In Vitro Chemical Degradation of Poly(Glycolic Acid) Pellets and Fibers

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Synopsis

The influence of macroscopic dimensions, heat treatment, and polymer morphology on the chemical degradation of poly(glycolic acid) (PGA) fibers and pellets was examined in media of different pH values by monitoring the sample mass, dimensions, crystallinity, mechanical strength, and surface character. The degradation was found to be chemically controlled and independent of fiber size. The rate was an order of magnitude faster in alkaline vs. acidic media. In general, the pellets degraded faster than fibers, and while the latter showed little surface deterioration, scanning electron photomicrographs of the pellets revealed considerable surface degradation with circumferential microcracks progressing into longitudinal cracks with increasing immersion times and pH. Concomitantly, DSC measurements showed a steady increase in crystallinity for both fibers and pellets. The fiber tensile strength decline was independent of diameter and more drastic in alkaline media. Additionally, the heat-treated fiber was always stronger than the non-heat-treated one. It is concluded that crystallinity and polymer chain orientation, in addition to immersion media, influence PGA degradation. Also, the loss in strength results from chain scission in the amorphous regions while mass loss occurs when polymer chains become small enough to be soluble. These different variables offer a means of modifying PGA fiber tensile properties.

INTRODUCTION

Poly(glycolic acid) is the simplest linear aliphatic polyester of glycolic acid. It is biocompatible, and, in the body, it slowly degrades into nontoxic products. Due to these desirable properties, it is used in surgical sutures[1] and is also a candidate for use in implants and in controlled release drug delivery formulations.[2] For all these applications, it is clearly desirable that the mechanism of digestion be understood and the rate of degradation be predictable. However, even in the case of sutures, which appear to have been studied the most, there does not seem to be a unity of opinion, especially with regard to the rate of decay of mechanical strength. This latter quantity has been shown to be influenced by suture size, polymer crystallinity,[3] temperature,[4] pH and the presence of buffers,[5] enzymes,[6] and bacteria.[7] All these studies have provided a wealth of data, both *in vivo* and *in vitro*, but the findings have often been in conflict with each other.

In the literature, the influence of suture size on the degradation kinetics has been controversial. Although several studies using commercially available multifilament sutures[4,8,9] showed that the retention of tensile strength and the rate of suture absorption were independent of the suture diameter, other investigators[3,10] reached exactly the opposite conclusion. In addition to this, the effect of pH is still unclear. While Holm-Jensen and Agner[11] and Reed and Gilding[4] reported no dependence of the process of polymer degradation on pH

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TABLE I
Properties of Poly(glycolic Acid) Pellets

Melting point	225–230°C
Weight average molecular weight (M_w)	~ 60,000
Number average molecular weight (M_n)	~ 20,000–30,000
Density (g/cc)	1.569
Percent crystallinity	38
Glass transition temperature	37°C

in the pH ranges 2–11 and 5–9, respectively, Chu[5] found that the degradation was pH-sensitive, being much more rapid in alkaline than in acidic or neutral media.

The purpose of the present investigation was to resolve some of the above-mentioned anomalies and to develop a consistent model for the degradation of poly(glycolic acid). As a part of this work, the effect of size, polymer morphology, and solution pH on polymer desterification was investigated *in vitro* for poly(glycolic acid) fibers as well as for pellets.

EXPERIMENTAL

Materials

Pellets of poly(glycolic acid), having a weight average molecular weight of 60,000, were obtained from Polysciences Inc., of Warrington, Pa. The physical properties of the material, as supplied by the manufacturer, are listed in Table I. Fiber monofilaments were made from this polymer by melt spinning as described below. Four different buffer solutions were prepared: (1) acetic acid–sodium acetate with a pH of 4.7; (2) potassium phosphate–potassium diphosphate with a pH of 7.0; and (3) sodium carbonate–sodium bicarbonate with pH values of 9.2 and 10.6. In each case, the molar concentration of the buffer solutions was 0.25.

Isothermal Fiber Spinning and Heat Treatment

An Instron capillary rheometer was used to melt-spin and extrude poly(glycolic acid) into fibers. Polymer pellets were dried overnight at about 90 °C to eliminate the moisture and were placed in the rheometer barrel. Extrusion was carried out at 228 ± 3 °C through a circular capillary having a diameter of 0.0762 cm and a length to diameter ratio of 64.5. The polymer filament passed through a set of guide rollers and was subsequently wound on a bobbin driven by a 1/4 HP motor. The total length of the spin line was 50–60 cm, and the take-up velocity was about 25–30 cm/s.[12]

By varying the operating conditions, fibers of two different diameters, 0.0155 and 0.0203 cm, were obtained; this corresponds to the USP sizes of 4-0 and 3-0, respectively. Some of the larger diameter fiber was heat-treated in an oven at 195 ± 5 °C for 5 h to induce additional crystallization. The heat treatment resulted in an increase in crystallinity from an initial value of 37% to a final value of 42%.

Specimen Preparation and Testing

Weighed fiber samples, about 25–35 cm long, were immersed in 15 cc of each of the buffer solutions, and this was done for all the three kinds of fibers. The pH of the buffers was monitored periodically to ensure that it remained unchanged. Five samples of each kind of fiber were used with each buffer solution, and these were harvested at the end of 1, 2, 3, 4, and 6 weeks of immersion. On removal from solution, the fibers were washed thrice with distilled water and then dried under vacuum in a desiccator filled with Drierite (anhydrous calcium sulfate). In separate tests, samples of PGA pellets (each sample containing 12 pellets having a total mass of about 0.2 g) were also studied in a similar fashion.

A Quantimet 720 image analyzer was used to characterize the PGA pellets and fibers dimensionally. In its most basic form it consists of an optical microscope, a scanner, a processor, and a calculator. The processor derives geometric data from images produced by the microscope on the scanner. Ten individual scans were taken for each area and perimeter measurement for a given sample. For the pellets, it is assumed that, while the individual orientation of the samples would change, the average values obtained are a fair measure of the sample dimensions.

A Perkin-Elmer differential scanning calorimeter, Model DSC-2, was used to characterize the degree of crystallinity, heat of fusion, and melting temperature of both the pellets and the fibers. The sample size was typically 3–10 mg, and the sample was scanned from 150 to 240 °C at the rate of 10 °C/min. The percent crystallinity was expressed as the percent ratio of the measured heat of fusion of the sample to the heat of fusion of a hypothetical 100% crystalline sample of PGA (49.34 cal/g).[13,14]

A Model 1000 Instron tensile testing machine was used to determine the mechanical properties of the fiber. About 2.5–5.0 cm of the fiber was clamped between the rubber faced jaws of the lower and upper grips such that the fibers experienced neither slack nor tension prior to the application of the load. The upper grip which is attached to the crosshead was moved at the rate of 1 cm/min, and the resulting extension curve was recorded by a strip chart recorder. The testing was done at ambient condition at 21 ± 2 °C and 68% RH. The reported values are averages of three separate runs.

An AMRAY 1000 scanning electron microscope was used to examine the surface of the pellets and fibers. The specimen was sputter-coated with a 20-μm layer of gold and then examined at an accelerating voltage of 5 kV. An automatic Polaroid camera was used to record the micrographs on black and white Polaroid PN 55 film.

RESULTS

Mass Loss. Typical mass loss profiles for both the pellets and the fibers are shown in Figures 1(a) and 1(b). While there are differences between the behavior of the pellets and the fibers, the general trend is that of increasing mass loss with increasing pH, particularly as the medium becomes alkaline. For pH 10.6, the loss in mass is especially drastic and occurs between 2 and 6 weeks after immersion. The behavior of the three different fibers seem to be qualitatively similar, except perhaps in the slightly alkaline medium (pH 9.2),

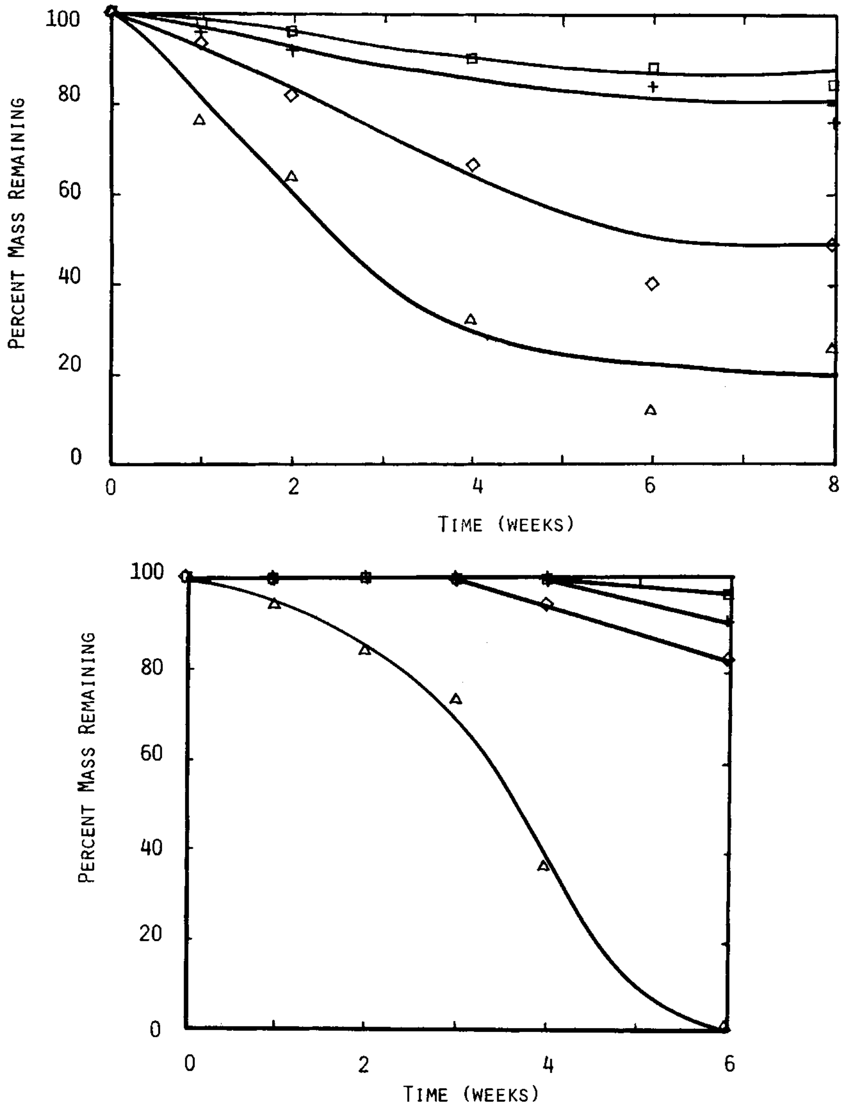


Fig. 1. Comparison of the mass loss data for PGA pellets and fibers: (a) pellets; (b) fiber of diameter 0.0203 cm. pH; (□) 4.7; (+) 7.0; (◇) 9.2; (△) 10.6.

where the thicker fiber shows a smaller loss in mass. At pH 10.6, both the thicker and the thinner fibers showed almost identical rates of mass loss, whereas the heat-treated fiber showed a slightly faster rate of mass loss when compared with the non-heat-treated sample. However, there is no question that the pellets behave differently from the fibers and show a much earlier and more rapid loss in mass than the fibers.

Changes in Size. The changes in the average area and the average perimeter of the pellets were tracked by an image analyzer, and the results for the area are displayed in Figure 2. Initially, all the pellets showed some swelling so that, for the first 2 weeks, both the area and the perimeter

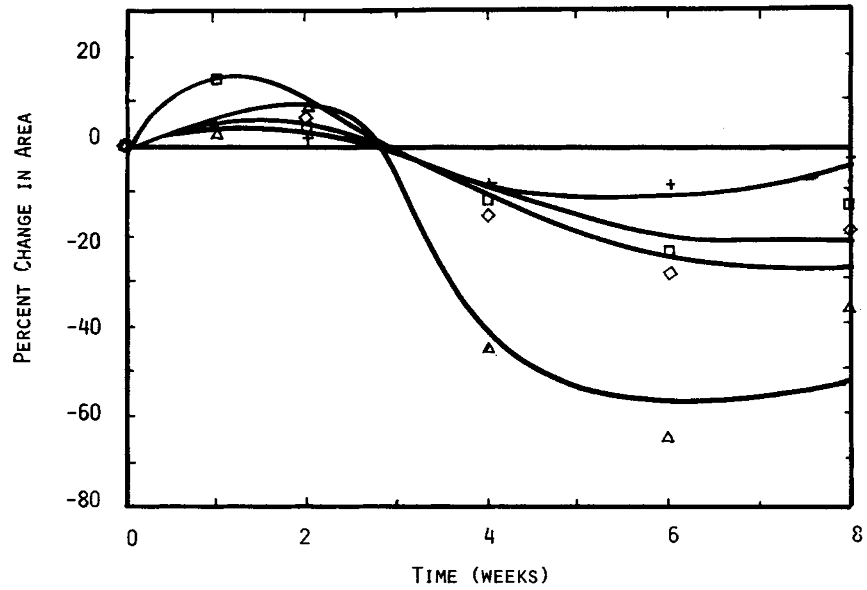


Fig. 2. Changes in area for PGA pellets. pH; (□) 4.7; (+) 7.0; (◇) 9.2; (△) 10.6.

exceeded their respective starting values. The trend was one of increasing swelling with decreasing pH. Beyond the first 2 weeks, however, the area and the perimeter started decreasing, more rapidly now with increasing pH. After 6 weeks of immersion, the dimensions again increase, but, by now, the pellets have begun to disintegrate into fine particles so that data interpretation is difficult.

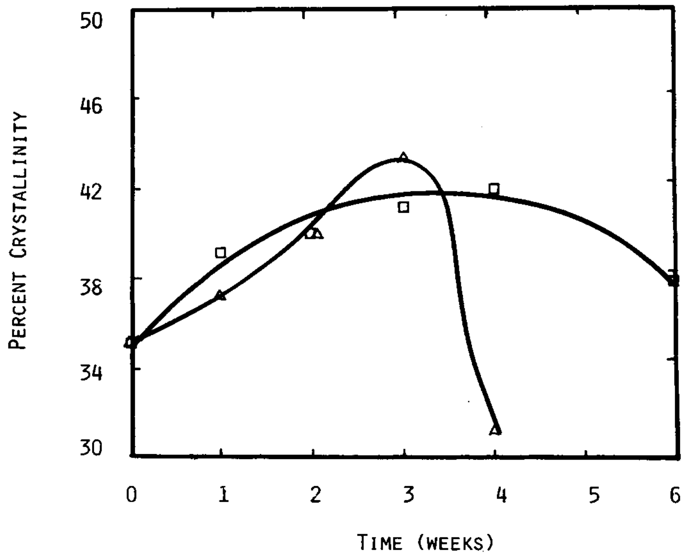


Fig. 3. Changes in percent crystallinity for PGA fibers (0.0203 cm). pH: (□) 4.7; (△) 10.6.

The changes in the diameter of the fibers were more difficult to follow since the fibers became brittle with time and did not permit proper measurement. Initially, though, the fibers did show a slight increase in diameter, but the data were erratic and, consequently, they are not reported here.

Changes in Crystalline Content. The changes in the heat of fusion of the poly(glycolic acid) were followed with the help of a differential scanning calorimeter, with two thermograms being obtained for each sample tested.

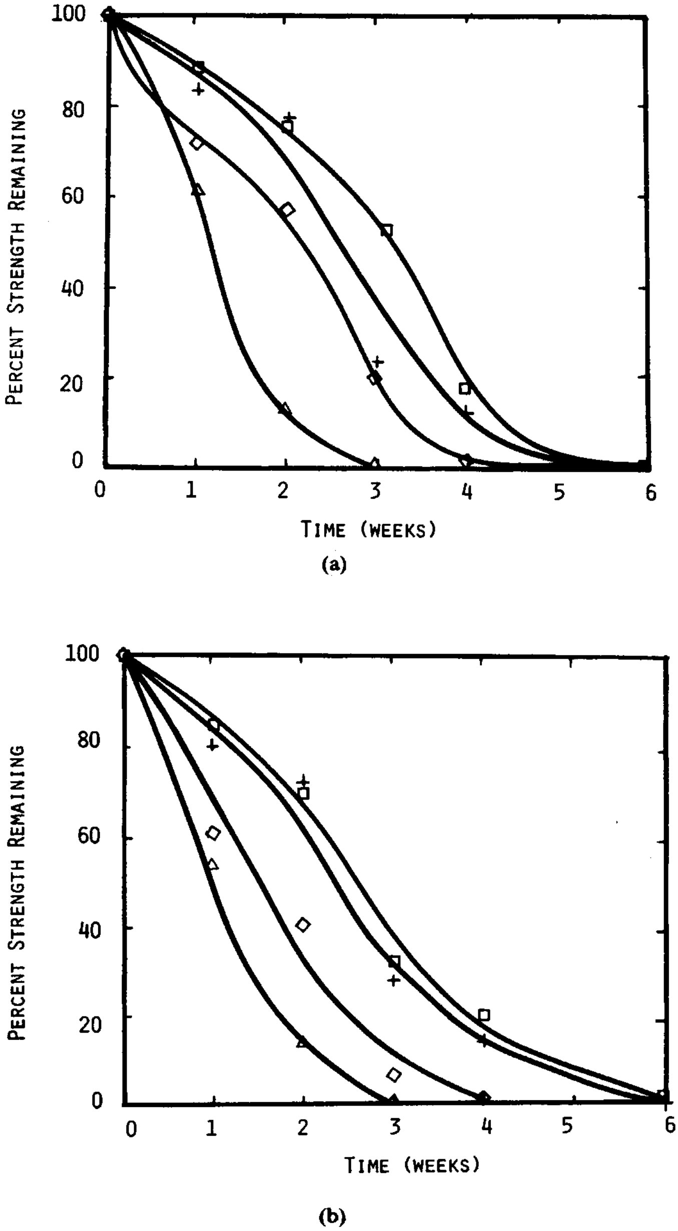


Fig. 4. Comparison of the tensile strength retention data for PGA fibers: (a) 0.0203 cm; (b) 0.0155 cm; (c) 0.0203 cm, heat-treated. pH: (□) 4.7; (+) 7.0; (◇) 9.2; (△) 10.6.

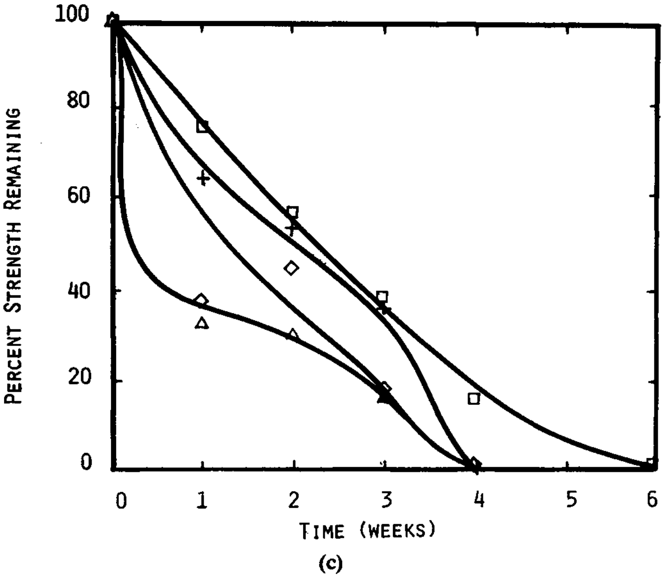


Fig. 4. (*Continued from the previous page.*)

These data were later converted into plots of percent crystallinity vs. time, and a typical profile for the thicker fiber is shown in Figure 3. The profiles for the pellets and the other fibers were similar and are, therefore, not shown. It may be mentioned, however, that the multiple endothermic fusion peaks were observed for the heat-treated fiber, indicating the presence of crystals formed during the heat treatment. All the data show a general increase in crystallinity with both time and pH, especially in the alkaline media. In most cases, maxima are also obtained, but the time at which maximum crystallinity occurs varies: It is about 3 weeks for both the non-heat-treated fibers, about 4 weeks for the heat-treated fibers, and about 6–8 weeks for the pellets. The data beyond 6 weeks, though, have to be treated with caution due to the possibility of complete disintegration of the sample, particularly in the more alkaline media.

Mechanical Properties. The stress at break (based on the initial area) and the initial (elastic) modulus for each of the fibers was obtained from the stress–strain curves. While the stress at break is termed as the tensile strength, the initial modulus is the slope of the stress–strain curve at zero strain. The percent change in these quantities upon immersion, as a function of time, is depicted graphically in Figures 4–6. Other data are listed in Table II.

The data at day zero clearly show the beneficial effect of heat treatment: The tensile strength increases by almost 40% due to annealing. The decline in strength of all the fibers, though, is similar, as shown in Figure 4. There is a progressive decline in both the mechanical properties, and this is hastened with increasing pH. It is found that while the initial strength is dependent on the fiber diameter, the rate of deterioration at a given pH is independent of this quantity. Surprisingly, the heat-treated fiber did not show a good retention of tensile strength when compared to the unannealed fiber, at least in the

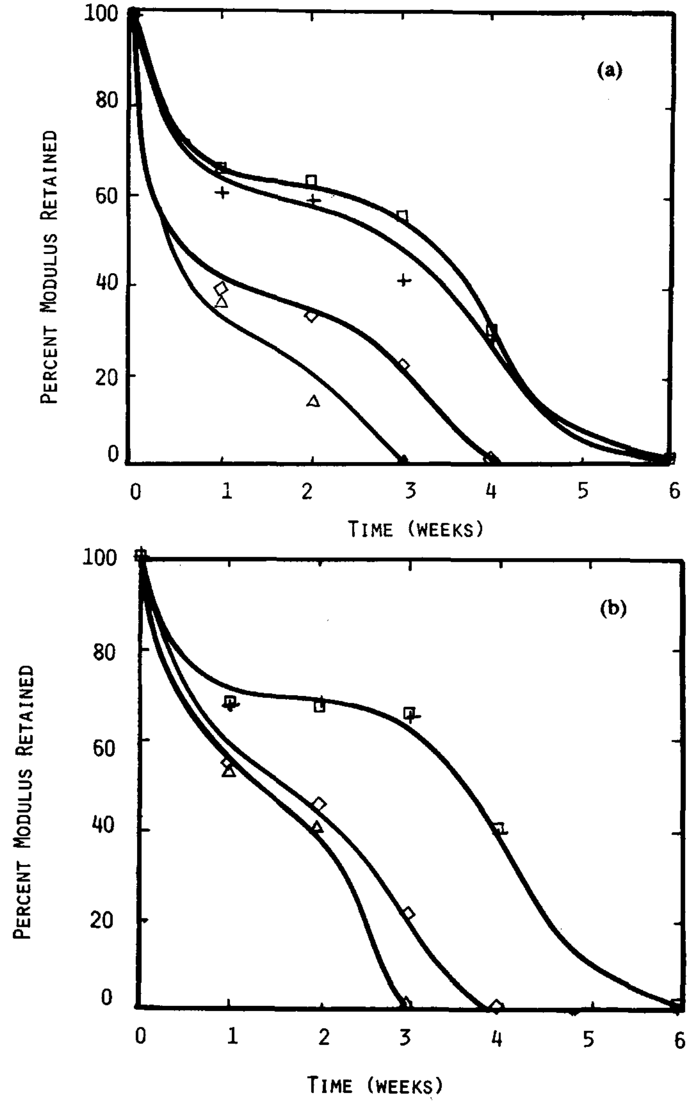


Fig. 5. Comparison of the initial modulus retention data for PGA fibers (a) 0.0203 cm; (b) 0.0155 cm; (c) 0.0203 cm, heat-treated. pH: (□) 4.7; (+) 7.0; (◇) 9.2; (△) 10.6.

initial stages, although its strength was greater than that of the unannealed fiber at all times (see Fig. 6). This may be due to the fact that the tensile strength is an ultimate property which depends strongly on the sample preparation and the presence of flaws and defects. The initial modulus, on the other hand, is a material property, and here the heat-treated fiber is clearly superior, as shown in Figure 5. All this appears to be in accord with other *in vitro* tensile data reported in the literature.[2,5,15-17]

Surface Deterioration. The changes in the surface structure of the polymer were observed with a scanning electron microscope. Three series of photomicrographs of the longitudinal views, for the pellets and the thicker fiber, are shown in Figures 7-11

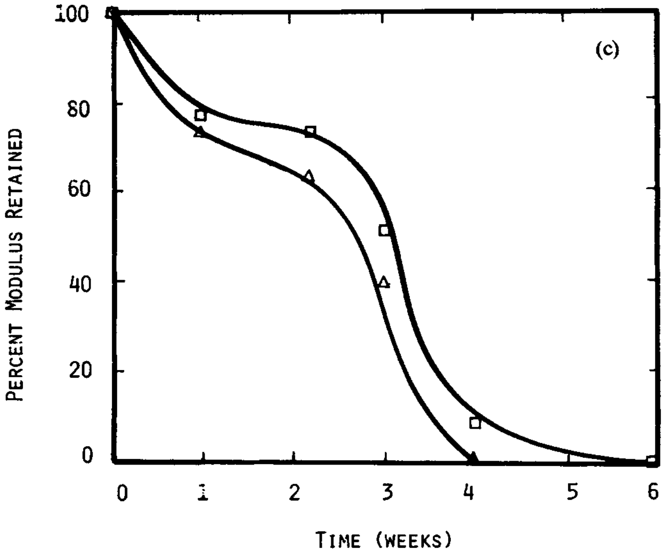


Fig. 5. (*Continued from the previous page.*)

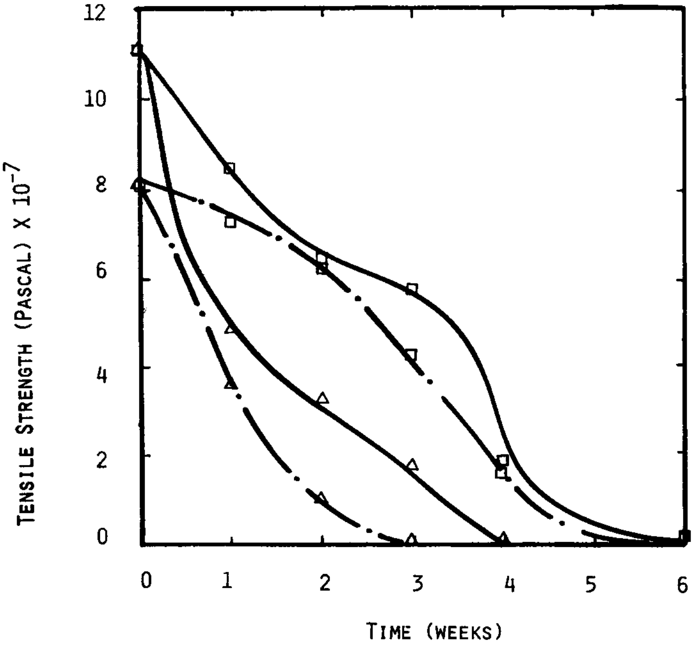


Fig. 6. Effect of heat treatment on the tensile strength retention of PGA fibers: (—) heat treated fiber; (---) non heat-treated fiber; diameter = 0.0203 cm for both fibers. pH: (□) 4.7; (△) 10.6.

TABLE II
Tensile Strength and Initial Modulus of the Fibers at Day 0

Fiber diameter (cm)	Tensile strength at day 0 (Pa)	Initial modulus at day 0 (Pa)
0.0203	7.94×10^7	9.52×10^9
0.0155	8.85×10^7	9.01×10^9
0.0203 (heat-treated)	1.12×10^8	1.02×10^{10}

As Figure 7 shows, the pellets initially have a smooth and regular structure. In the acidic medium, a gradual surface degradation takes place, with the initial circumferential cracks progressing into longitudinal cracks with increasing times of immersion [see Figs. 8(a)–8(e)]. A similar behavior is observed in physiological saline up to 4 weeks. Beyond this, deep and progressive circumferential cracks appear, a behavior that becomes even more acute in the alkaline media. For a pH of 10.6, deep surface cracks develop by the fourth week (see Fig. 9), and these become intense to a point of reaching a regular honeycomb pattern by the sixth week. Ultimately, the pellet disintegrates.

As far as the fibers are concerned, it was found that within the range of pH studied (4.7–10.6), and for times of immersion up to 6 weeks, no surface degradation was observed [compare Figs. 10 and 11(a)]. Only at very high magnification (125,000 ×), the fiber immersed in the alkaline media for 3 weeks showed some surface roughness. However, no cracks were observed at any time.

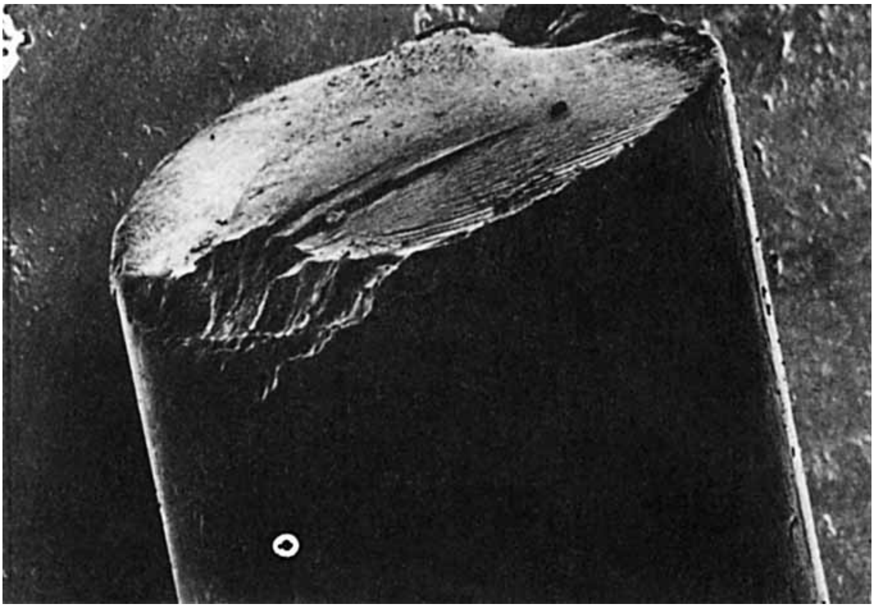
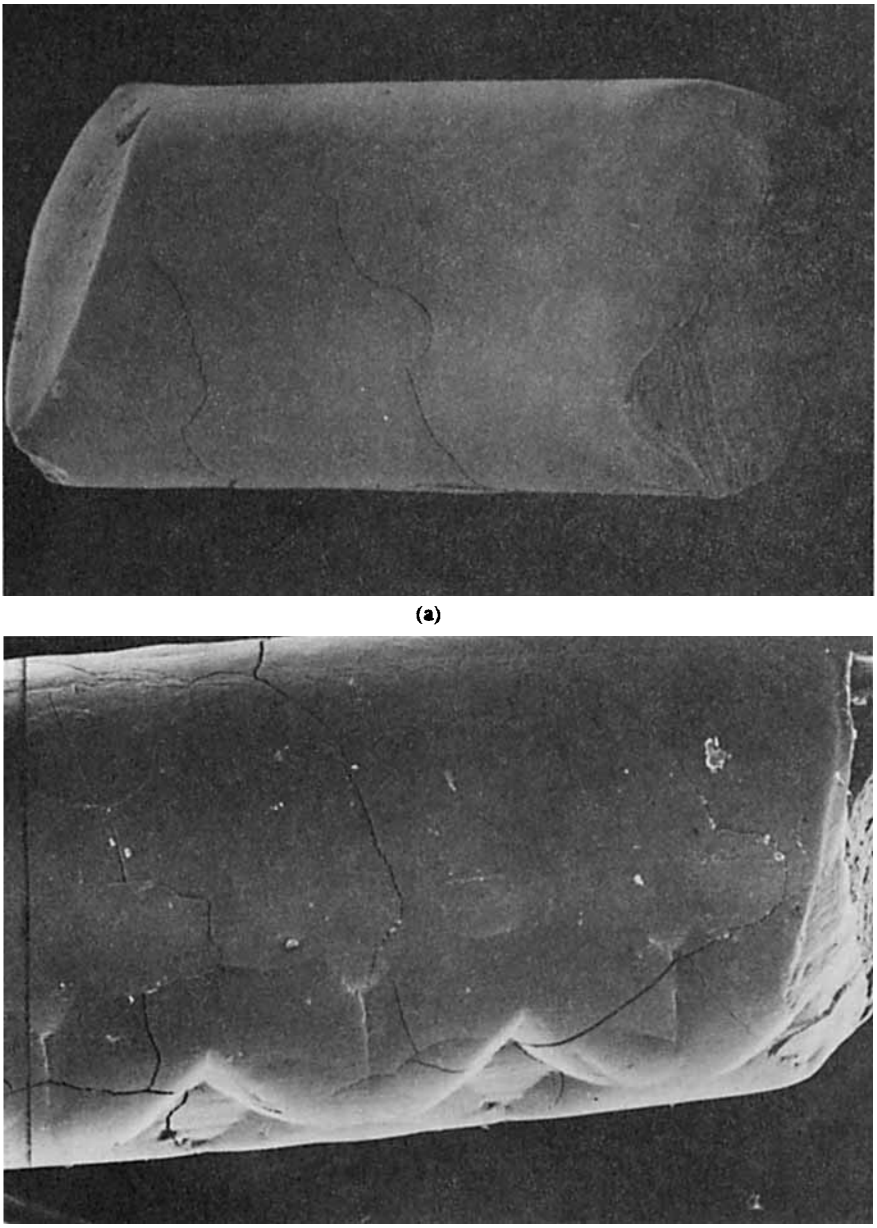


Fig. 7. Photomicrograph of the pellet surface at day 0 (50 ×).



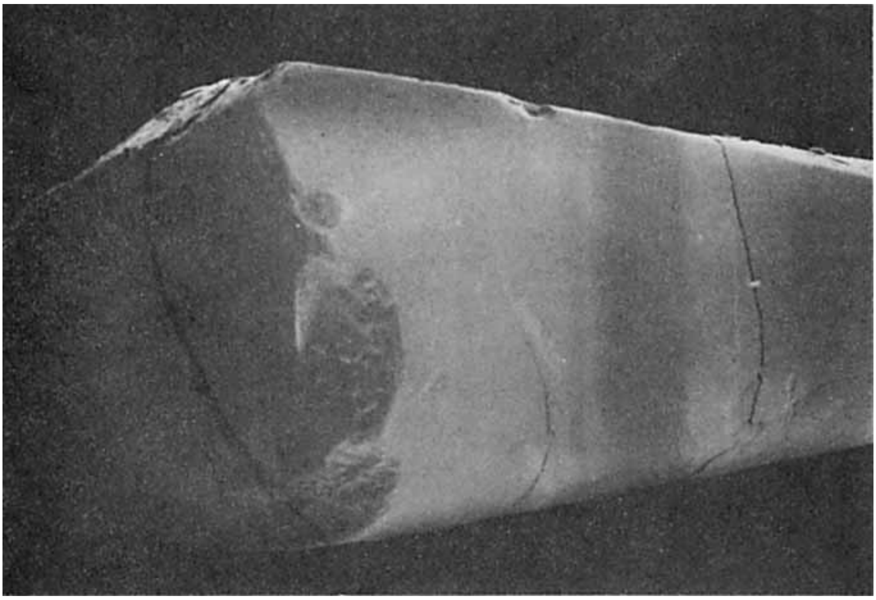
(a)

(b)

Fig. 8. Photomicrographs of the pellet surface after: (a) 7 days, (b) 14 days, (c) 28 days, (d) 42 days, and (e) 56 days *in a buffer of pH* 4.7 (50 ×).

DISCUSSION

Poly(glycolic acid) can undergo hydrolysis both in the presence of the hydrogen as well as the hydroxyl ions.[19] Hydrolyis usually leads to the rupture of the ester linkages which results in the catastrophic loss of tensile strength and other mechanical properties.



(c)

(d)

Fig. 8. (*Continued from the previous page.*)

Since the hydrolysis of poly(glycolic acid) is a heterogeneous, noncatalyzed, solid–liquid reaction, there is a possibility that the reaction may be diffusion-limited. However, the mass loss, crystallinity, and tensile data show no dependence of the rate of hydrolysis on the fiber diameter for the acidic as well as the alkaline case. The SEM photomicrographs also showed no significant surface deterioration in the case of the fibers. Similar studies with poly-


(e)

Fig. 8. (*Continued from the previous page.*)

(ethylene terephthalate)[18] and poly(lactic acid)[19,20] showed that the chemical degradation was independent of the fiber diameter, and that the reaction rates were at least 2–3 orders of magnitude slower than the diffusion rates. Thus, the hydrolysis of simple polyesters, such as poly(glycolic acid), appears to be a chemically controlled reaction and is neither diffusion-limited nor is it limited to the fiber surface.

The acid and the alkaline hydrolysis of poly(glycolic acid) is believed to take place by the following mechanisms[19]:

$$\mathrm{H{-}CHOH{-}COOH} + \mathrm{H}^+ \leftrightarrow \mathrm{H{-}CHOH{-}COOH^+H}$$

$$\mathrm{H{-}CHOH{-}COOH^+H} \leftrightarrow \mathrm{H{-}CHOH{-}C^+{=}O} + \mathrm{H_2O}$$

$$\mathrm{H{-}CHOH{-}COOH} + \mathrm{OH}^- \leftrightarrow \mathrm{H{-}CHOH{-}COO^-} + \mathrm{H_2O}$$

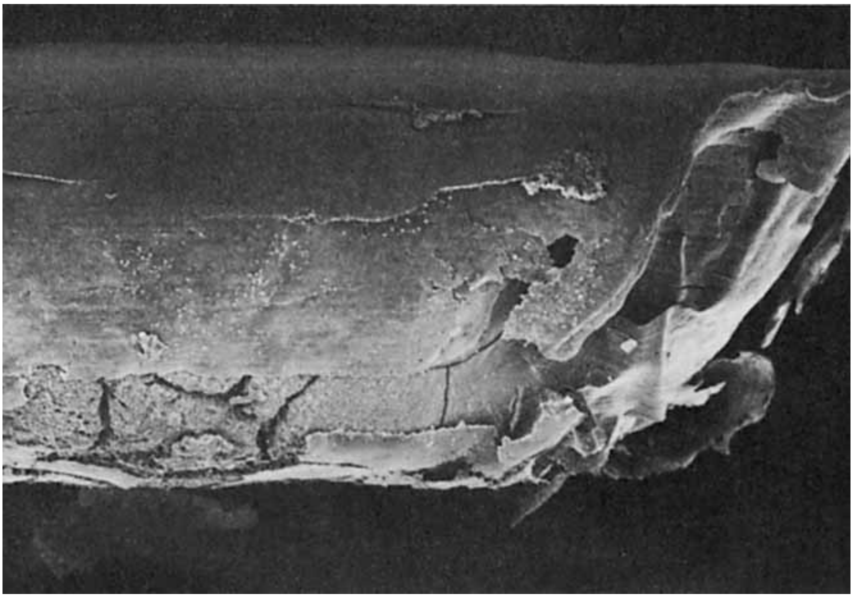
where the rate of the reaction $= -k(\mathrm{PGA})\,(\mathrm{H}^+ \text{ or } \mathrm{OH}^-)$. Since the pH of the medium remains constant, one can say that rate $= -k'$ (ester links)
or

$$\frac{dc}{dt} = -k'c$$

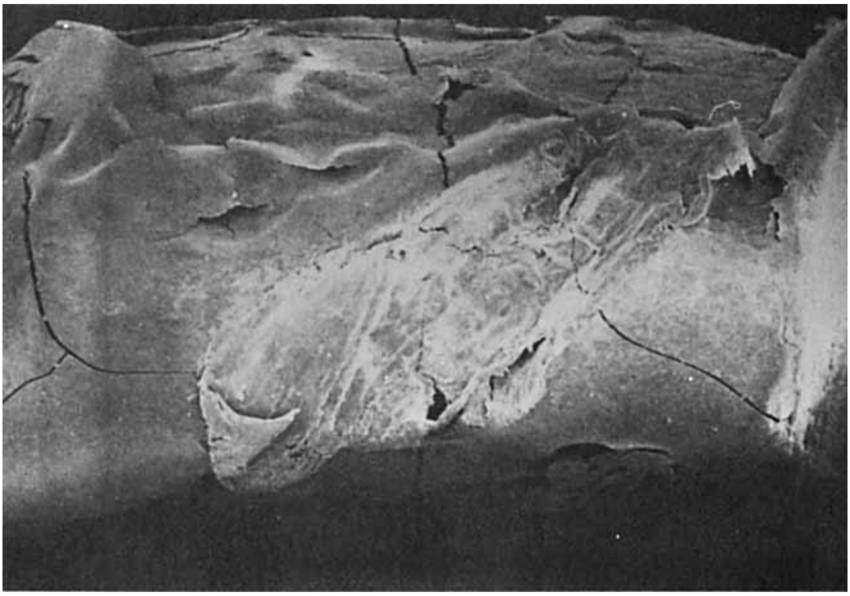
or

$$\ln\frac{c}{c_0} = -k't$$

If, for purposes of comparing the rates of reaction alone, one approximates the ratio of ester linkage concentration by m/m_0, where m/m_0 is the fraction



(a)

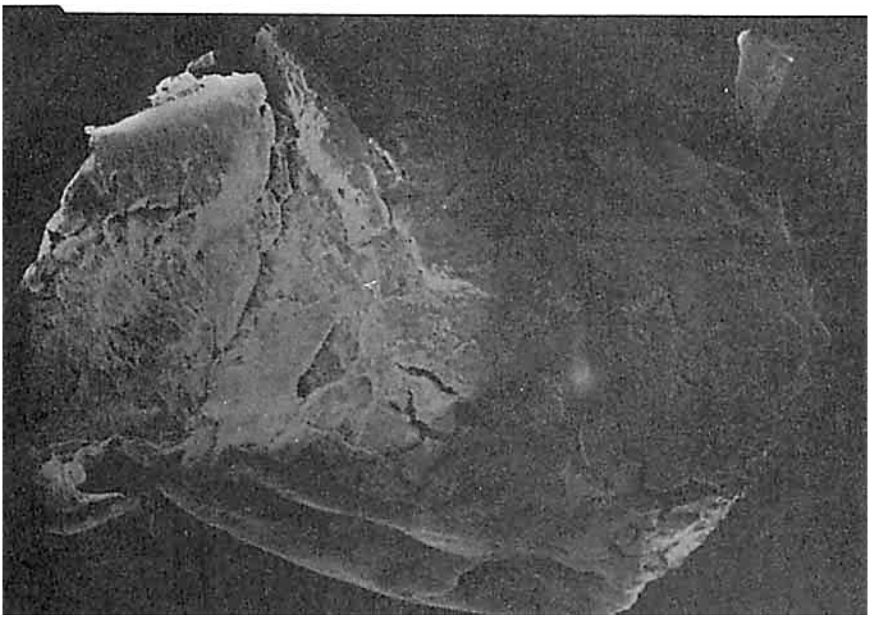


(b)

Fig. 9. Photomicrographs of the pellet surface after (a) 7 days, (b) 14 days, (c) 28 days, (d) 42 days, and (e) 56 days in a buffer of pH 10.6 (50 ×).

of polymer mass remaining, one can plot ln m/m_0 vs. time and obtain k' from the slope of the resulting straight line. Division of k' by the acid concentration would then yield the second-order rate constant k.

The second-order rate constants for the pellets and the fiber were calculated from the mass loss data and are displayed in Table III. In general, the rate constants increased with increasing pH, and were at least 1 order of magni-



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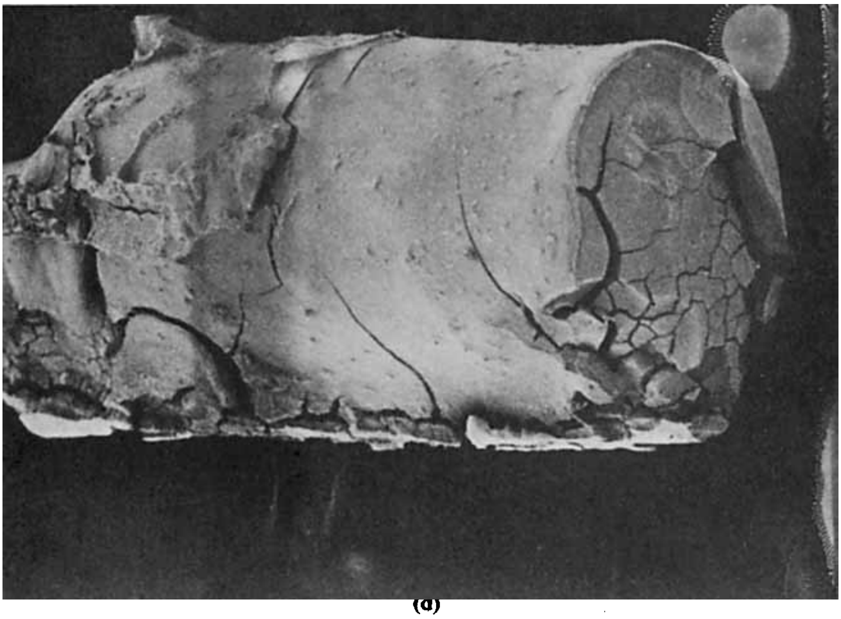
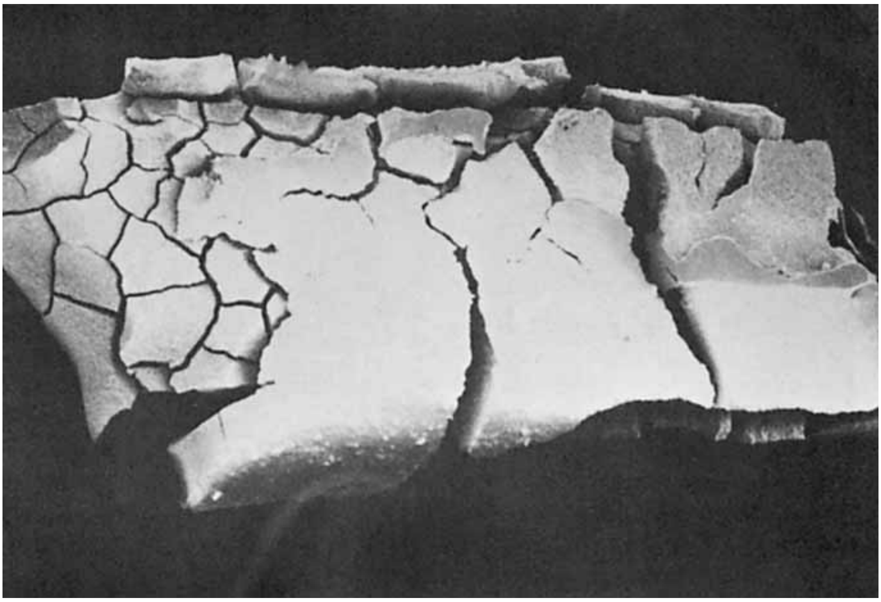


(d)

Fig. 9. (*Continued from the previous page.*)

tude higher in the alkaline media (pH 10.6) than in the acidic media (pH 4.7) for all cases. The rate of reaction was much faster in the pellets than in the fiber, presumably because of the lack of long range order in the former case. The physical properties of the starting materials prove that this is indeed the case. Although the commercially obtained pellets were slightly more crystalline (38%) when compared with the melt-spun fiber (35%), small angle X-ray



(c)

Fig. 9. (*Continued from the previous page.*)

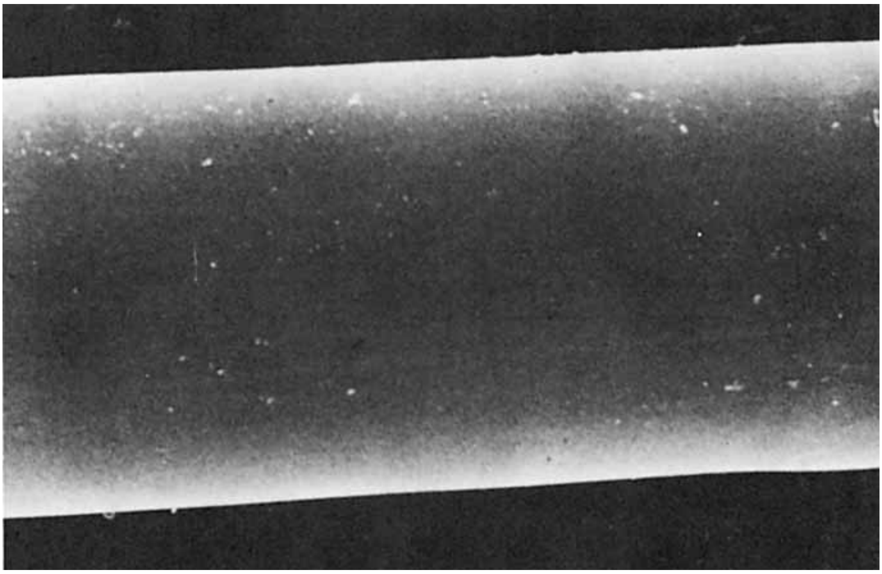
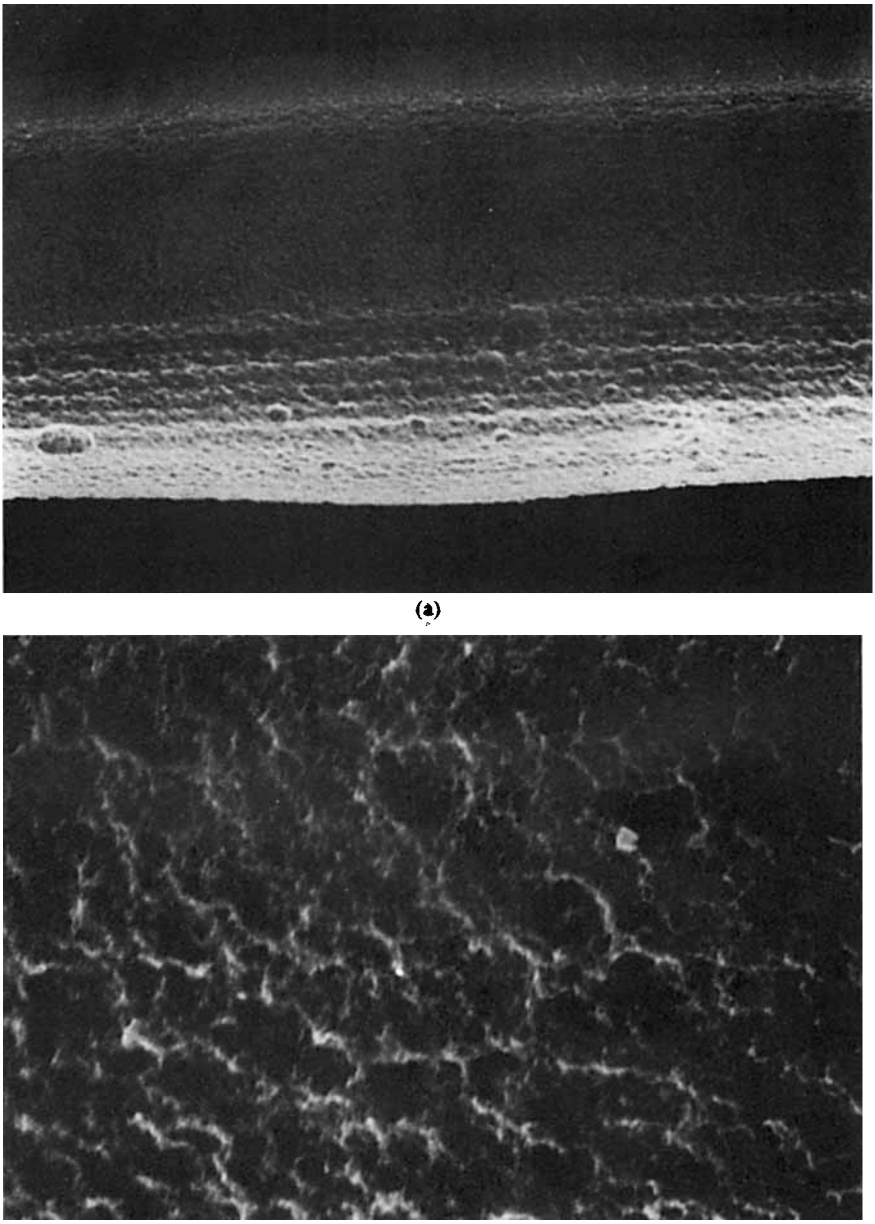


Fig. 10. Photomicrographs of the fiber surface at day 0 (250 ×).



(a)

(b)

Fig. 11. Photomicrographs of the fiber surface (a) 250 × and (b) 125,000 × after 28 days in a buffer of pH 10.6

diffraction showed the lack of orientation in the case of pellets, and this appears to lead to the drastic degradation of the pellets as compared to the fibers. It, therefore, appears that morphological considerations other than those of crystallinity alone influence the rate of polymer hydrolysis. Since polymer molecules get stretched and oriented in the process of melt spinning, we conclude that polymer chain orientation plays an important role in

TABLE III
Rate Constants for the Hydrolysis of Poly(glycolic Acid) in Acidic and Basic Media

		Rate constants (Li mol^{-1} day^{-1}) × 10^3 for		
pH	Pellets	Fiber (0.0203 cm)	Fiber (0.0155 cm)	Heat-treated fiber (0.0203 cm)
4.7	13.00 ± 0.24	3.16 ± 0.08	4.16 ± 0.21	5.88 ± 0.26
7.0	17.20 ± 0.93	8.64 ± 0.23	7.00 ± 0.42	n/a[a]
9.2	58.88 ± 3.83	12.84 ± 1.49	n/a[a]	n/a[a]
10.6	148.96 ± 9.02	46.08 ± 1.79	45.08 ± 1.46	53.32 ± 3.99

[a] n/a = data not available. The data are erratic and, hence, the values are not reported.

resisting hydrolytic deesterification. That the reaction rate constants for the heat-treated fiber are larger than those of the non-heat-treated one is most likely due to chain disorientation in the process of annealing. This assertion is supported by literature data[21] on the heterogeneous hydrolysis of poly(ethylene terephthalate).

Within the range of experimental error, the reaction rates were independent of the fiber diameter for the entire range of pH studied. The heat-treated fiber showed a slightly faster rate of reaction than its non-heat-treated counterpart, and this may be due to loss of order resulting from the thermal treatment.

The degradation of mechanical properties appears to be independent of the rate of mass loss. Although heat treatment of the fiber resulted in higher absolute values of the tensile properties than the non-heat-treated fiber, it did not affect the rate of mechanical degradation of the fiber.

The above observations and the general trend of the deterioration of mechanical properties can be rationalized by the microfibrillar model of the fiber. The model assumes that the fiber consists of well-aligned microfibrils in which alternate crystalline and amorphous regions are arranged in a direction parallel to the fiber axis. The tie chain molecules which connect the crystalline blocks together are believed to support and transmit tensile loads to the crystalline regions.

The disordered amorphous regions are most vulnerable to attack by the buffers. The diffusion of the liquid medium into the polymer results in the initial swelling seen in Figure 2. That the pellets swell more than the fibers suggests that the mass loss for the former would be more than that for the latter. This is indeed clear from a comparison of Figure 1(a) with Figure 1(b). Since the hydrolysis reaction would occur randomly along the polymer chain, the number of low molecular weight molecules would be small initially but grow rapidly leading to the rapid mass loss witnessed in Figure 1(a). As the amorphous regions are attacked and mass is lost due to dissolution of the low molecular weight fragments, the fraction of material that is crystalline has to increase, as seen in Figure 3. Eventually, the crystalline regions are attacked as well, more so at the higher pH, and maxima are observed. Figures 5 and 6 merely document the deterioration of the fiber tensile properties due to polymer chain scission; the plateaux observed in Figure 6 hint at the presence of a two-step degradation process postulated above.

CONCLUSIONS

The *in vitro* degradation of PGA was followed by observing the changes in the mass, dimensions, crystallinity, tensile strength, and surface structure. The profile of mechanical degradation was found to be independent of the initial fiber diameter. There was a steady decrease in tensile strength with time, and the alkaline medium had more drastic affect on the mechanical properties than the acidic or neutral media. It was found that one could increase the absolute value of the tensile strength by heat treatment, and, although the profile of mechanical degradation was slightly erratic, the absolute value of the breaking stress for the heat-treated fiber was always greater than that of the non-heat-treated counterpart.

The mass loss profiles for the PGA pellets and the PGA fibers showed that orientation of the fiber was more effective in decreasing the degradation rates than crystallinity. The degradation of PGA, in both the acidic and the alkaline media, was found to be a chemically controlled second-order reaction. The SEM photomicrographs conclusively showed that the degradation of PGA fibers is not a surface reaction which, although contrary to the data reported in literature,[3,10] helps explain the independence of the degradation rates on the initial diameters.

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