Amorphous and crystalline morphologies in glycolic acid and lactic acid polymers

D. Cohn, H. Younes and G. Marom
Casali Institute of Applied Chemistry, Graduate School of Applied Science and Technology, The Hebrew University, 91904 Jerusalem, Israel

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This paper describes an investigation of a number of parameters which affect the physical structures of glycolic acid (GA) and lactic acid (LA). It has been found that the cooling rate of a quenching process determines the amorphous–crystalline morphology balance, and that the effect of a similar quenching process will vary with the molecular weight of the polymer. At very high molecular weights, even very rapid quenching does not produce higher degrees of amorphous phase. Copolymerization of PGA or of PLA with poly(ethylene oxide) results in either phase blending or phase separation, depending on the copolymer composition and the segmental chain length. The degree of crystallinity of the PGA or PLA component in the copolymer is mostly affected by copolymerization in a state of phase blending.

(Keywords: poly(glycolic acid); poly(lactic acid); poly(ethylene oxide); biodegradable polymers)

INTRODUCTION

Poly(glycolic acid) (PGA) and poly(lactic acid) (PLA) are well established as very useful biodegradable polymers, covering a wide range of applications, such as dental, orthopaedic and drug delivery[1–7] which have emerged from the original suture development[8–10]. The scientific literature offers a vast amount of data and information on these polymers, and readers may refer to reviews[11–12].

A particular aspect which seems to have been rather neglected in the literature is the morphological structure of these materials. PGA and PLA appear with different degrees of crystallinity, from completely amorphous to a maximum of 52% crystallinity in the PGA and of 37% in the poly(L-lactic acid), while poly(DL-lactic acid) is always amorphous[13].

The practical significance of the variable crystallinity has been discussed by Gilding and Reed[13]. They pointed out that the amorphous state is ideal for applications where it is necessary to have mass loss simultaneously with molecular weight degradation, or for applications such as drug delivery, where it is important to have a homogeneous dispersion of the active species in a monophasic matrix. The partially crystalline morphology is relevant to uses where high mechanical properties are required, i.e. in sutures and in orthopaedic or dental applications. In addition to these examples, it is expected that the degree of crystallinity will influence chemical and physical properties, such as swelling behaviour and the hydrolytic sensitivity of these polymers and, consequently, their rate of biodegradation.

Gilding and Reed also showed[13] that the degree of crystallinity in cast polymer films was controllable by copolymerization of GA with LA at different compositions, with those of 22–66 wt% GA being fully amorphous. They also found that quenching of copolymer compositions, which were potentially to produce partially crystalline morphologies, resulted in amorphous polymers. However, when these polymers were implanted in the physiological environment or placed in water, they crystallized partially over 24–72 h, hence it was impossible to retain quenched morphologies under those conditions.

The present study investigated further a number of parameters that may potentially control the amorphous/crystalline morphologies in glycolic acid and lactic acid polymers. These parameters are the rate of quenching, the molecular weight of the polymer and copolymerization of GA or LA with poly(ethylene oxide), parameters which are known to substantially affect the morphology developed by polymeric matrices.

EXPERIMENTAL

Materials

PGA and PLA with high molecular weight ($MW > 20000$) were obtained from Polysciences, Inc. The low molecular weight samples ($MW \leq 10000$) were prepared in our laboratory by simple polycondensation reactions using glycolic acid (Fluka) and a 90% solution of (L^+) lactic acid (Merck); poly(ethylene oxide) with different molecular weights were obtained from Aldrich. The Sb_2O_3 catalyst was supplied by Fluka.

Analytical methods

Carboxylic end-group analysis. Samples of PLA with different molecular weights were dissolved in approximately 20 ml of a 1:1 solution of benzyl alcohol (Merk, Analar grade) and chloroform (Frutarom, Analar grade) and titrated against 0.05 M KOH in benzyl alcohol solution in the presence of phenolphthalein indicator. The number of COOH end groups present in each polymer sample was calculated and the molecular weight (M_n) determined.

Thermal analysis. A Mettler TA3000 differential scanning calorimeter (d.s.c.) calibrated with indium was used to determine the glass transition (T_g), the melting

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(T_m) and crystallization (T_c) temperatures and the heat of fusion (H_f) of the various materials investigated. Three different cooling rates were used: fast cooling (60°C min^{-1}), medium (20°C min^{-1}) and slow cooling (10°C min^{-1}). When not stated, the slowest cooling rate was used.

T_g was obtained from the thermograms, using the middle point between the intersections of the two parallel baselines, before and after T_g, and the d.s.c. trace. T_m and T_c were determined as the intersection of the baseline and the edge of the fusion peak. The heat of fusion was estimated from the area enclosed by the d.s.c. curve and the baseline.

All samples were heated (in nitrogen atmosphere) to 20–30°C above the melting point of the polymer for $\approx$ 10 min to ensure that no trace of crystallinity remained. The melted samples were then cooled at three different rates, 60, 20 and 10°C min^{-1}, to the desired temperature, which was about 50°C below the T_g.

RESULTS AND DISCUSSION

PGA and PLA homopolymers

Figure 1 presents a typical d.s.c. trace of high molecular weight (HMW) PGA. The main feature is a melting endotherm at 222°C, while a small glass transition is present at 45°C. This thermogram is indicative of a substantially crystalline material, and is in full agreement with the results of Gilding and Reed[13].

Figure 2 shows the d.s.c. traces during reheating and after a heating–cooling cycle for a medium molecular weight (MMW) PGA, at three different cooling rates. *Table 1* summarizes the main data obtained from the results in *Figure 2*. The clear and relatively sharp glass transition exhibited by the quenched samples and the large crystallization exotherms are indicative of a polymer that contains a large amorphous phase. The increasingly important crystalline character of PGA samples which underwent slower cooling cycles is evidenced by the pronounced decrease of both features. When the molten PGA is cooled rapidly to below 0°C, the crystallization process is hindered, and an amorphous morphology is frozen in. Upon reheating, the amorphous phase will recrystallize at a typical temperature, T_c, above T_g. In fact, two recrystallization points are evident, one around 90°C, T_{c1}, and another in the 160–180°C range, T_{c2}. The proportion of the amorphous phase strongly depends on the cooling rate and, for a maximum proportion, a quenching rate faster than 60°C min^{-1} is required, as shown by the large exotherm, which is still present at 212°C. The final degree of crystallinity, X_c, was calculated from the heat of fusion, H_f, compared with the 72.3 J g^{-1} value, measured for HMW PGA of maximum 52% crystallinity. Our findings show that X_c increases slightly, from 13.4 to 16.3%, as the cooling rate decreases from 60 to 10°C min^{-1}. As one would expect, the melting endotherms are only marginally affected by the cooling procedure, no significant shift or increase in the peaks being evident. This is due to the fact that much of the effect of the cooling rate on the morphology of the sample is eliminated during the reheating cycle; once the system approaches the melting temperature and various crystallization phenomena have already taken place, much of its thermal history has been erased. Still, the trend in X_c results from the fact that reheating at 10°C min^{-1} in the d.s.c. experiment does not allow sufficient time for full crystallization. Finally, at this state the origin of the separate T_{c1} and T_{c2} crystallizations is still unclear.

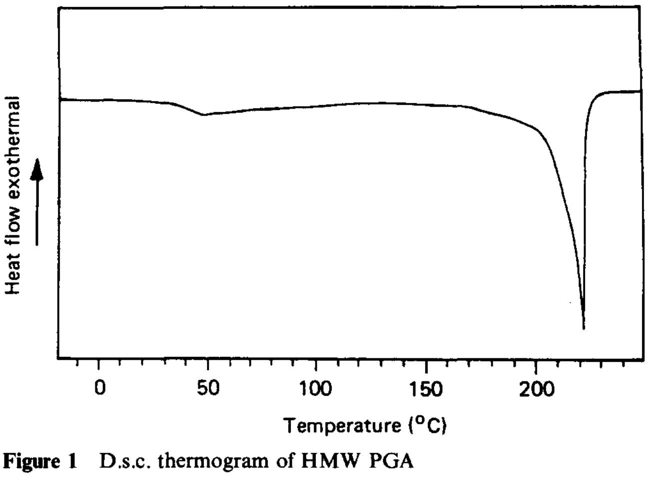

Figure 1 D.s.c. thermogram of HMW PGA

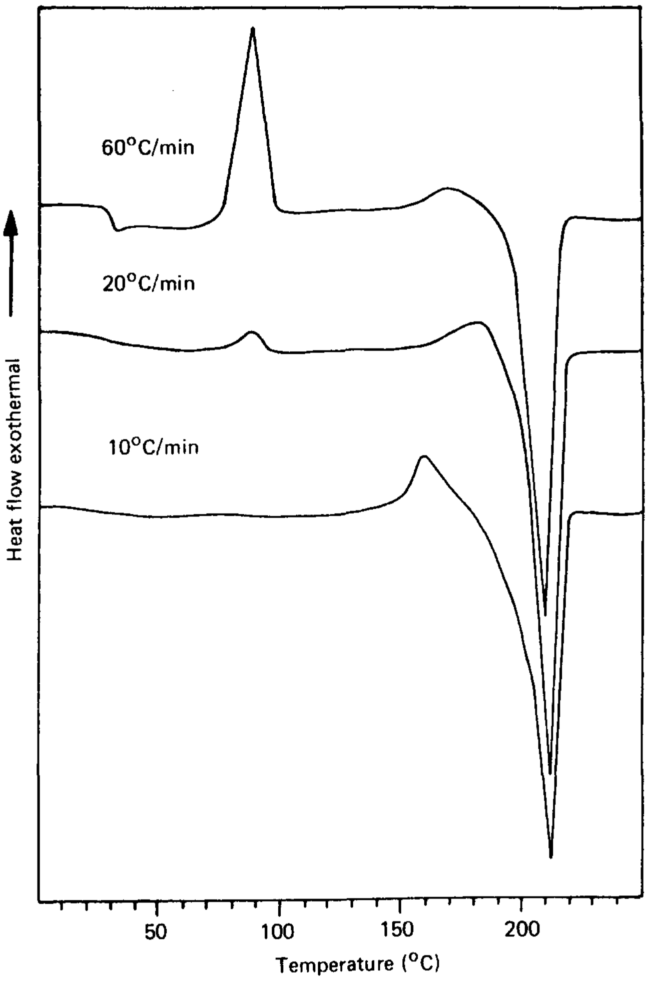

Figure 2 Effect of cooling rate on PGA's thermal behaviour

Table 1 D.s.c. data of MMW PGA

Cooling rate (°C min^{-1})	Temperature (°C)				H_f (J g^{-1})	X_c (%)
	T_g	T_{c1}	T_{c2}	T_m		
60	30	89	170	208	18.6	13.4
20	31	89	180	212	20.1	14.5
10	–	–	158	213	22.7	16.3

Figure 3 and *Table 2* present the thermal behaviour and the morphological data for PGA samples having different molecular weights. The d.s.c. traces are for reheating after cooling the sample from the melt at a 60°C min^{-1} cooling rate. The main observation is that all four transition temperatures, as well as the degree of crystallinity, increase with the molecular weight. The crystalline phase of PGA is better developed and more homogeneous as the molecular weight increases, as revealed by the sharper melting endotherms, which steadily shift to higher temperatures. The broadening of the peak displayed by the low molecular weight polymer is indicative of different sizes of crystallites.

It is worth noting that sample VI, which has the highest molecular weight, does not go through any crystallization process during reheating. This is probably due to the high molecular weight of PGA and the consequent very low concentration of chain ends, which minimizes their interference with the crystalline array of the chains.

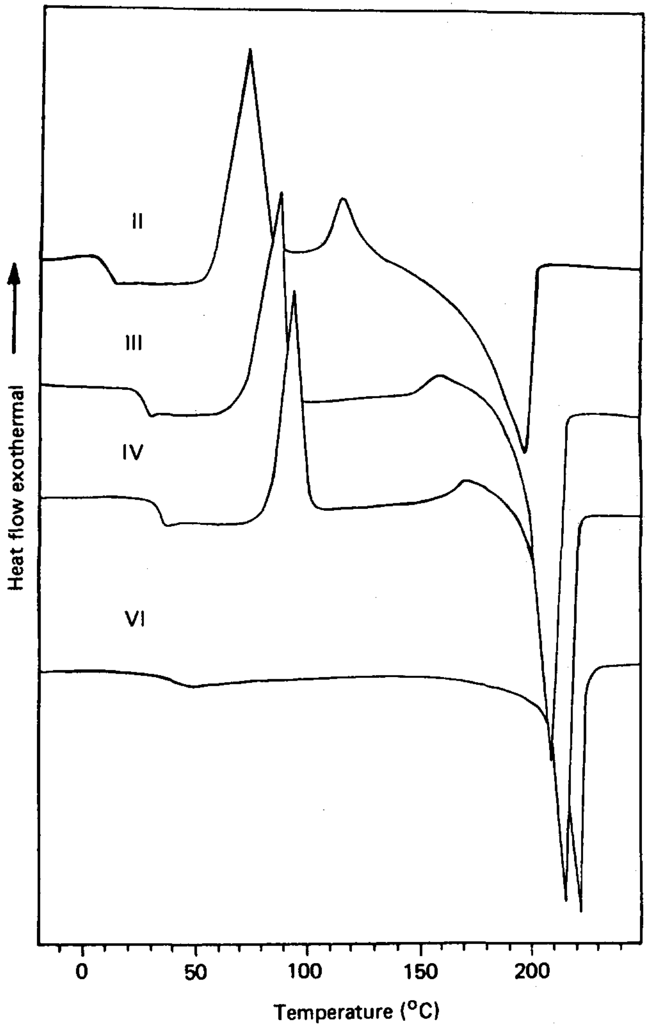

Figure 3 Effect of molecular weight on PGA's thermal behaviour

Table 2 D.s.c. data of different molecular weight PGA samples. Molecular weight increases with sample number

PGA sample	Temperature (°C)				H_f (J g^{-1})	X_c (%)
	T_g	T_{c1}	T_{c2}	T_m		
I	10	68	108	187	12.6	9.0
II	11	72	114	198	20.6	14.8
III	26	85	158	209	23.2	16.7
IV	33	91	173	214	26.7	19.2
V	40	104	177	221	37.2	26.8
VI	42	–	–	222	72.3	52.0

Table 3 D.s.c. data of different molecular weight PLA samples

M_n	Temperature (°C)				H_f (J g^{-1})	X_c (%)
	T_g	T_{c1}	T_{c2}	T_m		
1 000	38	–	100	135	18.1	12.2
2 500	45	–	110	138	19.1	12.9
4 000	46	–	110	140	21.1	14.1
6 500	50	–	112	142	23.9	16.1
9 500	53	–	115	145	27.6	18.6
28 000	56	95	155	170	55.0	37.0

The glass transition temperature, its location and breadth supply valuable information about the homogeneity of the amorphous phase and the degree of interaction between the crystalline and amorphous phases. While the low molecular weight PGA shows a clear glass transition at 10°C, T_g shifts to higher temperatures, up to 45°C for the longest PGA chains. The glass transition is affected by the length of the crystalline blocks: the longer they are, the higher the T_g. This is attributed to the increasing constraints imposed to the mobility of PGA amorphous chains by the rigid blocks as X_c increases.

Clearly, a high molecular weight PGA is essential for applications that require good mechanical properties, which in turn depends on the degree of crystallinity.

Table 3 summarizes the thermal behaviour and the morphological data for PLA having different molecular weights. These data were obtained in the same way as for PGA, calculating X_c from the H_f values, compared to the value of 55.1 J g^{-1}, measured for HMW PLA of maximum 37% crystallinity. The picture presented by the PLA data is consistent with that for the PGA data. Here too, the transition temperatures and the degree of crystallinity increase with the molecular weight. One difference, though, is that PLA exhibits two crystallization regions only at the highest molecular weight examined.

PGA and PLA copolymers with PEO

It has been shown[13] that copolymerization of PGA with PLA results in a wide range of copolymer compositions that do not crystallize. Copolymerization is therefore a powerful tool for controlling polymer morphology, and it is investigated here in block copolymers of either PGA or PLA containing poly(ethylene oxide) (PEO) segments.

As an example, *Figure 4* presents the d.s.c. traces of a PGA/PEO (6000) copolymer and that of both homopolymers. The thermogram of crystalline PGA has already been discussed above (see *Figure 1*); the d.s.c. trace of PEO (6000) shows a sharp melting endotherm at 69°C and a very small glass transition at approximately −60°C. The thermogram of the copolymer is under reheating of a 50:50 wt% composition after a heating–cooling (60°C min^{-1}) cycle. The copolymer exhibits substantially different thermal behaviour, with the melting endotherm at 39°C, and the absence of another melting at a higher temperature being of particular significance. Hence, it is evident that the incorporation of the PEO oligomer into the PGA chain causes a shift of the melting point of the first to a lower temperature, while that of the latter polymer disappears in this particular composition. These phenomena are taken as indications of some degree of phase blending occurring in the copolymeric matrix.

The behaviour of the copolymer is expected to be highly sensitive to the composition. Hence, the 60:40 wt% PGA/PEO (6000) composition shown in *Figure 5*, compared with the 50:50 composition (*Figure 4*), is characterized by a shift of the thermal transitions to higher temperatures. It is seen that T_g is shifted from -43°C to -32°C, and T_m, which is associated with fusion of the PEO segments, is shifted from 39°C to 47°C. These phenomena are attributed to the anchoring effect that the hard PGA blocks have on the mobility of the PEO segments. Another important feature of the copolymer is expressed through the effect of the presence of PEO on the crystallizability of the PGA. Whereas the 50:50 wt% composition does not exhibit any signs of PGA crystallization or melting, the 60:40 wt% composition, which has relatively less PEO, already exhibits a crystallization peak (T_{c1}) around 70°C and a broad endotherm around 175°C; these transitions indicate an incipient crystallinity of the PGA, and some degree of phase separation in the copolymer. It should be stressed, however, that the copolymer is generally characterized by large phase blending, which is anticipated in view of the solubility parameters of the components[14].

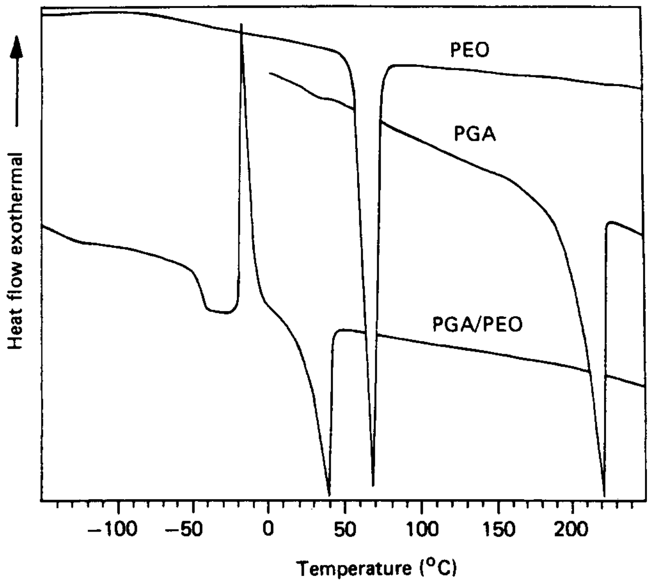

Figure 4 D.s.c. thermograms of a 50:50 (wt%) PGA/PEO(6000) copolymer and that of both homopolymers

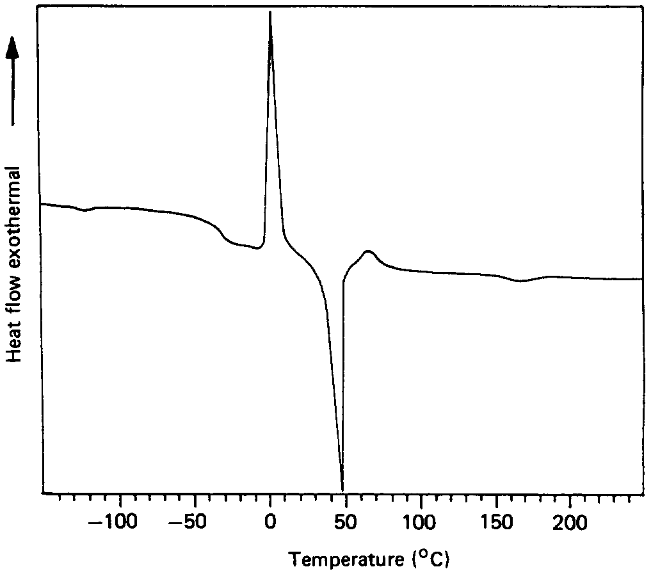

Figure 5 D.s.c. thermogram of a 60:40 (wt%) PGA/PEO(6000) copolymer

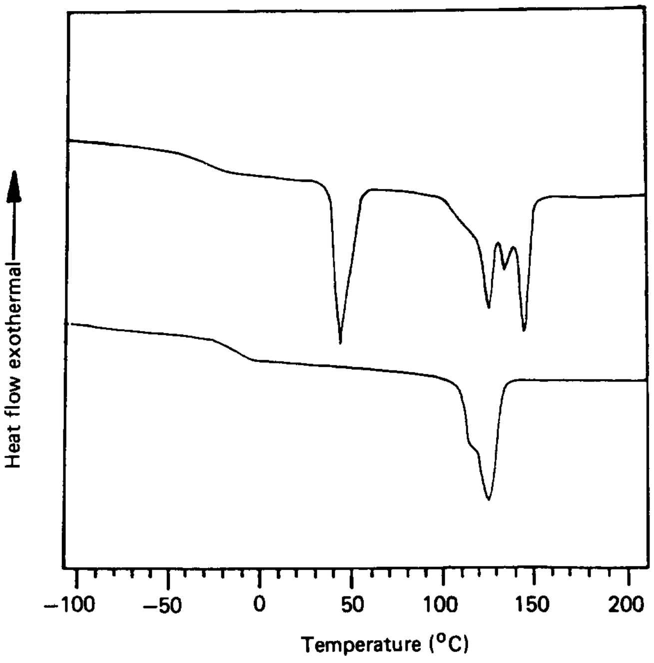

Figure 6 D.s.c. thermograms of two PLA/PEO copolymers

In parallel with the PGA/PEO copolymers, a series of PLA/PEO copolymers covering a wide range of compositions and segmental lengths was investigated in detail[15,16]. The results of these studies are consistent with the conclusions drawn for the PGA/PEO copolymers. An additional insight into the effect of copolymerization is gained from an investigation in the PLA/PEO series of a range of segmental lengths for a constant copolymer composition. This is demonstrated in *Figure 6*, which shows the d.s.c. thermograms of two PLA/PEO copolymers, exhibiting clearly different behaviours. The copolymers shown, while being characterized by an almost identical overall composition, differ in the length of the blocks along the chain. The lower trace corresponds to a monophasic semicrystalline polymer, containing PEO 3400 soft segments, the melting point at 126°C being associated with the fusion of PLA blocks. The material containing PEO 6000 and PLA longer segments (upper thermogram) exhibits a different morphology, where a two phase matrix is evident, with both components being able to crystallize. The presence of two separate melting endotherms, one at 40°C and the other over the 125–140°C range, due to the PEO and PLA segments, respectively, demonstrates the existence of microphase separation phenomena in this PLA/PEO matrix. Even though characterized by the same overall composition, the morphological differences of these matrices will strongly affect both the mode and the kinetics of their biodegradation.

CONCLUSION

Biodegradability and other essential properties of biomedical polymers depend on their physical structure. It is, therefore, important to be able to control the amorphous–crystalline morphology balance. It is shown here that in PGA and PLA homopolymers this control is achieved by selecting an appropriate quenching rate, according to the molecular weight of the polymers. At very high molecular weights, however, the degree of crystallinity is insensitive to the cooling rate. In copolymers of PGA and PLA with PEO, two basic possibilities exist, namely, phase blending and phase separation of the copolymer components. The degree of crystallinity of the PGA or PLA component is mostly affected by the presence of the comonomer, in a state of phase blending. The achievement of phase separation versus that of phase blending depends on both the copolymer composition and the segmental length.

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