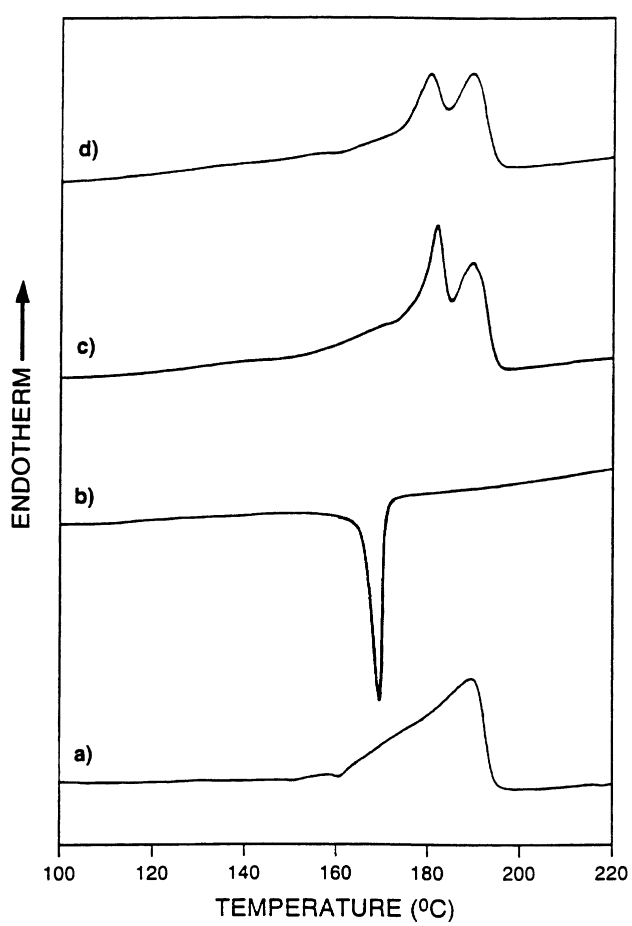

Fig. 4. Sequence of four DSC scans carried out with the $PDA_{70}AHA_{30}8$ sample: (a) heating run at 20°C/min; (b) cooling run at 10°C/min after keeping the sample in the melt state for 2 min; (c) reheating run at 20°C/min; (d) heating run at 20°C/min after quenching the sample from the melt state.

reduces the melting temperature, in agreement with the fusion data of polyethylene and polyesters [18]. Note in this sense that the unit repeat lengths of both polymers are similar, as well as the density of hydrogen bonds.

(b) PAHA8 shows the lowest melting temperature (Fig. 5) due to its CH_3 side groups that hinder chain packing and consequently decrease the heat of fusion. Note also that polymers of the PDA_xAHA_y8 series with x lower than 50 cannot crystallize from the melt state (second and third DSC runs). However, all these samples could be induced to crystallize by a 3 h annealing at 80°C. The deduced crystallinities obtained after this treatment were always slightly higher than those of the initial solution-crystallized samples. For example, a crystallinity of 26% was estimated for PAHA8 obtained directly from polymerization, whereas an increase towards 30% was estimated after annealing a quenched sample.

(c) Melt-crystallized samples show a lower degree of crystallinity than that coming from polymerization.

(d) A double melting peak, as is characteristic of polyamides, is found for polymers with a composition close to both Nylon 12 10 or PGHG8. The ratio between the two peaks is influenced by the crystallization process. Note for example, that the solution-crystallized Nylon 12 10 shows only a peak at 192°C, but a second peak at a lower temperature (184°C) is observed for the melt-crystallized sample. This peak has been associated to a population of less perfect crystals, that is, with a smaller lamellar thickness. So, a double peak implies recrystallization rather than the presence of two different crystal structures.

(e) For a given series, crystallinity decreases as x or y tends to 50.

(f) Melting temperatures are very close to that of the

Table 5
Main calorimetric data of the polymers studied in this work (heating and cooling rates were 20 and 10°C/min, respectively)

Polymer	First run			Second run		Third run			$T_{d,0}$ (°C)	$T_{d,1/2}$ (°C)
	T_f[a] (°C)	ΔH_f (kJ/mol)	χ (%)[b]	T_c (°C)	ΔH_f (kJ/mol)	T_f[a] (°C)	ΔH_f (kJ/mol)	χ (%)[b]		
$PDA_0GHG_{100}8$	138, *147*	28.6	45	108	19.5	*132*, 145	20.1	32	340	417
$PDA_{10}GHG_{90}8$	138, *165*	27.5	42	122	17.9	137, *165*	18.2	28	345	425
$PDA_{20}GHG_{80}8$	138, 179	23.8	36	118	17.9	*138*, 143, *168*	18.1	27	350	436
$PDA_{50}GHG_{50}8$	*135*, *167*, 190	20.5	28	167	17.0	*133*, *167*, 180, *190*	17.8	25	350[c]	472
$PDA_{70}GHG_{30}8$	191	22.7	29	174	17.6	181, *190*	22.0	28	355	484
$PDA_0AHA_{100}8$	90	16.8	26	–	–	–	–	–	320	408
$PDA_{10}AHA_{90}8$	90	12.5	19	–	–	–	–	–	325	423
$PDA_{20}AHA_{80}8$	*86*, 90	11.0	17	–	–	–	–	–	355[c]	433
$PDA_{50}AHA_{50}8$	*123*, *169*, *178*, 186	10.3	14	165	11.2	*126*, *166*, *178*, 188	12.3	17	352[c]	468
$PDA_{70}AHA_{30}8$	191	20.3	26	170	15.3	*182*,190	22.1	28	351[c]	480
Nylon 12 10	192	27.5	33	176	23.5	*184*, 194	24.5	29	400[c]	485

[a] When multiple peaks are observed, the less intenses are indicated by italics.

[b] Crystallinity.

[c] Temperature corresponds to a decomposition lower than 4%.

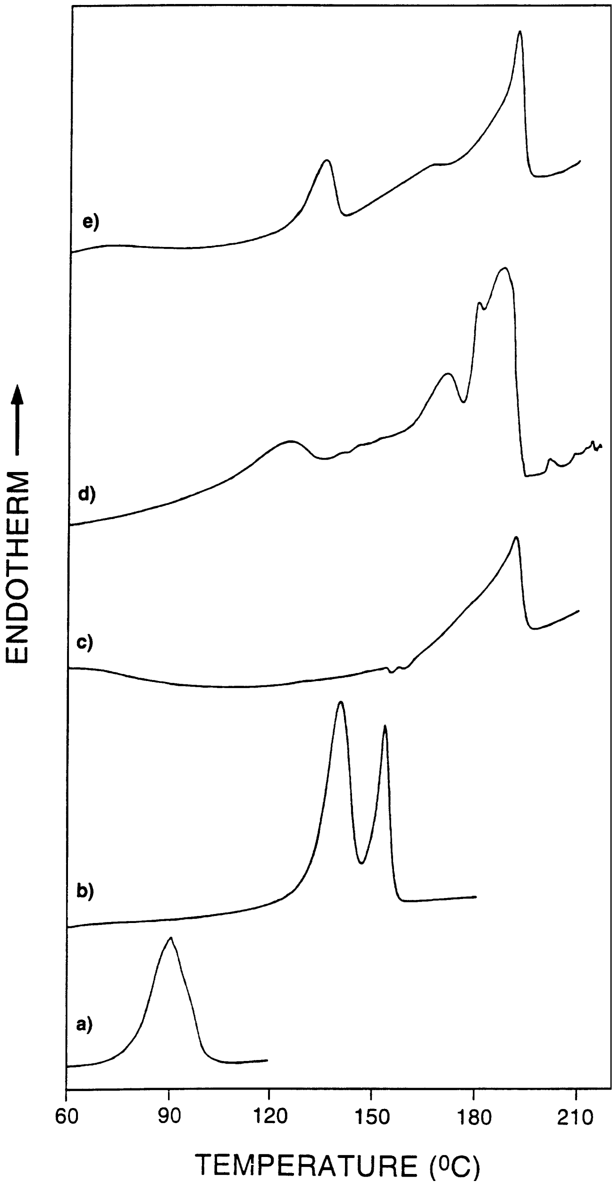

Fig. 5. First heating DSC scans corresponding to: (a) PAHA8; (b) PGHG8; (c) Nylon 12 10; (d) $PDA_{50}AHA_{50}8$ and (e) $PDA_{50}GHG_{50}8$. Heating rates were 20°C/min.

corresponding homopolymers (Nylon 12 10, PGHG8 or PAHA8) when x or y tends to 100. However, the appearance of an additional intermediate and broad fusion peak near 165–170°C for both $PDA_{50}GHG_{50}8$ and $PDA_{50}AHA_{50}8$ samples (Fig. 5) suggesting new chain interactions, probably as a consequence of some statistical distribution of the two different diamines, is very significant.

Thermogravimetric analysis, performed at a heating rate of 10°C/min under a flow of dry nitrogen, demonstrated the thermal stability of all the studied polymers. The values summarized in Table 5 indicate that the temperature at which the weight loss reaches 50% ($T_{d,1/2}$) increases with the proportion of 1,12-dodecanediamine residues (or with the decrease in the amino acid content). Furthermore, no significant differences are found between the equivalent polymers of the two series. The temperature at which decomposition begins is not clear because a slight weight loss (less than 4%) is detected in some polymers at a temperature close to 220°C. Since this decomposition is observed when polymers have a low intrinsic viscosity, we associate it with a process involving the terminal groups, most likely post-condensation. Once the indicated temperature has been reached, the weight remains practically constant until the temperature indicated as $T_{d,0}$ is reached (Table 5). Note that this value is close to 350°C for all polymers, except Nylon 12 10 (400°C), and higher than the melting temperature. The profile of the thermogravimetries (Fig. 6) shows that decomposition takes place in two steps that begin at ca. 350 and 400°C, respectively. The former may be associated to the thermal degradation of units that involve α-amino acids. Note also that the weight loss in the first step decreases as the ratio of 1,12-dodecanediamine residues increases.

3.4. Degradation studies

Both weight loss and changes in the intrinsic viscosity of samples exposed to the hydrolytic degradation medium were evaluated for different exposure times (up to 110 days). Our results indicate that PGHG8 and PAHA8 homopolymers degrade slowly but steadily. Fig. 7 shows a similar drop of intrinsic viscosity versus degradation time for both polymers. Note that although the initial viscosities are different, the profiles are basically the same. Thus, after an initial step (10 days) where the viscosity change is remarkable, the variation goes at a slower rate. However, the weight of the samples remains practically constant (results not shown) during degradation. In fact, viscosity changes correspond to a reduced number of bond cleavages and consequently the degradation products are still insoluble in the medium. When the amide content increases, the degradation rate diminishes, as shown in Fig. 7 for $PDA_{20}AHA_{80}8$. Although this polymer has a low proportion ($x = 20$) of 1,12-dodecanediamine residues, the viscosity profile is less sharp than the related PAHA8 sample. Nylon 12 10 corresponds to the end of both series, and it is known that the hydrolysis of polyamides is very slow and consequently no noticeable change was found in this case.

We used $PDA_{20}GHG_{80}8$ and $PDA_{20}AHA_{80}8$ samples to test the activity of different enzymes on the degradation of the polymers. Basically, both polymers form good films (with a constant thickness) when they are processed and have a comparable 1,12-dodecanediamine content. Papain and proteinase K were selected as enzymes with a proteolytic activity, whereas lipase from *C. cylindracea* was taken as enzyme with an esterase activity. Due to the fact that enzymatic degradation

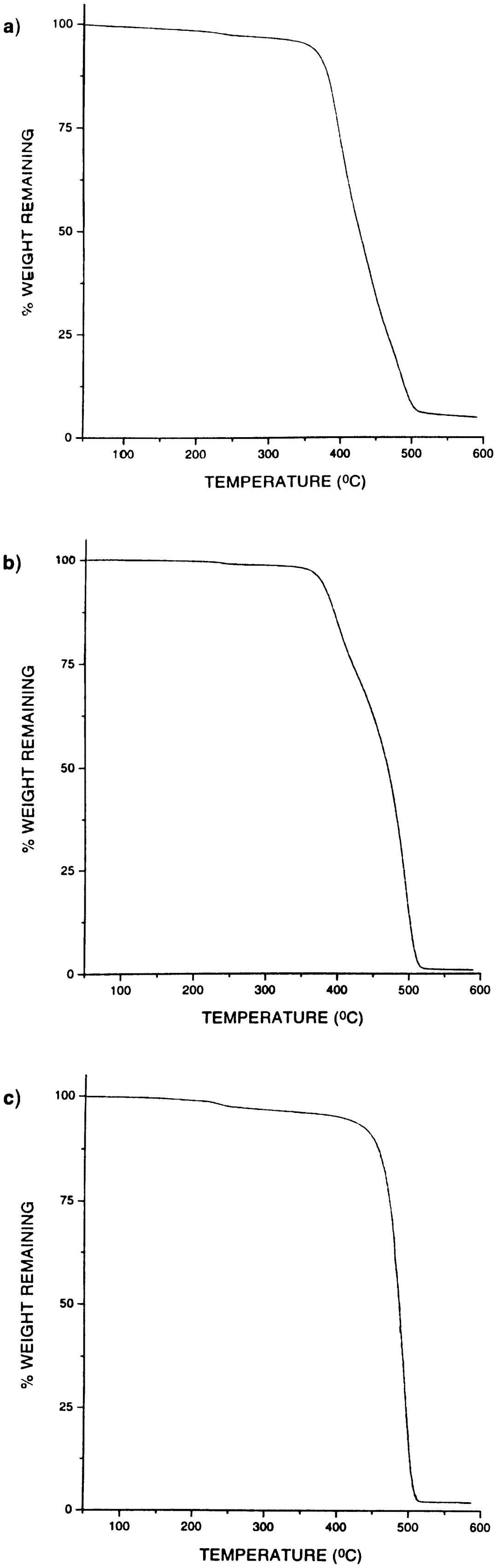

Fig. 6. Representative thermogravimetries of: (a) $PDA_{20}AHA_{80}8$; (b) $PDA_{50}AHA_{50}8$ and (c) Nylon 12 10.

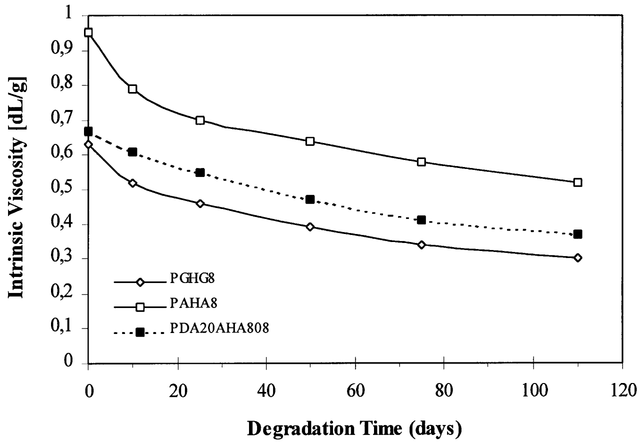

Fig. 7. Changes in intrinsic viscosity (dl/g) during hydrolytic degradation in a pH 7.4 sodium phosphate buffer at 37°C of films corresponding to the sequential poly(ester amide)s PAHA8 (□) and PGHG8 (◇), and the random poly(ester amide) $PDA_{20}AHA_{80}8$ (■).

is a surface process, the viscosity of samples must be practically constant during exposure to the media. Hence, only the weight loss of the remaining samples was evaluated. Results are shown in Fig. 8a and b for glycine and alanine derivatives, respectively. Several observations should be pointed out:

(a) An appreciable degradation rate is only found with proteolytic enzymes. Note that in all cases, a significant weight loss is found after only 15 days of exposure. This result contrasts with the data obtained in the hydrolytic degradation medium.

(b) Alanine derivatives degrade faster than polymers based on glycine. The main explanations for this behavior can be attributed to differences in crystallinity of samples and above all to the different activity of enzymes towards the two amino acids. Thus, papain is the most efficient enzyme for degrading the glycine derivative, whereas proteinase K is the most effective for $PDA_{20}AHA_{80}8$. In this sense, note that practically 70% of this sample solubilizes after only 15 days of exposure.

The degradation process of both films was also monitored by scanning electron microscopy (Fig. 9), since the superficial texture during degradation with proteolytic enzymes changed significantly. The rugous aspect of the surface and the appearance of crevasses and holes were the main features of the $PDA_{20}AHA_{80}8$ sample after 15 days of exposure to proteinase K. Furthermore, only small fragments could be recovered since most of the sample was solubilized. On the contrary, the whole plates of $PDA_{20}GHG_{80}8$ were recovered after 15 days of exposure to papain; only some fissures and pores were detected on the surface of the films.

Enzymatic degradability of the different polymers was compared by using powder samples due to the difficulty

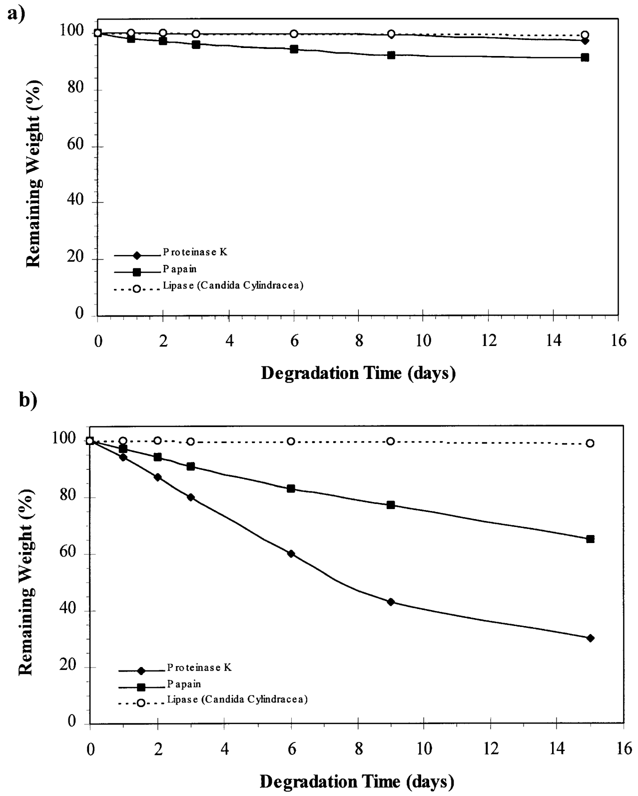

Fig. 8. Plot of the remaining weight (%) versus degradation time (days) in different enzymatic media for $PDA_{20}GHG_{80}8$ (a) and $PDA_{20}AHA_{80}8$ (b) films.

of preparing films with similar characteristics from polymers of different composition. Thus, processing into films became more difficult for samples with higher 1,12-dodecanediamine content due to the decrease on molecular weight and the increase in the melting temperature. Moreover, degradation was studied in the same papain enzymatic medium, since it was reasonably effective for both alanine and glycine derivatives, as explained above. As the exposed surface of powder samples increased, a higher degradation rate was found in these experiments. The results, shown in Fig. 10, clearly demonstrate that enzymatic degradability strongly depends on composition. Thus, both series degrade faster when x (ratio of 1,12-dodecanediamine residues) decreases, which corresponds to the increase of the amino acid content. Note that no significant degradation was found for $x = 100$ (Nylon 12 10). In the same way, it can also be concluded that polymers of the alanine series degrade faster than the equivalent ones of the PDA_xGHG_y8 series. It is also worth noting that PAHA8 degrades completely after only 3 days of exposure to enzymatic media.

4. Conclusions

The results presented in this paper can be summarized as follows:

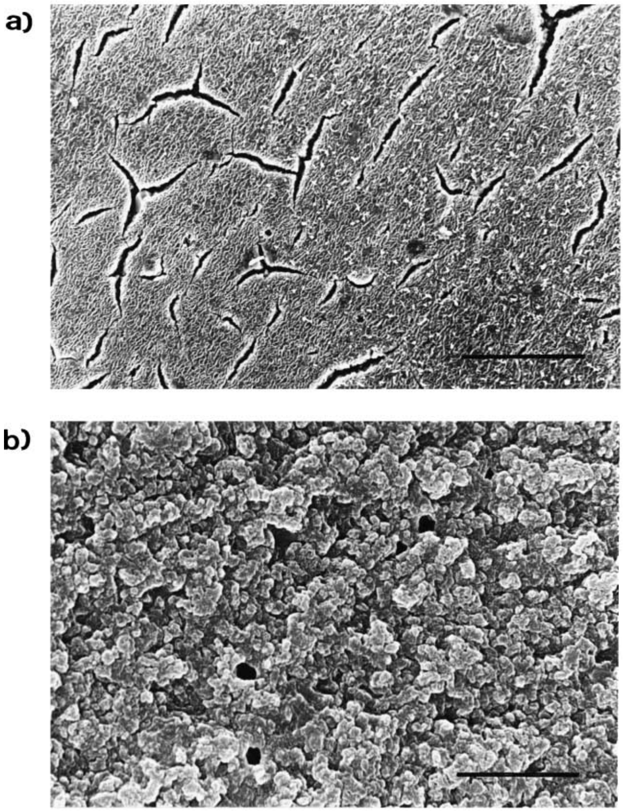

Fig. 9. Scanning electron micrographs of $PDA_{20}GHG_{80}8$ (a) and $PDA_{20}AHA_{80}8$ (b) films after 15 days of exposure in a papain and proteinase K medium, respectively. Scale bars: 10 μm for (a) and 100 μm for (b).

1. Two series of poly(ester amide)s with variable amide/ester ratio and derived from glycine or L-alanine have been synthesized by interfacial polymerization with high yields (60–75%). Molecular weights were higher for alanine derivatives and for polymers with lower amide/ester ratio.
2. Infrared spectra indicate that hydrogen bonds could be well established in each series, in spite of the two kinds of diamines ($NH_2(CH_2)_{12}NH_2$ and $NH_2CHRCOO(CH_2)_6O$-$COCHRNH_2$) involved.
3. ^{1}H-NMR spectra always show a good agreement between polymer composition and monomer feed ratio.
4. Melting temperature increases as the amide/ester ratio does. Polymers derived from alanine have lower melting temperatures and crystallinities than those derived from glycine due to the worse chain packing caused by the CH_3 side groups. Moreover, glass transition temperature slightly increases for polymers with methyl side groups.
5. Calorimetric scans of poly(ester amide)s with equal ratio of the two kinds of diamines are rather complex. Melting peaks associated to homopolymers (block sequence), together with new peaks indicative of a statistical distribution are found.

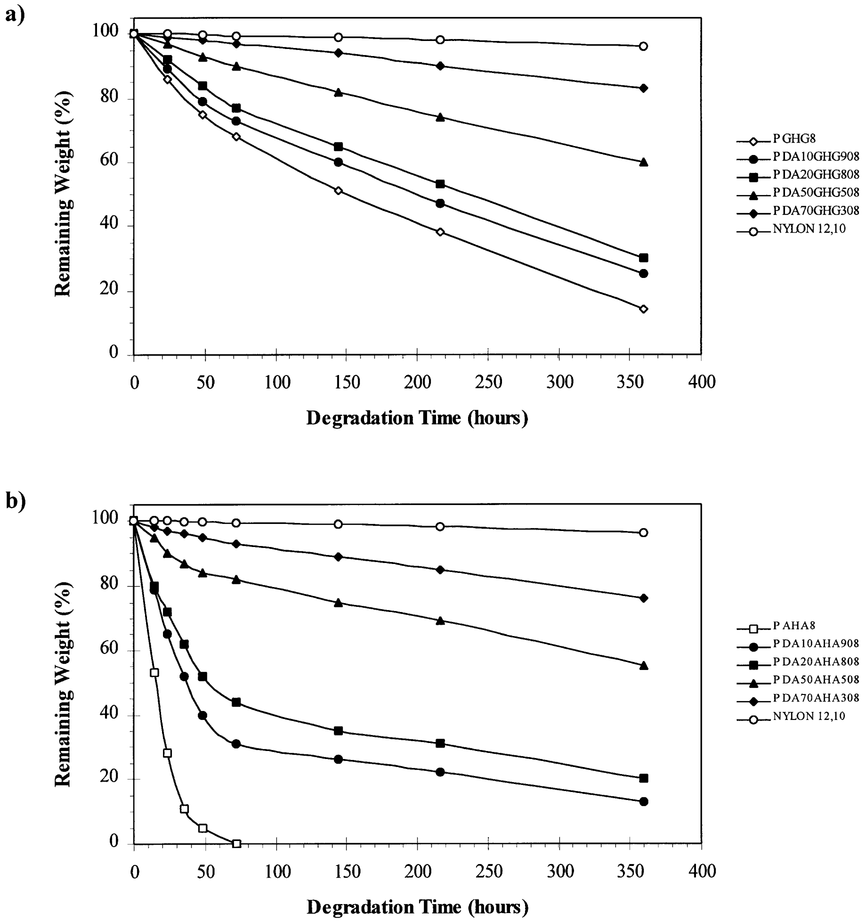

Fig. 10. Plot of remaining weight (%) versus degradation time (h) in a papain enzymatic medium for powder samples of PDA$_x$GHG$_y$8 (a) and PDA$_x$AHA$_y$8 (b) series.

6. Thermogravimetric analyses indicate that all polymers have a good thermal stability, since decomposition temperatures are always higher than melting temperatures, and consequently their melt processing is not hindered. Thermal stability increases as amino acid content decreases.
7. The new poly(ester amide)s are degraded slowly but steadily under hydrolytic conditions simulating physiological media.
8. Proteolytic enzymes such as papain and proteinase K degrade both series of poly(ester amide)s. The degradation rate strongly depends on the proportion of amino acid and its nature, being the sequential poly(ester amide) derived from alanine (PAHA8) the most degradable.

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