Hydrolytic Degradation of Polyglycolic Acid: Tensile Strength and Crystallinity Study

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Synopsis

The hydrolytic degradation of polyglycolic acid (PGA) was studied by examining the changes of tensile strength and the level of crystallinity of the suture material. It was found that the breaking stress decreased from 6.369×10^{-1} at 0 day to 3.97×10^{-3} Newton/Tex at 49 days. The sigmodial shape of the stress–strain curves gradually disappeared with increase in the duration of *in vitro* degradation. The endpoint titration method used to assess the degree of degradation beyond the period of measurable tensile strength showed that the percent of PGA degraded were 42, 56, and 70% at 49, 60, and 90 days, respectively. The level of crystallinity of PGA at various durations of degradation exhibited an initial increase in the degree of crystallinity from 40% at 0 day to an upper limit of 52% at 21 days, then gradual decrease to 23% at 90 days. This observation is essentially parallel to hydrolysis of cellulose and polyethylene terephthalate. The concept of microfibrillar structure of fibers provides the basis for the proposed degradation mechanism of PGA *in vitro*. It is believed that degradation proceeds through two main stages which are different in rate of degradation.

INTRODUCTION

A typical application of fibrous materials in biomedical science is as suture materials for closing surgical wounds. Two synthetic biodegradable polymeric materials have been successfully developed as absorbable suture materials and have become widely available. They are polyglycolic acid (Dexon) from American Cyanamid Co. and its lactide copolymer (Vicryl) from Ethicon. Polyglycolic acid (PGA) is polymerized through ring-opening polymerization of glycolide. The properties of the resulting polymer have been reported by Chujo and coworkers[1,2] and Frazza and Schmitt.[3] Polyglycolic acid is the simplest aliphatic polyester; it has a melting point ranging from 224 to 227°C. Because of its simple chemical structure and stereoregularity, it usually occurs in the semicrystalline form. Chatani and coworkers[4] determined the crystal structure of PGA by x-ray diffraction; the dimensions of the orthorhombic unit cell are a = 5.22 Å, b = 6.19 Å, and c (the fiber axis) = 7.02 Å. Two macromolecular chains in planar zig–zag conformation passing through the unit cell permit tight molecular packing and the close approach of ester groups.

The requirements for a suture material depend to some extent on the type of wound to be closed. The suture material must, in any case, retain adequate tensile strength over the critical period of wound healing; it also should induce minimal tissue reaction that might interfere with the healing process. Because of PGA hydrolytic instability, it loses tensile strength as it biodegrades. The rate at which PGA sutures weaken as they are absorbed is a vital factor in their usefulness in wound healing. For noncritical surgical conditions such as small-vessel ligature or the coaptation of uncomplicated wounds in rapidly

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healing tissues, the rate of loss of tensile strength is probably of little importance. For more critical surgical wounds, however, the difference among suture materials in the rate of loss of tensile strength may be highly significant, particularly in tissues slow to heal, for example, those with neoplasia, hypoproteinemia, etc. Thus, the rate at which PGA sutures weaken as they are biodegraded is a vital factor in their usefulness in would healing and reflects the importance of the need to understand the phenomena.

Published reports on PGA biodegradation have reached two general conclusions. First, PGA sutures exhibit virtually no strength by about 21 days after implantation.[5–10] However, Katz and Turner reported that PGA lost strength much more slowly through the first 11 days than did catgut sutures.[8] Second, the hydrolytic degradation of ester bonds is apparently the means by which PGA is degraded.[9,11]

Although significant progress toward the understanding of PGA biodegradation has been achieved mainly through clinical investigation, a coherent picture of the biodegradation mechanism of PGA is still unavailable because of the lack of important information relating to the basic properties of this polymer. A few research reports published very recently have begun to recognize the importance of gaining more fundamental information on this material in order to facilitate a better understanding of the biodegradation mechanism of PGA.[5,11–15]

Since tensile strength of PGA after several weeks of degradation becomes too weak to measure, it is difficult to assess the degree of degradation in terms of the loss of tensile strength after that period of degradation. Although visual comparison of the cross-sectional area of sutures had been used to assess the extent of degradation,[9] considerable uncertainty has resulted, particularly because of the differences in microspaces between the multifilaments of a strand and those between the strands that make up the braid. It is believed that the use of a cross-sectional area as a means for determining the degree of degradation is more appropriate in monofilament than in braided sutures. It has been reported previously that the degradation products of PGA are of acidic nature[15]; therefore, neutralization titration can be used to assess the degree of degradation of PGA beyond the measurable tensile strength stage.

It is the purpose of this article to report how the crystallinity of PGA, a basic property of a semicrystalline polymer, changes during the *in vitro* degradation; how the decrease in tensile strength is related to the changes in crystallinity; and how to assess the degree of degradation quantitatively after tensile strength becomes unmeasurable. The information gained could offer a much-needed insight into the degradation process in PGA.

EXPERIMENTAL PROCEDURE

Sterilized Dexon sutures from American Cyanamid in size 2-0 were used in this study. Prior to immersion, sutures of 17 in. long were stored in a dessicator filled with a mixture of P_2O_5 and anhydrous $CaSO_4$. Distilled water (pH = 6.8) was used as the immersion medium because it was reported that the only requirement for PGA degradation is an aqueous environment.[16] Thus, its use could eliminate the complex condition involved in *in vivo* and allows us to examine the desired property adequately. All lab wares were sterilized by autoclave

and the glassware containing 30 ml of distilled water and 0.191313 g of Dexon sutures were sealed in a septical hood before incubation. This precaution was taken because of the reported fact that the presence of bacteria has been shown to reduce the rate of degradation of PGA, both *in vitro* and *in vivo*.[17]

The suture specimens were immersed in each medium for 7, 14, 21, 28, 49, 60, or 90 days, and kept at 37 ± 1°C in a constant-temperature oven. At the end of each immersion period, the level of crystallinity, tensile strength of the specimens, and pH of the solutions were determined by differential scanning calorimeter, Instron tensiometer, and pH meter, respectively.

For crystallinity measurement, 7–8 mg of dry PGA sutures were weighed with a Cahn microbalance and then packed in an aluminum sample pan; the pan was then crimped shut. A Perkin–Elmer differential scanning calorimeter (DSC) model 1B was used, calibrated with the standard Indium supplied by the manufacturer. The specimens were placed inside the sample holder of the DSC and kept at 167°C for 3 min to reach thermal equilibrium. The DSC was programmed to increase the temperature at a scan speed of 10°/min, a range of 16, and a recording chart speed of 1 in./min. A melting curve would be produced during the crystallization–melting transiton. After the baseline had been attained, the heat of fusion, ΔHu, and the percentage of crystallinity were calculated in the usual manner.[18,19] A value of 49.34 cal/g for ΔHu of 100% crystallized PGA was used to calculate the level of crystallinity.[20]

The tensile properties of suture materials were determined on an Instron tensometer table model TM at 21 ± 1°C and 65 ± 2% RH. The gauge length was 7.62 cm; crosshead speed, 2.54 cm/min. Slippage was avoided by making two throws of surgical knot which were tied just above the upper jaw of the tensometer, then the suture was wound around a metal pin at the base of the lower jaw, pulled through the jaw again, and clamped to it. Coplanar jaws lined with neoprene rubber were used. Each test was repeated five times. The pH of the solution was measured by a Corning pH meter, model 12. The pH meter was calibrated with Fisher's certified buffer solution at pH = 7.0 and 4.0. The solutions after 49 days immersion were titrated with 0.1*N* NaOH, and the concentration of the degradation products was thus calculated. The percent of degradation was calculated by dividing the amount of degradation products in grams by the initial amount of sutures before immersion.

RESULTS

The stress–strain curves of Dexon 2-0 at various stages of degradation in aqueous solution are shown in Figure 1. As suggested previously, a stress unit called Newton/Tex was used instead of Pascal.[15] Tex is defined as the weight in grams of a fibrous material of 1000 m long. A series of stress–strain curves, all of similar shapes, was observed at the various durations of immersion. The breaking stress decreased from 6.369×10^{-1} at zero day to 5.536×10^{-1} at 7 days, 3.07×10^{-1} at 14 days, 1.43×10^{-1} at 21 days, 5.58×10^{-2} at 28 days, and 3.97×10^{-3} N/Tex at 49 days. The stress–strain curve at 49 days was too small to be graphed in Figure 1. The corresponding percent of retention of original tensile strength were 87% at 7 days, 48% at 14 days, 23% at 21 days, 9% at 28 days, and 0.6% at 49 days. The largest drop in tensile strength occurred between 7 and 14 days; more than half was lost at 14 days. The breaking strain also decreased

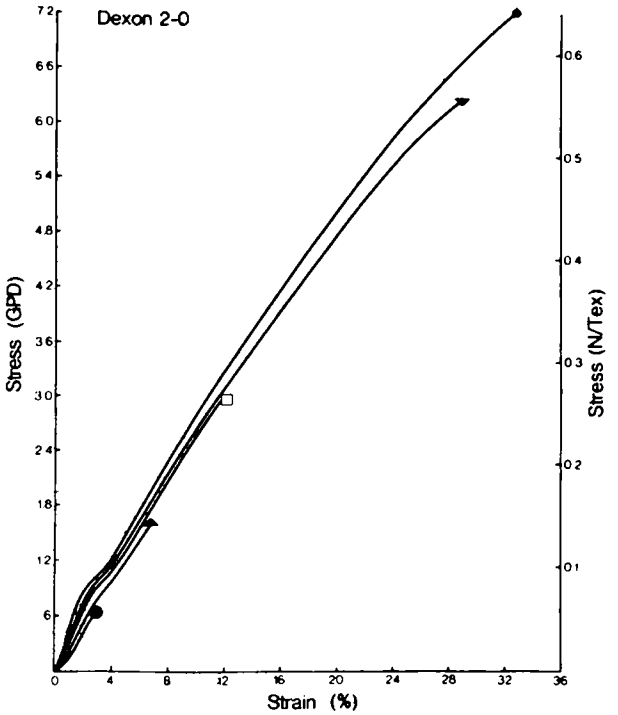

Fig. 1. Stress–strain curves of Dexon 2-0 suture immersed in distilled water at 37°C. ⊙, 0 day; ▲, 21 days; ▼, 7 days; ●, 28 days; ■, 14 days.

with duration of immersion; and the values were 32.5% at zero day, 29% at 7 days; 14% at 14 days; 7% at 21 days; and 2.7% at 28 days. Similarly, the largest drop in strain occurred between 7 and 14 days.

The shapes of the stress–strain curves were similar prior to 14 days of degradation. A well-defined plastic flow region beyond yield point was retained in this period of hydrolytic degradation. As degradation proceeded further, however, this characteristic region disappeared, as shown at 21 and 28 days degradation. The initial moduli of the stress–strain curves decreased with increasing duration of degradation.

The endpoint titration method used to assess the degree of degradation of PGA beyond the period of measurable tensile strength showed that the percent of PGA degraded were 42, 56, and 70% at 49, 60, and 90 days, respectively. Although almost no tensile strength was detected at 49 days of immersion, more than half of the original suture material was still undegraded. Even after 90 days degradation, 30% of PGA remained undegraded.

The degree of crystallinity of PGA at various durations of immersion showed a rather unique feature. There was an initial increase in the degree of crystallinity from 40% at 0 days to an upper limit of 52% at 21 days, then gradual decrease to 23% at 90 days. Consequently, a maximum in crystallinity was observed as the duration of immersion proceeded. The decrease in the level of crystallinity was not drastic, particularly between 60 and 90 days of degradation.

A summary of tensile strength, percent of degradation, and level of crystallinity is given in Table I.

TABLE I
In vitro Degradation Data of Dexon 2–0 Suture

Property	Duration of Immersion, days							
	0	7	14	21	28	49	60	90
Retention of tensile strength, %	100	87	48	23	9	0.6	—	—
Retention of elongation, %	100	89	43	22	8	2	—	—
Level of crystallinity, %	40	—	45	52	42	33	26	23
Degradation, %	—	—	—	—	—	42	56	70

DISCUSSION

One of the basic physical properties of a semicrystalline polymer like PGA is the degree of crystallinity. The importance of this property on polymer degradation has initially been recognized by Atlas and Mark on the hydrolytic degradation of cellulose.[21] Since hydrolytic degradation would destroy the crystalline structure of the polymer, it is believed the level of crystallinity must change with duration of degradation.

Research on semicrystalline polymers have given rise to many models of fiber structure, such as the model proposed by Bonart and Hosemann[22] and recently revised by Kausch–Schmeling,[23] the fringed micelle fibrillar model suggested by Hess, Mahl, and Guter,[24] and finally the microfibrillar model proposed by Peterlin.[25–28] Among all the models proposed, the microfibrillar one which combines the concepts of the folded chain and fringed micelle models has taken account of the space requirement for the accommodation of tie-chain segments[29] as well as the anisotropy of mechanical properties.

On the basis of this microfibrillar model as shown in Figure 2, the basic element is the microfibrils in which alternative crystalline and amorphous regions arrange in the direction of the fiber axis. In each microfibril, some polymer chains will pass through several crystalline and amorphous regions along the fiber axis and other chains will return to the crystallite of original but not necessarily in juxtaposition. The crystalline regions are composed of chain sequences in ordered or preferred conformation. The amorphous regions containing chain folds, chain ends, and tie-chain segments are in characteristically disordered conformations. They have thermodynamic, spectral, and mechanical properties which are relatively similar to those in the pure melt. In the microfibrillar model, two types of tie-chain segments can be formed: interfibrillar and intrafibrillar as indicated by (A) and (B) in Figure 2. Their major function is to tie crystalline blocks together and to support and transmit tensile loads to the crystalline regions.

This model of fiber structure provides the basis for the proposed degradation mechanism of PGA *in vitro*. It is believed that degradation proceeds through two main stages: the first stage is in the amorphous region; the second in the crystalline regions. When the material is immersed in aqueous solution, the water molecules which diffuse through the polymer accommodate themselves readily in the amorphous zone, and not at all in the crystalline zone. The structure of the amorphous zone is the most open of the two: water penetrates easily. The crystalline region is highly packed, with a densely ordered crystalline structure; little or no water penetrates there.

Because of this difference, hydrolytic degradation starts in the amorphous regions, as the tie-chain segments in these regions degrade into fragments. This

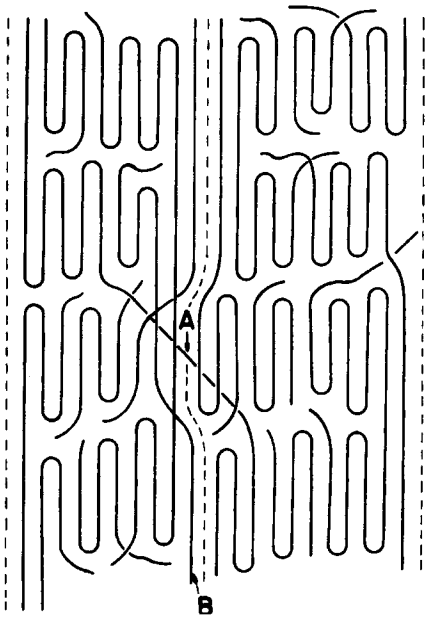

Fig. 2. Schematic drawing of microfibrillar structure of fibers: (A) interfibrillar, (B) intrafibrillar tie molecules. (Courtesy of *Tex. Res. J.*)

chain scission results in a lesser degree of entanglement of long-chain molecules located in the amorphous regions. Therefore, the remaining undegraded chain segments in the amorphous regions obtain better chain mobility; they can move and reorganize themselves from a disordered to an ordered state. Further crystallization is induced and an increase in crystallinity is thus observed.

This observation is not an isolated case. Similar results of increase in the degree of crystallinity due to the hydrolytic degradation of cellulose,[30] and poly(ethylene terephthalate),[31] and other kinds of degradation of bulk and solution crystallized polyethylene[32–35] have been reported by several different groups of investigators. In the hydrolytic degradation of cellulose and poly(ethylene terephthalate), mineral acids were used to selectively hydrolyze the polymers; the noncrystalline regions were preferentially degraded and removed. Induced crystallization was found which is shown by an increase in the crystallinity. Therefore, two competing processes, hydrolysis and induced crystallization, were observed in the hydrolytic degradation of PGA.

Along the scission of the chain segments which connect the crystal blocks in the axis direction, lower axial elastic moduli and tensile strength should be found. This was exactly what we observed.

When all the amorphous regions have been removed by hydrolysis, the second stage of degradation starts. The degree of crystallinity would reach a maximum at the end of the first-stage degradation; and it would then start to decrease, as hydrolysis destroyed the crystalline lattice. Owing to the existence of imperfections and defected crystalline regions, however, a few portions of the crystalline region could also be destroyed simultaneously, but more slowly, during the hydrolytic degradation of the noncrystalline regions. The fact that no level of crystallinity higher than 52% could be obtained demonstrates that both regions

are attacked in the later stages of hydrolysis. Consequently, a strict demarcation of the second-stage hydrolytic degradation from the first stage is difficult to assess. From the observed changes of the degree of crystallinity, the first-stage degradation was predominant during the 21-day immersion period, while the second-stage degradation became important after the 21-day degradation period. The first-stage degradation still proceeded, but at a much lesser degree, until all the tie-chain segments located in the amorphous regions were degraded. The material then exhibited no tensile strength. This corresponded to approximately 49 days *in vitro* degradation in this study.

The 42% degradation at 49 days suggests that approximately 60% of the original material remained after 49 days immersion. The degraded products predominately came from the noncrystalline region of the semicrystalline polymer. An examination of the initial degree of crystallinity of PGA at zero day further demonstrates this point of view.

The advantage of using the acid–base titration method for assessing the extent of degradation, particularly in the degradation period that tensile strength becomes unmeasureable, is clearly evident. It provides quantitative data that are needed for acquiring an overall picture of PGA degradation. After 60 days degradation, there was still slightly less than 50% of the suture remaining undegraded. This may be why it is commonly observed that the gross morphological shape of the suture is still largely preserved after a prolonged period of degradation, even when the tensile strength of the suture has already become zero.

The gradual disappearance of the sigmodial shape (more specifically, the plastic flow region) of the stress–strain curves with increase in the duration of degradation might be due to the removal of the noncrystalline portion of the fiber. In the plastic flow region, some of the most highly strained crosslinked chain segments in the noncrystalline regions break first when the applied stress increases; this results in a greater degree of straightening of the chain segments located in the noncrystalline regions. As a result, extension becomes less difficult and a plastic flow region is observed. Upon hydrolytic degradation of PGA, the chain segments in the noncrystalline regions will initially degrade into smaller fragments. Consequently, molecules are shorter and become less entangled. This shortening of the molecules results in a lesser degree of straightening of the molecules in the noncrystalline regions with external force. A less profound plastic flow region would thus result as observed in Figure 1.

It is proposed that a better understanding of the PGA degradation mechanism could be achieved by correlating some fundamental physical properties with the variation of mechanical properties of the material. Although the previously proposed mechanism is oversimplified and lacks details, it does suggest several additional approaches to investigate further the hydrolytic degradation phenomena of PGA for a better understanding of the mechanism and to aid in the design of even better materials. Those approaches are currently under investigation.

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