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Correlation of hydrolytic degradation with structure for copolyesters produced from glycolic and adipic acids

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Abstract Copolyesters based on glycolic acid (G) combined with adipic acid (A) and ethylene glycol (E) were synthesized in different percentage of molar ratios (A: 100–50% and G: 100%) and their hydrolytic degradation was studied and correlated with their structures. According to the DSC, the production of polyesters leads to the formation of copolyesters and not to mixtures of homopolyesters. The crystallites in the copolyesters mainly consist of continuous sequences of ethylene adipate structural units. The hydrolytic degradation of the polyesters was followed by their weight loss during hydrolysis and by the FTIR spectra of the initial polyesters compared with that of the degraded polyesters at equilibrium. The region between 1142 and 800 cm^{-1} can be utilized to evaluate the extent of degradation of polyesters after their hydrolysis. The absorption bands at 1142, 1077 and 850 cm^{-1} due to the amorphous region decrease after hydrolysis, whereas those at 972, 901 and 806 cm^{-1} due to the crystalline region increase. The experimental data of the hydrolytic degradation were fitted with exponential rise to maximum type functions using two-parameter model, which describes very well mainly the initial part of the degradation, and four-parameter model (containing two exponential terms), which is appropriate for fitting the hydrolytic degradation on the entire time period (including the equilibrium). Furthermore, the kinetics of the hydrolytic degradation of the polyesters for the initial time period based on both models results to similar values of the rate constant, k. The synthesized copolyesters of glycolic acid combined with adipic acid and ethylene glycol are soluble in many common organic solvents opposite to PGA, leading to modified biodegradable polyesters and therefore they can be easily processed.

1 Introduction

Polyesters are one of the most significant class of polymers, used both as thermoplastics (such as polyethylene terephthalate, PET) and as thermosets (unsaturated polyesters, UP). They are produced for more than 50 years in industrial scale by direct condensation of mixtures of diacids and/or anhydrides (such as adipic acid, maleic acid, terephthalic acid, phthalic anhydride etc.) with diols (such as ethylene glycol, propylene glycol etc.), using the azeotropic distillation method [1–3]. Among the polyesters, the category of degradable synthetic aliphatic polyesters is very important, since they were adopted in surgery and in pharmacology 30 years ago and remain among the most widely used degradable synthetic polymers [4, 5].

Poly(lactic acid) (PLA) and poly(glycolic acid) (PGA) belong to the family of aliphatic polyesters commonly made from α-hydroxy acids. They have received a large amount of attention in the field of medical applications because they degrade in the body by simple hydrolysis of the ester backbone to non-harmful and nontoxic compounds [6–9]. They are used in various biomedical, pharmaceutical and technical applications including packaging materials, implants, scaffolds for tissue engineering, resorbable sutures and drug delivery devices [5, 10, 11]. The application of these materials has extended in bone fixation devices (plates, screws, pins, nails etc.) [5, 10, 12].

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PGA is a highly crystalline polymer (45–55% crystallinity) and therefore exhibits a high tensile modulus with very low solubility in organic solvents. The glass transition temperature of the polymer ranges from 35 to 40°C and the melting point can be greater than 200°C. In spite of its low solubility, this polymer has been fabricated into a variety of forms and structures. Extrusion, injection and compression molding as well as particulate leaching and solvent casting, are some of the techniques used to develop polyglycolide-based structures for biomedical applications. Due to its excellent fiber forming ability, PGA was initially investigated for developing resorbable sutures [11, 13]. Apart from PGA and PLA homopolymers, extensive research has been performed in developing a full range of poly(lactide-co-glycolide) polymers (PLGA). Different ratios of poly(lactide-co-glycolides) have been commercially developed and are being investigated for a wide range of biomedical applications. The major advantages of these copolymers are that due to the different crystallinity and hydrophobicity of the lactic and glycolic acid components, their application permits the preparation of ‘custom made’ carriers according to the specific needs [13–15].

The degradable polymers are insoluble in water but they can degrade by hydrolytic attack of the ester bond [4, 5, 13]. The degradation of the material due to its dissolution is accompanied by mass loss, reduction of the molecular weight, changes in the implant’s structural configuration, changes in mechanical properties such as reduction in strength and stiffness etc. [12, 16]. Water access to the ester bond is governed by hydrophobicity of the monomers, the crystallinity of the sample and the bulk sample dimensions. Because water rapidly plasticizes these polymers, degradation proceeds through the entire mass simultaneously, often ultimately leading to mechanical distortion, cracking, pitting and fissure of the material in uncontrolled ways [4]. There have been a number of reports that provide strong indications that the degradation kinetics cannot only be described by random chain scissions, but that the end groups may play an important role in the process. The degradation process is influenced by many factors, including water accessibility, molecular mobility, etc. [5, 16–19]. The mechanical properties and the degradation of the polymers are affected by the combined effects of the crystallinity, the molecular weight (M_w), the glass transition temperature (T_g), and the monomer hydrophobicity [4, 5, 16–18].

On the other hand, aliphatic polyester made from diacids, such as adipic acid [20] and sebacic acid [21] and diols is expected to be one of the most economically competitive biodegradable polymers and it can be degraded and assimilated completely by microorganisms [20]. Thermoset elastomers such as poly(glycerol sebacate) (PGS) have shown to primarily degrade by surface erosion, retaining their structural integrity and form stability during degradation in vivo. Therefore, biomaterials based on these elastomers hold great promise in soft tissue applications that require small features, such as gecko-inspired surgical adhesives, microfabricated scaffolds, cardiovascular tissue engineering applications and small diameter nerve grafts [22].

The aim of this work is to synthesize copolyesters based on glycolic acid combined with adipic acid and ethylene glycol in different molar ratios. Since PGA is insoluble in many common organic solvents and thus it cannot be easily processed by thermal and solvent-based methods, such copolymers are expected to have improved solubility and therefore convenient processability. Moreover, their hydrolytic degradation would be altered compared to that of PGA, leading to modified biodegradable polyesters.

2 Experimental

Glycolic acid (p.a. Fluka), adipic acid (p.a. Merck) and ethylene glycol (p.a. Merck) were used as monomers. The polyesterification was carried out in a 0.5 l vapor reflux reactor by the azeotropic distillation method according to a proper procedure previously described in detail [3, 23, 24]. Since glycols are generally volatile and they co-distill with the water, the initial amount of glycol was in a molar excess of 10% over the stoichiometry (i.e., the molar ratio of ethylene glycol to the adipic acid was 1.10:1). Toluene (p.a. Merck) was used as the azeotropic agent in a ratio of 3.5 wt% over the total weight of the monomers. The polyesters were produced by prolonged heating of the reaction mixture at temperatures up to 200°C. The acid number (A.N.) of the polyesters, dissolved in toluene/methanol (1/2 v/v), was determined by titration with 0.5 N KOH alcoholic solution, indicating the progress of the polyesterification. The molecular weight of the polyesters, M_n, was estimated from the A.N. using the equation [3, 23, 24]:

$$\overline{M}_n = \frac{56000}{A.N.} \tag{1}$$

The hydrolytic degradation of every polyester was studied by using an amount of 1.8 g of polyester as specimen in the form of tablet (diameter: 20 mm, height: about 1 mm), in deionized water at 50°C. The proportion of the initial weight of polyester to water volume was equal to 1 g:150 ml and its weight loss was determined by weighting the tablet at certain time intervals.

The two homopolyesters of poly(ethylene adipate) and of poly(glycolic acid) were produced by polyesterification of ethylene glycol with adipic acid and glycolic acid, respectively. Copolyesters were produced by polyesterification of ethylene glycol, adipic acid and glycolic acid, in different molar ratios. Mixtures of the homopolyesters poly(ethylene adipate) and poly(glycolic acid) having the same molar ratios as those of the copolyesters were produced by grinding, mixing the appropriate amounts of the homopolymers at room temperature and homogenizing the mixtures.

The polyesters were studied by Differential Scanning Calorimetry (DSC) under nitrogen flow, with a Netsch DSC 200 apparatus in the temperature range of 0°C up to 250°C, with a heating rate of 10°C/min. Furthermore, the polyesters were characterized by Fourier Transform Infrared Spectroscopy (FTIR) with a Perkin Elmer GX, in the form of tablets with KBr.

3 Results and discussion

Table 1 presents the monomers used for the synthesis of homopolyesters and copolyesters and their characteristics. At room temperature, the polyesters produced are wax-like solids, except them of A60G40, A50G50 and A30G70, which resemble to viscous liquids. The acid number (A.N.) of the polyesters is below 40, as is valid for commercial polyesters [3, 23, 24] and their molecular weight ($\overline{M_n}$) is between 1500 and 2500. The mean number degree of polymerization of polyesters is determined as:

$$\overline{X_n} = \frac{\overline{M_n}}{m_o} \tag{2}$$

where m_o is the molecular weight of the mean structural unit. For the homopolyester A100, the corresponding m_o is equal to $m_{o,A} = 86$ (ethylene adipate structural unit) and for the homopolyester G100 is equal to $m_{o,G} = 58$ (glycolate structural unit). For the copolyesters, the corresponding $m_{o,A}$ and $m_{o,G}$ are determined supposing that the ratio between both structural units is equal to the feed ratio of the monomers.

$$\overline{X_{n,A}} = \frac{f_A \cdot \overline{M_n}}{m_{o,A}} \tag{3}$$

and

$$\overline{X_{n,G}} = \frac{f_G \cdot \overline{M_n}}{m_{o,G}} \tag{4}$$

where $\overline{X_{n,A}}$, $\overline{X_{n,G}}$ is the mean number degree of polymerization of ethylene adipate and glycolate, respectively and f_A, f_G is the molar feed ratio of adipic acid and glycolic acid, respectively, i.e., $f_A + f_G = 1$. The values of $\overline{X_{n,A}}$, $\overline{X_{n,G}}$ of the polyesters are presented in Table 1.

The results of the DSC scans are shown in Figs. 1, 2, and 3 and are summarized in Table 2. The latter contains separately for ethylene adipate and glycolate units their characteristic data, i.e., the melting temperature (T_m), the heat of fusion determined by DSC ($\Delta H_{DSC,A}$ and $\Delta H_{DSC,G}$) and the expected heat of fusion ($\Delta H_{expect,A}$ and $\Delta H_{expect,G}$)

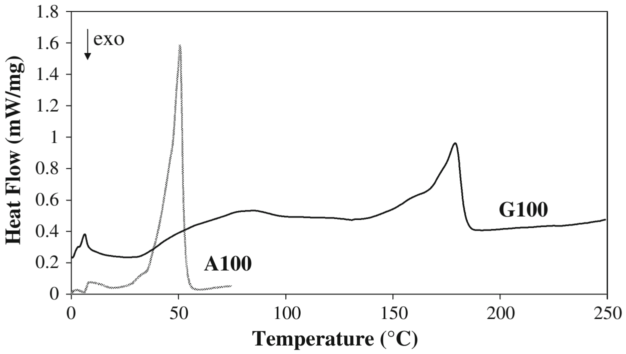


Fig. 1 DSC scans for the initial polyesters A100 and G100

Table 1 Monomers used for the synthesis of polyesters, their acid number (A.N.), molecular weight (M_n) and mean number degree of polymerization

Code of polyesters	Monomers (mol)			Acid number A.N.	Molecular weight $\overline{M_n}$	Mean number degree of polymerization of:	
	Adipic acid (A)	Glycolic acid (G)	Ethylene glycol $Et(OH)_2$			Ethylene adipate $\overline{X_{n,A}}$	Glycolate $\overline{X_{n,G}}$
A100	100	–	110	26	2154 → 2150	25.05	–
A90G10	90	10	99	27	2074 → 2100	21.70	3.57
A80G20	80	20	88	37	1514 → 1500	14.08	5.22
A70G30	70	30	77	24	2333 → 2350	19.00	12.06
A60G40	60	40	66	23	2435 → 2450	17.00	16.80
A50G50	50	50	55	29	1930 → 1950	11.22	16.64
A30G70	30	70	33	25	2240 → 2250	7.81	27.03
A10G90	10	90	11	37	1515 → 1500	1.76	23.51
G100	–	100	–	*	*	–	*

* Polyester G100 is insoluble in solvents (e.g., toluene/methanol)

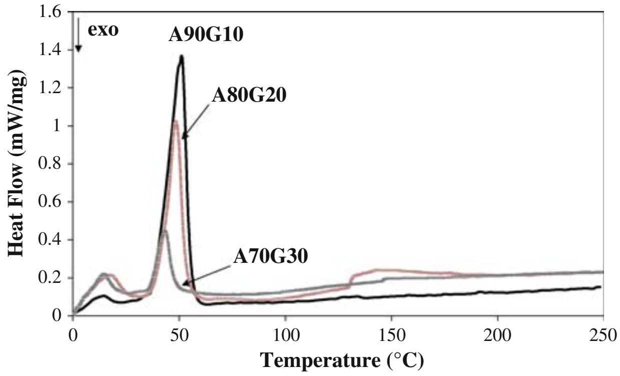


Fig. 2 DSC scans for the initial polyesters A90G10, A80G20 and A70G30

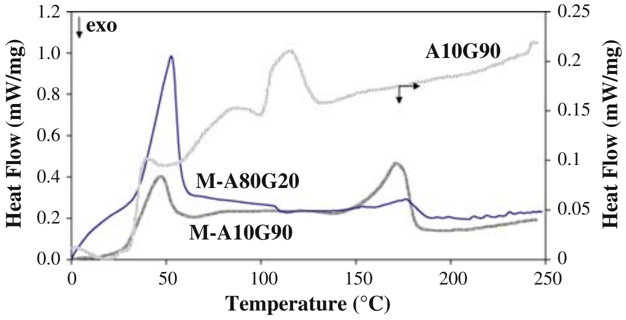


Fig. 3 DSC curves of the polyester A10G90 and the mixtures M-A80G20 and M-A10G90 of homopolyesters A100 and G100

which was calculated for every copolyester or mixture from the equations:

$$\Delta H_{expect,A} = f_A \cdot \Delta H_{DSC,A100} \quad (5)$$

$$\Delta H_{expect,G} = f_G \cdot \Delta H_{DSC,G100} \quad (6)$$

where $\Delta H_{DSC,A100}$, $\Delta H_{DSC,G100}$ is the heat of fusion of poly(ethylene adipate) or poly(glycolic acid) determined by DSC, respectively.

According to Fig. 1, the poly(ethylene adipate) (A100) and the poly(glycolic acid) (G100) show a distinct endothermic peak at about 50°C and at 170°C, respectively, due to the melting of their crystallites. The melting temperature (T_m) of polyester A100 is in accordance to the values given in the literature, varying between 47 and 65°C, whereas that of G100 is somewhat lower than the values given in the literature, varying between 180 and 233°C depending on the molecular weight [5, 25, 26]. The latter is difficult to be determined due to the insolubility of PGA to many common organic solvents [4]. In most polyesters, multiple melting behaviors are observed and two or more endothermic peaks appear, which make it difficult to determine the heat of fusion by DSC [27]. Furthermore, the glass transition temperature (T_g) of polyesters is difficult to be determined by DSC. The T_g of G100 is about 35°C, which agrees with the literature referring to the T_g of poly(glycolic acid) in the range of 35–40°C [13], whereas for poly(ethylene adipate) the value of −46°C has been reported [5, 25]. The lower values of T_m and T_g for A100 compared to G100 are due to the higher flexibility of the ethylene adipate structural unit compared to that of the glycolate structural unit. The flexibility increases by increasing the number of inserted methylene groups between the ester groups [28]. Therefore, poly(ethylene adipate) containing ethylene adipate structural units with six and with two methylene units between the ester groups (originating from adipic acid and ethylene glycol, respectively) is more flexible compared to poly(glycolic acid) containing glycolate structural unit with only one methylene unit between the ester groups.

According to Fig. 2 and Table 2, the copolyesters A90G10, A80G20, A70G30 and A60G40 exhibit an endothermic peak between 35 and 50°C, attributed to the melting of crystallites. The values of T_m of the copolyesters are nearer to that of A100 ($T_{m,A} = 50.6$°C) than that of G100 ($T_{m,G} = 170.2$°C). Consequently, the crystallites in the copolyesters mainly consist of continuous sequences of ethylene adipate structural units. Furthermore, the absence of the corresponding peak of poly(glycolate) indicates that the glycolate structural units were incorporated in the copolymer backbone, without forming continuous sequences. By decreasing the molar feed ratio of adipic acid in the composition of the copolyester, the $T_{m,A}$ and the $\Delta H_{DSC,A}$ decrease. The copolyesters A50G50 and A30G70 do not show any endothermic peaks, whereas the A10G90 shows an endothermic peak at 115.2°C, which is nearer that of G100.

By comparing the values of $\Delta H_{DSC,A}$ and $\Delta H_{expect,A}$ presented in Table 2, it can be seen that the heat of fusion determined by DSC for the copolyester A90G10 is very close to the expected value, while by decreasing the molar feed ratio of adipic acid the divergence between the expected and determined values is significant. Specifically, the difference is significant for A80G20, more intense for A70G30 and very abrupt for A60G40, A50G50 and A30G70. The polyester A10G90, containing high molar ratio of glycolic acid exhibit an endothermic peak around 115°C, which cannot be attributed to neither poly(glycolic acid), with $T_m = 170$°C, nor poly(ethylene adipate), with $T_m = 50$°C. This means that in this case, ethylene adipate structural units are incorporated into the poly(glycolic acid) crystallites, leading to the formation of copolymer. The endothermic peak due to ethylene adipate units ($\Delta H_{DSC,A}$), i.e., the crystallinity, decreases by decreasing the molar feed ratio of adipic acid.

Figure 3 shows the DSC curves of the polyester A10G90 and the mixtures M-A80G20 and M-A10G90. The mixtures exhibit two endothermic peaks, the first at about

Table 2 Results of the DSC analysis of homopolyesters, copolyesters and mixtures of homopolyesters of poly(ethylene-adipate) and poly(glycolic acid)

Code of polyesters	Endothermic peaks due to					
	Ethylene adipate units			Glycolate units		
	$T_{m,A}$ (°C)	$\Delta H_{DSC,A}$ (J/g)	$\Delta H_{expect,A}$ (J/g)	$T_{m,G}$ (°C)	$\Delta H_{DSC,G}$ (J/g)	$\Delta H_{expect,G}$ (J/g)
Homopolyesters and copolyesters						
A100	50.6	74.3	74.3	–	–	–
A90G10	50.3	66.4	66.7	–	–	3.7
A80G20	48.3	44.6	59.4	–	–	7.5
A70G30	43.3	15.0	52.0	–	–	11.2
A60G40	35.7	0.7	44.6	–	–	15.0
A50G50	–	–	37.2	–	–	18.7
A30G70	–	–	22.3	–	–	26.2
A10G90	–	–	7.4	115.2	6.1	33.7
G100	–	–	–	170.2	37.4	37.4
Mixtures of homopolyesters						
M-A90G10	50.7	66.5	66.7	142.6	3.0	3.7
M-A80G20	52.7	53.1	59.4	176.5	7.0	7.5
M-A70G30	50.7	50.3	52.0	180.7	5.8	11.2
M-A60G40	50.2	42.0	44.6	136.8	11.0	15.0
M-A50G50	48.1	34.8	37.2	166.3	18.0	18.7
M-A30G70	43.6	19.2	22.3	173.7	26.0	26.2
M-A10G90	47.0	6.3	7.4	171.1	33.0	33.7

T_m melting temperature, ΔH_{DSC} heat of fusion determined by DSC, ΔH_{expect} expected heat of fusion

50°C due to the poly(ethylene adipate) macromolecules and the second at temperatures between 140 and 180°C due to poly(glycolic acid) macromolecules. The second peak is also observed even in the mixtures with low molar ratio of poly(glycolic acid), e.g., in the mixture M-A90G10, contrarily to the copolyesters. Furthermore, for both the endothermic peaks of the mixtures, the values of the heat of fusion determined by DSC (ΔH_{DSC}) are very close to those theoretically expected (ΔH_{expec}), indicating that the two homopolymers in the mixtures behave independently, i.e., they do not interact. All these facts strongly indicate that the production of polyesters with adipic acid and glycolic acid leads to the formation of copolymers and not to a mixture of homopolymers.

The FTIR spectra of the polyesters are shown in Figs. 4, 5, and 6. Figure 4 shows the FTIR spectra of the initial polyesters A100, G100 and A90G10. The polyester A100 exhibit the absorption bands of the corresponding stretching vibrations : –OH from glycolic acid and/or ethylene glycol (at 3400–3200 cm^{-1}), –CH_2– (at 2980–2850 cm^{-1}) and >C=O from ester groups (at 1750–1735 cm^{-1}) [29–31]. There is also an absorption band of –CH_2– bending vibrations around 1460 cm^{-1} and a less intense peak of the carboxylic –OH bending vibrations at 1415 cm^{-1}. Around 1385 cm^{-1} appears the peak of –OH in plane bending vibrations due to glycolic acid (polyester G100) or ethylene glycol (polyester A100). Two peaks arising from C–O stretching vibrations of carboxyl groups appear at 1275 and 1255 cm^{-1} [29]. Moreover, two peaks at 1142 and 1077 cm^{-1} can be assigned to C–O stretching modes in ester and oxymethylene groups, respectively [31]. Finally, the absorption bands at 972, 901, 850, 806, 745 and 735 cm^{-1} are attributed to –C–H rocking vibrations [29–31]. The FTIR spectra of the polyester G100 is slightly different than that of A100. Specifically, the absorption band at 1460 cm^{-1} due to –CH_2– bending vibrations is not present in the FTIR spectrum of G100, whereas that at 1415 cm^{-1} due to carboxylic –OH bending vibrations is very intense. Moreover, in the fingerprint region (1300–900 cm^{-1}) of FTIR spectrum of G100, the absorption bands at 1275, 1255 cm^{-1} due to C–O stretching vibrations of carboxyl groups [29] are exhibited as one broad peak at 1220 cm^{-1} and those at 1142, 1077 cm^{-1} due to stretching vibrations of the ester groups [31] are exhibited as one broad peak at 1090 cm^{-1}. The FTIR spectrum of the copolyester A90G10 is similar to that of A100.

Figures 5 and 6 show the FTIR spectra of the initial and the hydrolytically degraded polyesters A100 and G100, respectively. According to the literature [31], the four bands at 850, 753, 713 and 560 cm^{-1} are associated with

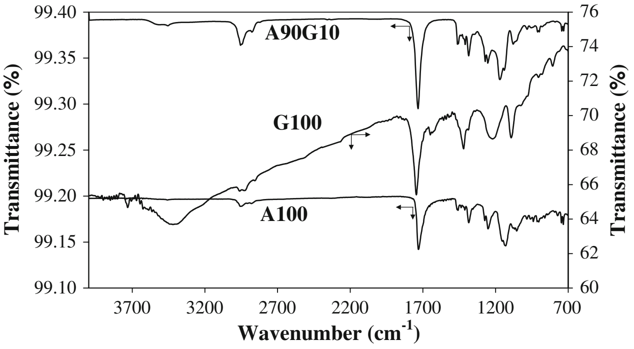


Fig. 4 FTIR spectra of the initial polyesters A100, G100 and A90G10

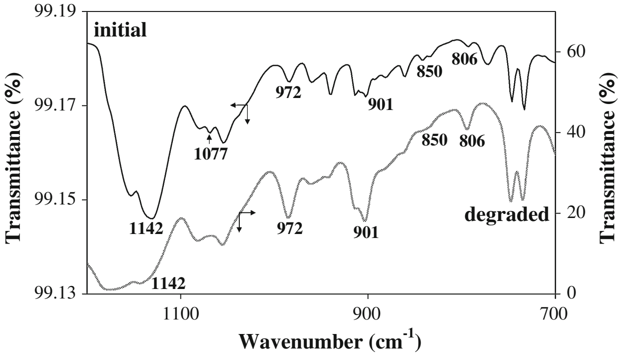


Fig. 5 FTIR spectra of the initial and degraded A100 polyester

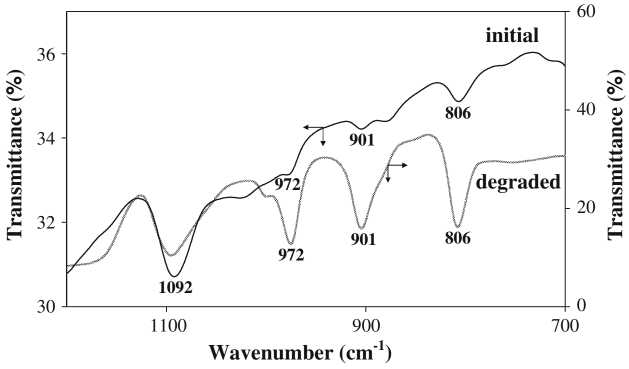


Fig. 6 FTIR spectra of the initial and degraded G100 polyester

the amorphous regions of the poly(glycolic acid) and could be used to assess the extends of the hydrolysis. Peaks associated with the crystalline phase included those at 972, 901, 806, 627 and 590 cm^{-1}. As mentioned above, the two broad intense peaks at 1142 and 1077 cm^{-1} can be assigned to C–O stretching modes in the ester and oxymethylene groups, respectively and are associated mainly with ester and oxymethylene groups originating in the amorphous domains. Hydrolysis could cause both of these C–O stretching modes to substantially decrease in intensity. Therefore, the region between 1142 and 800 cm^{-1} can be utilized to evaluate the extent of degradation of polyesters after their hydrolysis. Concerning the initial polyester A100 and the corresponding degraded (Fig. 5), the absorption bands at 1142, 1077 and 850 cm^{-1} due to the amorphous region decrease after hydrolysis, whereas those at 972, 901 and 806 cm^{-1} due to the crystalline region increase. It is known that the amorphous region is preferably attacked during hydrolysis [32]. For the initial polyester G100 and the corresponding degraded (Fig. 6), the absorption band at 1090 cm^{-1} due to the amorphous region decreases after hydrolysis, whereas the absorption bands at 972, 901 and 806 cm^{-1} due to the crystalline region increase.

Figure 7 shows the hydrolytic degradation expressed as W ($W = (W_o - W_t)/W_o$, where W_o: initial weight of sample and W_t: weight of sample at time t) of the polyesters A100, A80G20, A30G70 and G100 versus time. The hydrolytic degradation of the polyesters increases and after a certain time (equilibrium time, t_{eq}) reaches its maximum value of $W_m = (W_o - W_{eq})/W_o$, where W_{eq}: weight of sample at equilibrium time. Poly(ethylene adipate) (i.e., polyester A100) shows lower degradation, W_m, than poly(glycolic acid) (i.e., polyester G100). The copolyester A80G20, which contains more ethylene adipate units, shows lower degradation, W_m, than the copolyester A30G70 containing more glycolate units.

The experimental data can be fitted with exponential rise to maximum type functions. As a first approximation, a simple model with two parameters was used for the fitting:

$$\frac{W_o - W_t}{W_o} = a \cdot (1 - \exp(-b \cdot t)) \qquad (7)$$

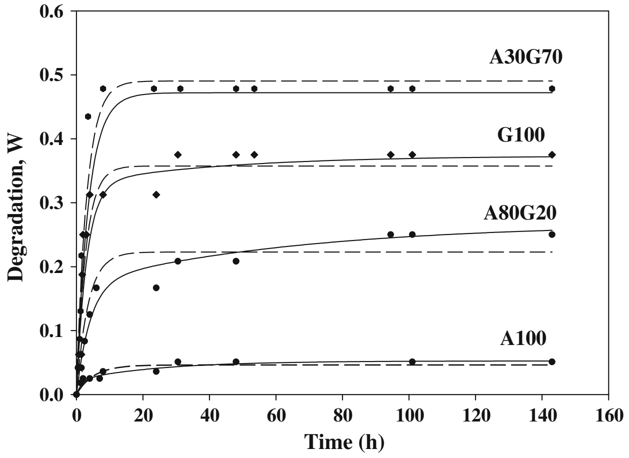


Fig. 7 Hydrolytic degradation W, of the polyesters A100, A80G20, G100 and A30G70 versus time [$W = (W_o - W_t)/W_o$, where W_o initial weight of sample and W_t weight of sample at time *t*] Experimental data (*points*) and their fitting with two-(*dotted lines*) or four-parameter (*continuous lines*) models

where: a = pro-exponential parameter; b = empirical parameter for the fitting of the experimental data (h^{-1}); t = time (h). From Eq. 7, when time $t \to \infty$, then $\exp(-bt) \to 0$, thus the maximum degradation according to the model, W_a, corresponds to the parameter a. In Fig. 7 the two-parameter model is shown with the dotted lines.

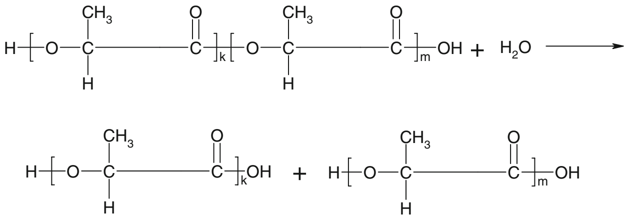
As a second approximation, a more complex, four-parameter model was used for the fitting:

$$\frac{W_o - W_t}{W_o} = a \cdot (1 - \exp(-b \cdot t)) + c \cdot (1 - \exp(-d \cdot t)) \tag{8}$$

where: a, c = pro-exponential parameters; b and d = empirical parameters for the fitting of the experimental data (h^{-1}). From Eq. 8, when time $t \to \infty$, then $\exp(-bt) \to 0$ and $\exp(-dt) \to 0$, thus the maximum degradation according to the model, W_{a+c}, corresponds to the sum of the parameters a and c. In Fig. 7 the four-parameter model is shown with the continuous lines.

The experimental data of the hydrolytic degradation and the parameters of Eqs. 7 and 8 for the polyesters are summarized in Table 3. Polyester A100 compared to the other polyesters shows the lowest value of W_m. The latter increases by increasing the percentage molar feed ratio of glycolic acid from 10% (A90G10) up to 50% (A50G50), whereas above 50% up to 90% (A10G90) the value of W_m decreases. The relative variation between the experimental maximum degradation W_m (Table 3, column 3) and the maximum degradation according to the two-parameter model, W_a (Table 3, column 4), expressed as $[(W_m - W_a)/W_m]*100$ (Table 3, column 6), is up to 12% (in absolute value). Similarly, the relative variation between the experimental maximum degradation W_m (Table 3, column 3) and the maximum degradation according to the four-parameter model, W_{a+c} (Table 3, column 11), expressed as $[(W_m - W_{a+c})/W_m]*100$ (Table 3, column 12), is up to 7.2% (in absolute value). The two-parameter model describes very well mainly the initial part of the degradation, indeed up to the initial 10 h, whereas the four-parameter model is appropriate for fitting hydrolytic degradation on the entire time period (including the equilibrium).

Besides the fitting of the experimental data previously described using the two- and four-parameter models, it is of great importance to determine the kinetics of the hydrolytic degradation of the polyesters. The latter is a complicated phenomenon which belongs to the heterogeneous, non-catalyzed reactions. These reactions take place between the solid state of the polyester and the liquid phase of the water and, indeed, between an ester group containing into the macromolecule of polyester and a molecule of water, according to the reaction for the polyester G100 [33]:



The attack of the water molecule occurs to a random ester group of the macromolecule (having k and m structural units on the left or right side, respectively). Similar reactions take place for the polyester A100 or the copolyesters. The previously described FTIR spectra for the degraded polyesters are in accordance with this reaction.

The chemical reaction rate which is used in single phase reaction systems can be used also for multiphase reaction systems (as in the hydrolytic degradation of the polyester) and is then characterized as effective reaction rate [34]. Below, the chemical reaction rate is used under this meaning.

Based on the unit surface of solid in liquid–solid systems, the expression of the reaction rate r_i is defined as [35]:

$$r_i = \frac{1}{S}\frac{dN_i}{dt}\left[\frac{\text{moles\_}i\text{\_formed}}{(\text{surface})(\text{time})}\right] \tag{9}$$

In the case of hydrolysis of polyester, N_i are the moles of the remaining (unreacted) ester groups (symbolized in below as N) and S is the surface of the solid polyester in the form of tablet ($6.91 \cdot 10^{-4}$ m^2) and the reaction rate r is:

$$r = -\frac{1}{S}\frac{dN}{dt} \tag{10}$$

The general expression of the reaction rate is:

$$r = k \cdot N^a \cdot C^b \tag{11}$$

where k is the rate constant of the hydrolytic degradation, C is the concentration of water and a, b are the corresponding partial orders. The hydrolytic degradation of polyesters (such as poly(lactide-co-glycolide) [36, 37] or unsaturated polyesters of the type of fumarates, phthalates etc. [38]) is zero- order with respect to the solid polyester (i.e., a = 0) and first-order with respect to the water (i.e., b = 1) and therefore the final expression of the reaction rate is:

$$r = k \cdot C \tag{12}$$

Combining Eqs. 11 and 12:

$$r = -\frac{1}{S}\frac{dN}{dt} = k \cdot C \tag{13}$$

It is accepted [38] that in the case of semi-dilute solutions of the polyesters it could be considered that water

Table 3 Results of hydrolytic degradation of polyesters at 50°C: Experimental data, their fitting with two- or four-parameter model and calculated and simulated rate constant for the degradation

Code of polyesters	Equilibrium parameters of the experimental data		Two-parameter model (Eq. 7)			Four-parameter model (Eq. 8)						Rate constant (k) of hydrolytic degradation at 50°C (Eq. 17, 18) based on:			
												Two-parameter model		Four-parameter model	
	Equilibrium time t_{eq} (h)	Degradation at maximum, W_m	$a = W_a$	b (h^{-1})	$\frac{W_m - W_a}{W_m} * 100$	a	b (h^{-1})	c	d (h^{-1})	$a + c = W_{a+c}$	$\frac{W_m - W_{a+c}}{W_m} * 100$ (%)	k (kg/m^2*s)	(s^{-1})	k (kg/m^2*s)	(s^{-1})
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)
A100	28.0	0.051	0.046	0.192	+9.8	0.023	0.566	0.030	0.039	0.053	−3.9	0.47E-05	1.82E-06	0.12E-05	4.65E-06
A90G10	24.0	0.188	0.198	0.233	−5.3	0.183	0.123	0.014	0.011	0.197	−4.8	0.69E-05	2.66E-06	0.42E-05	1.60E-06
A80G20	100.0	0.250	0.223	0.280	−10.8	0.174	0.242	0.094	0.015	0.268	−7.2	0.90E-05	3.46E-06	0.67E-05	2.58E-06
A70G30	43.0	0.385	0.357	0.299	+7.3	0.288	0.380	0.112	0.022	0.400	−3.9	1.08E-05	4.15E-06	0.97E-05	3.73E-06
A60G40	48.0	0.400	0.352	0.377	+12.0	0.281	0.555	0.120	0.024	0.401	+0.3	1.65E-05	6.31E-06	1.71E-05	6.56E-06
A50G50	53.5	0.500	0.451	0.342	+9.8	0.303	0.707	0.200	0.041	0.503	−0.6	1.83E-05	7.01E-06	1.99E-05	7.64E-06
A30G70	22.0	0.480	0.492	0.318	−2.5	0.292	0.318	0.180	0.216	0.472	+1.7	2.96E-05	11.3E-06	2.57E-05	9.84E-06
A10G90	7.0	0.280	0.300	0.300	−8.0	0.240	0.230	0.050	0.260	0.290	−3.6	2.24E-05	8.58E-06	1.79E-05	6.87E-06
G100	30.5	0.375	0.358	0.348	+4.5	0.327	0.327	0.046	0.025	0.373	−0.5	1.88E-05	7.22E-06	1.68E-05	6.45E-06

$W_m = (W_o - W_{eq})/W_o$, where W_o initial weight of sample and W_{eq} weight of sample at equilibrium time

W_a maximum degradation according to the two-parameter model

W_{a+c} maximum degradation according to the four-parameter model is in large excess, so that C is constant and close to 1/18 mol/g or 55.5 mol/kg.

Taking into consideration that one structural unit contains one ester groups, then N moles of ester groups correspond to N moles of structural units. One mole of structural units of polyester corresponds to the molecular weight of the structural unit m_o in grams, N moles of structural units of the macromolecules of polyester (referred to the total number of structural units and not in a single macromolecule, i.e., for all macromolecules) correspond to the weight W (g) of polyester. Then, Eq. 13 is written :

$$\frac{1}{S}\frac{d\frac{W}{m_0}}{dt} = -k \cdot C \tag{14}$$

or

$$\frac{1}{S \cdot m_0}\frac{dW}{dt} = -k \cdot C \tag{15a}$$

or

$$\frac{dW}{dt} = -k \cdot S \cdot m_0 \cdot C \tag{15b}$$

or

$$dW = -k \cdot S \cdot m_0 \cdot C \cdot dt \tag{15c}$$

For the polyester A100, m_o is equal to $m_{o,A} = 86$ (ethylene adipate structural unit) and for the polyester G100 is equal to $m_{o,G} = 58$ (glycolate structural unit). For the copolyesters :

$$m_o = f_A \cdot m_{o,A} + f_G \cdot m_{o,G} \tag{16}$$

Taking S, m_o and C as constants and integrating Eq. 15c between $t = 0 \rightarrow W = W_o$ up to $t = t \rightarrow W = W_t$, we have:

$$W_o - W_t = k \cdot S \cdot m_0 \cdot C \cdot t = K \cdot t \tag{17}$$

where:

$$K = k \cdot S \cdot m_0 \cdot C \tag{18}$$

By plotting $(W_o - W_t)$ versus t, using the initial linear part of the fitting curve (i.e., up to 5 h), the constant K is determined from the slope of the straight line. Then, the rate constant of polyesters degradation k is determined from Eq. 18 in units of kg/(m^2 s) or in s^{-1} by multiplying with S and dividing by the initial weight W_o ($1.8 \cdot 10^{-3}$ kg).

In the kinetics study only the initial time period is used, where the concentration is nearly equal to the initial, whereas afterwards the concentration changes with the progress of the phenomenon. Thus, for the calculation of the rate constant for the degradation, k, only the data from the initial linear part (which corresponds at time of about 3 h) was used. The results of the kinetics of the hydrolytic degradation for the polyesters are presented in Table 3 (columns 13, 14 for the two-parameter model and columns 15, 16 for the four-parameter model). The values of k calculated from the two models are similar. Thus, the two models, which were used for the fitting of the experimental data, can be used to determine the kinetics of the hydrolytic degradation of the polyesters.

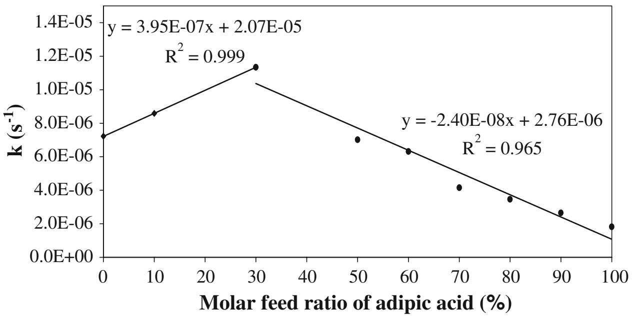


Fig. 8 Dependence of rate constant of degradation, k (s^{-1}), calculated with two-parameter model, of the polyesters versus molar feed ratio of adipic acid (%)

Figure 8 shows the dependence of k (s^{-1}), calculated with two-parameter model, of the polyesters versus molar feed ratio of adipic acid (%). By decreasing the molar feed ratio of the adipic acid from 100% (A100) to 30% (A30G70) the values of k increase linearly. By decreasing the molar feed ratio of the adipic acid from 30% (A30G70) to 0% (G100) the values of k decrease linearly.

The hydrolytic degradation of the polyesters is affected mainly by the crystallinity or the amorphous region of the polyester, respectively, and by the number of ester groups contained in the macromolecule. Other factors are the flexibility of the macromolecular backbone and the hydrophobicity of the macromolecule, which both influence the access of water in the vicinity of the ester groups where the hydrolysis reaction takes place. Concerning the two homopolymers, the degradation at maximum (W_m) of A100 is much lower than that of G100. The crystallinity of poly(ethylene adipate) has been determined as 74 ± 5% [39] and that of poly(glycolic acid) as 45 to 55% [13]. The lower crystallinity indicates higher amorphous region which is more preferably attacked during hydrolysis [32]. The degradation at maximum of the copolyesters increases by decreasing the molar feed ratio of adipic acid from 90 up to 50% (Table 3), which is interpreted by the decrease of crystallinity.

4 Conclusions

Copolyesters of glycolic acid combined with adipic acid and ethylene glycol were synthesized and their hydrolytic degradation was studied and correlated with their structures. According to the DSC, the production of polyesters leads to the formation of copolyester and not to mixtures of homopolyesters. The crystallites in the copolyesters mainly consist of continuous sequences of ethylene adipate structural units. The hydrolytic degradation of the polyesters was followed by their weight loss during hydrolysis and by the FTIR spectra of the initial polyesters compared with that of the degraded polyesters at equilibrium.

The region between 1142 and 800 cm^{-1} can be utilized to evaluate the extent of degradation of polyesters after their hydrolysis. The absorption bands at 1142, 1077 and 850 cm^{-1} due to the amorphous region decrease after hydrolysis, whereas those at 972, 901 and 806 cm^{-1} due to the crystalline region increase.

The experimental data of the hydrolytic degradation were fitted with exponential rise to maximum type functions using two-parameter model, which describes very well mainly the initial part of the degradation, and four-parameter model (containing two exponential terms), which is appropriate for fitting the hydrolytic degradation on the entire time period (including the equilibrium). Furthermore, the kinetics of the hydrolytic degradation of the polyesters for the initial time period based on both models results to similar values of the rate constant, k. By decreasing the molar feed ratio of the adipic acid from 100 to 30% the values of k increase linearly and from 30 to 0% the values of k decrease linearly. The lower crystallinity of the polyesters indicates higher amorphous region which is more preferably attacked during hydrolysis.

The synthesized copolyesters of glycolic acid combined with adipic acid and ethylene glycol are soluble in many common organic solvents opposite to PGA, leading to modified biodegradable polyesters and therefore they can be easily processed. They could be useful in various biomedical, pharmaceutical and technical applications including implants, scaffolds for tissue engineering, resorbable materials and drug delivery devices.

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