Degradation phenomena of two linear aliphatic polyester fibres used in medicine and surgery

C. C. Chu

Department of Design and Enviromental Analysis, Martha Van Rensselaer Hall, Cornell University, Ithaca, New York 14853–0218, USA

The changes of pH levels and tensile breaking strength of two synthetic biodegradable polymers, polyglycolic acid and poly(glycolide–lactide) were examined as a function of time of immersion and γ irradiation in *in vitro* conditions. It was found that (1) the pH of the solution containing the polymers would decrease with time as degradation proceeded; (2) all of the pH–time curves exhibited sigmoidal shape and consisted of three distinctive regions - early, accelerated, and later stages; (3) the lengths of these three regions were a function of γ irradiation and increasing the radiation dosage shortened the time required for the accelerated region to occur; and (4) the appearance of the drastic pH changes coincided with loss of tensile breaking strength. It was suggested that the destruction of the tie-chain segments in the first stage of degradation and the subsequent relaxation of crystal blocks were related to the drastic decrease in pH levels and loss of tensile breaking strength.

INTRODUCTION

All synthetic polymers are subject to degradation to different levels. For those polymers specifically designed for use in medicine and surgery, hydrolytic and enzymatic catalysed degradation is probably the most important concern. As a result of such degradation, not only the structure and properties of these polymers change with time but also their failure could severely hamper the wellfare of human beings. Clinical cases of the failure of implanted materials have been reported in the closure of surgical wounds, and the reconstruction of ligaments and blood vessels[1,2].

Degradation of synthetic polymers inside the human body or in a simulated biological environment can be intentional and unintentional. In the former, polymers are intentionally designed to degrade within the body for the purpose of either minimizing adverse reactions, such as foreign body reaction that the polymer could cause or serving the designated function through degradation. The polymers used to close wounds, and to deliver drugs in a controlled manner are two typical examples.

A recent series of studies of the degradation phenomena of polyglycolic acid[3–11], one of the synthetic degradable polymers, have not only improved the understanding of the degradation mechanism of this polymer but have also allowed the unique examination of the structure and morphology of fibrous polymers. However, all these studies were based on the examination of the change of mechanical properties of polymers with time. Rarely, if ever, were the degradation products of these polymers studied as a function of time in order to elucidate the degradation mechanism. One of the advantages of this approach is the ability to obtain degradation information beyond the measurable mechanical properties, such as

tensile strength. The degradation products of PGA have been shown to be glycolic acids. The continuous release of this acid into the medium during degradation would certainly change the pH level of the medium with time. Thus, the purpose of this study is to examine this pH change as a function of time, γ-irradiation treatment and polymer types; and compare the pH–time profiles with tensile strength data.

EXPERIMENTAL

Polyglycolic acid (PGA) and poly(glycolide–lactide) (PGL) in the form of sutures were obtained from David and Geck, and Ethicon, respectively. The corresponding trade names are Vicry[R] for the copolymer and Dexon[R] for the homopolymer. They have a multifilament braided structure. The copolymer (PGL) is randomly copolymerized from glycolide and L(-)lactide at a molar ratio 9:1. Because of their hydrolytic instability, they are double-sealed and packaged on both plastic film and aluminium foil.

Unopened packets of PGA sutures, obtained from the manufacturer, were subjected to $Co^{60}\gamma$ irradiation at a constant rate of 2.5 Mrad per 2 h of exposure. The dosages were 5, 10 and 20 Mrads. Undesirable oxidative degradation of these fibres during the radiation treatment was kept at a minimal and insignificant level by the manufacturer's double-sealed packaging of these fibres. The sealed packaging consists of both plastic film and the aluminium foil which could reduce diffusion of O_2 into the fibre specimens.

After Co^{60} radiation treatment, one suture sample 6 inches long (0.018 g) was placed in a glass jar filled with 50 ml of distilled sterile water of pH ranging from 6.05 to
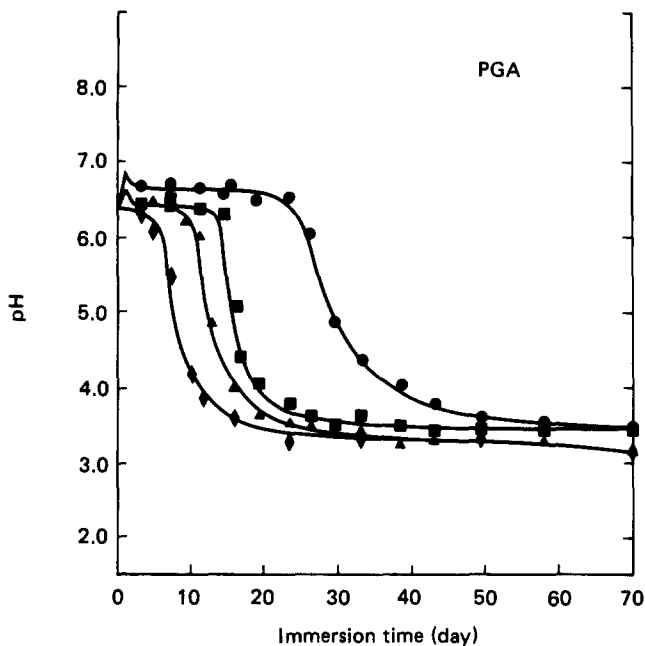
Figure 1 Change of pH levels of polyglycolic acid braided fibres as a function of in vitro immersion time. (●): 0 Mrad, (■): 5 Mrad, (▲): 10 Mrad, (◆): 20 Mrad

6.43. The jars were then sealed and placed in a hot-air circulated oven maintained at 37°C. All glassware was sterilized using an autoclave before use, to reduce bacterial contamination. The pH of the solution after predetermined periods of immersion was measured using a Fischer Accumet Model 630 pH meter. A control consisting of distilled water only (no polymers) was also used to measure the change of pH with time. With the aid of this control, the change of pH solely due to the hydrolytic degradation of these fibrous polymers can thus be determined precisely. The morphological appearance of the samples was also observed along with the pH measurement.

For tensile strength tests, 5 samples 15.24 cm long each were placed in a glass jar filled with 30 ml of phosphate buffer of pH 7.4. They were then placed in the same oven used for the pH study. After predetermined intervals of 7, 14, 21 and 28 days, the samples were removed and tested immediately for tensile strength by the Instron Tensile testing machine. The gauge length was 7.62 cm and crosshead speed was 2.54 cm/min. The tests were performed at 65±2% r.h. and 21±1°C.

RESULTS

The observed changes of pH values with the duration of immersion of the samples irradiated at various amounts of dosage are given in *Figures 1* and *2*. The corresponding tensile strength data are summarized in *Figure 3*. The pH of the control (no polymer sample, distilled water only) remained relatively constant over the period of study, particularly within the first 40 days. The largest fluctuation in pH values was 0.63 in this control.

It is evident that the pH–time curves of all tested samples have several characteristics. First, they all exhibit a sigmoidal shape and consisted of 3 distinctive regions— early, accelerated and later stages. The pH of the solutions remains the same at relatively constant values at both the early and later stages of immersion and the biggest change

in pH (the accelerated region) occurs in the middle stage. The length of the relatively constant pH region is shorter in the early stage than in the later stage and is a function of radiation dosage. In both the sample and control solutions there is a slight increase in the pH level one day after immersion when compared to day 0. The amount of this initial increase was the largest in the control and unirradiated specimens (about 0.34 to 0.27) and is reduced as the dosage of radiation is increased. Secondly, the time needed for the appearance of the accelerated region (defined as t_a) depended largely on the dosage level of γ-
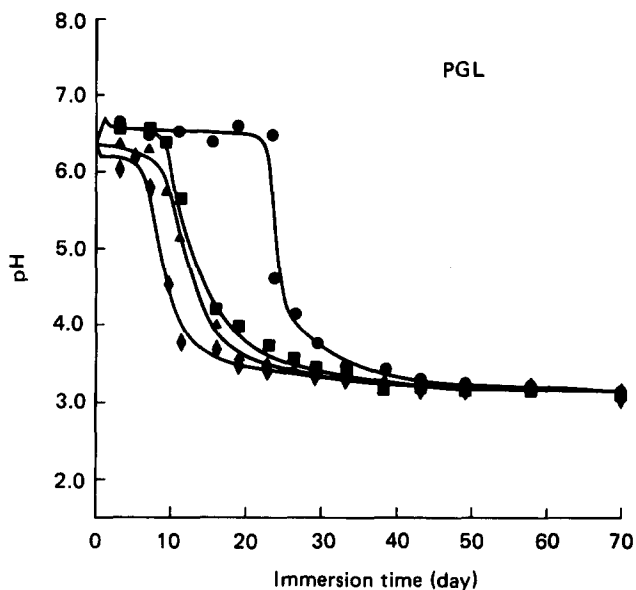

Figure 2 Change of pH levels of poly(glycolide-lactide) braided fibres as a function of in vitro immersion time. (●) 0 Mrad, (■) 5 Mrad, (▲) 10 Mrad, (◆) 20 Mrad
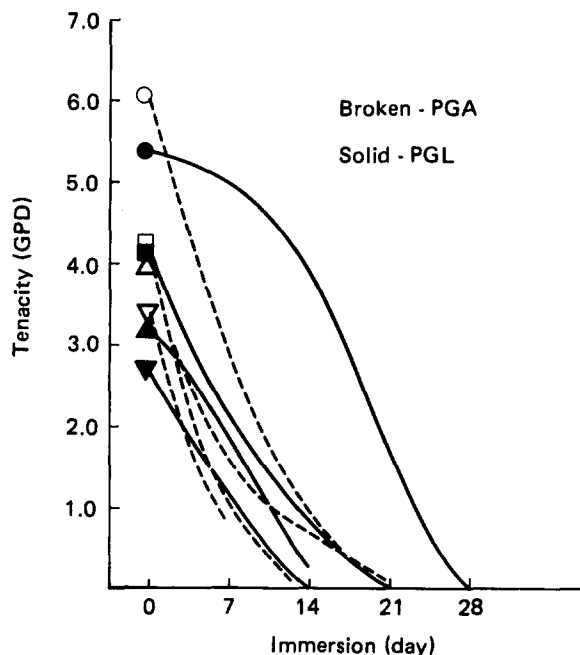

Figure 3 Effect of γ-irradiation on the change of tensile breaking strength of polyglycolic acid and poly(glycolide–lactide) braided fibres after predetermined period of immersion in buffer solution of pH=7.4. (– – –): PGA; (———) PGL; (●) and (○): 0 Mrad; (■) and (□): 5 Mrad; (▲) and (△): 10 Mrad; (▼) and (▽): 20 Mrad

irradiation. Increasing the radiation dosage shortens the time required for the accelerated region to occur. For example, T_c of the homopolymer was about 24, 14, 17 and 6 days for 0, 5, 10 and 20 Mrad treated samples. Thirdly, after the accelerated region, the pH of the solution became relatively constant again. Irrespective of the dosage of γ irradiation, the tail (or later) portions of the pH curves (corresponding to 4 different irradiation dosages), all reached a relatively common constant pH level. This is more apparent in PGL. Depending on the radiation dosages, these final pH levels (at 70 days) ranged from 3.12 to 3.17 for the copolymer and 3.21 to 3.48 for the homopolymer. The samples irradiated at the higher level of dosage, however, reached these final pH values earlier than those irradiated at the lower dosage levels. This was true for both the homopolymers and the copolymers. Fourth, although PGA appeared to maintain generally a slightly higher pH level over the entire duration of study (i.e., 70 days) than its corresponding lactide copolymer, the difference became smaller with increasing the dosage of γ-irradiation. There was virtually no difference between the two fibrous polymers at 20 Mrad.

The changes of tensile breaking strength with time of immersion of these two fibrous polymers irradiated at different levels were summarized in *Figure 3*. γ irradiation accelerated the hydrolytic degradation of these two fibrous polymers and the degree of acceleration depended on the dosage, duration of immersion, and the chemical structure of the polymers. Without immersion treatment, PGA samples were found to retain higher tensile breaking strength than their lactide copolymers over the tested range of γ-irradiation (0–20 Mrads). As immersion started to progress, the PGL copolymers, however, retained better strength, particularly with the unirradiated specimens. The difference between the two polymers, however, became smaller with an increase in radiation dosage and/or the duration of immersion. For example, after 14 days immersion, unirradiated PGL copolymer had strength four times greater than the unirradiated PGA. But there was virtually no difference in strength between the two polymers when irradiated at 5 Mrads and above at the same time interval. The 20 Mrad samples (including both PGA and its lactide copolymer) became too weak to measure their tensile strength at this time. No or very insignificant strength could be measured for 5 and 10 Mrads samples by 21 days and for 0 Mrad samples by 28 days.

DISCUSSION

The observed changes in pH values and tensile breaking strength of PGA and PGL fibres as a function of time and γ irradiation indicate that the degradation of these fibres involve more than one single stage. As pointed out by Chu[3], the degradation mechanism of this class of polymers proceeds through two main stages: first in the amorphous regions and then in the crystalline regions. Hydrolytic degradation starts in the amorphous regions, as the tie-chain segments in these regions degrade into fragments. Along the scission of the tie-chain segments which connect the crystal blocks in the axis (fibre) direction, lower tensile strength should be observed. This was exactly what was observed in this study.

This loss of strength is accompanied by the release of

glycolic and lactic acids into the medium resulting from this ester hydrolysis. Consequently, the pH of the solution would decrease. However, the observed drastic pH changes occurred after most of these fibres had already lost all or a majority of their tensile strength. In other words, there was relatively little decrease in the pH level during the period that these materials lost most of their strength. This would indicate that although the first stage of degradation, which occurs in the amorphous regions, released very little acids into the medium and hence resulted in slight pH change, it has the most important impact on the strength.

When most or all of the tie-chain segments located in the amorphous regions were broken through hydrolysis, the second stage of degradation starts as previously proposed by Chu[3]. It is unclear, however, why the pH level decreased so drastically at the end of the first stage of degradation. It is speculated that the destruction of tie-chain segments in the first stage of degradation frees the crystal blocks, which were previously tied together by tie-chain segments, from restricted motion. As a result, the crystals in the microfibrils are less densely and orderly packed, which renders them more susceptible to degradation. In addition, the crystalline regions contain more glycolic and lactide acids per unit volume than the amorphous regions (i.e., more densely packed) and more acids could be released through chain scissions. Thus, a combination of these two factors (i.e., relaxation of crystal blocks and more acids per unit volume) could drastically decrease the pH level as degradation proceeds through this stage.

The onset of the accelerated pH region of the un-irradiated PGA occurring at 21 days coincides with the previously reported time for the maximum crystallinity to develop[3]. The level of crystallinity of PGA reached a maximum and then started to decrease after 21 days according to that study. This decrease in the level of crystallinity due to the fragmentation of polymer chains in the crystalline region should release plenty of acids to lower the pH level of the solution significantly. The faster reduction in pH after 21 days in both unirradiated polymers demonstrates this point of view.

The decrease in the pH level in the medium as hydrolytic degradation proceeded could also contribute to the rate of degradation of PGA and PGL fibres. This autocatalysis phenomenon in polymers has been reported by Ravens *et al.* in their examination of aqueous hydrolysis of poly(ethylene terephthalate)[12]. In recent reported studies, Chu has also shown that acids catalyse the hydrolytic degradation of both PGA and PGL fibres as is evident in their faster loss of tensile strength in acidic buffer media when comparing with neutral buffer media[7,13]. In the present study, the specimens for tensile strength were immersed in a buffer solution maintained at a constant physiological pH level (7.4), while the specimens for pH test were immersed in aqueous media (not buffered). Therefore, the degradation observed in the pH test specimens is expected to be different from those for tensile strength specimens because of the autocatalytic nature of polyesters. Autocatalysis does not exist in the buffer medium.

From the equilibrium point of view although the hydrolysis of simple organic esters in neutral or acid media is reversible and reaches an equilibrium, it is suspected that in polymeric systems, the probability of

two chain ends after hydrolytic scission coming together again for reconnection is probably too small to be significant.

The study also showed that γ-irradiation treatment of these two fibres resulted in an early appearance of the accelerated pH region along the time scale. This is consistent with the observed faster loss of tensile strength due to γ-irradiation in this study and the morphological observation in a recent reported work[4]. In that study, Chu *et al.*, found that the length of immersion time needed to cause surface cracks on PGA fibres decreased with increasing irradiation dosages, and the number and regularity of these surface cracks increased with increasing irradiation dosages[4]. This shortening in the immersion time and increasing the degree of surface cracks would reflect in the early appearance of the accelerated pH region found in this study.

It is believed that γ-irradiation shortens the duration of the first stage of degradation through the preferential chain scission in the amorphous regions. Chu *et al.*, have recently reported that the predominant effect of γ-irradiation on PGA fibres is chain scission and was attributed to the weakened bond resonance[4]. Chu also suggested that due to the so-called 'cage effect', the scission of polymer chains would be more severe in the amorphous regions than in the crystalline regions. Such a preferential fragmentation (due to γ-irradiation) of the chain segments located in the amorphous regions would reduce the degree of chain entanglement in those regions and result in more open amorphous structure. Consequently, the irradiated specimens became more susceptible to hydrolysis, and was reflected in the earlier appearance of the accelerated pH region as well as the faster loss of tensile strength.

Due to the presence of lactic acid component in PGL fibres, it was found that PGL fibres were more susceptible to radiation degradation than PGA fibres, but the former was more resistant to hydrolytic degradation than the latter as evident in the tensile strength data. An examination of the chemical structure of the constituents (glycolic and lactic acids) indicates that the difference in response to radiation and hydrolysis lies in the methyl group of the lactic acid. This methyl group could lower the probability for recombination of radical pairs resulting from radiation chain scission because of steric hindrance and hence increase degradation probability. This same methyl group could also inhibit or lower the rate of hydrolysis because of steric hindrance and its hydrophobicity.

ACKNOWLEDGEMENT

REFERENCES

1   Scholz, K. and Lewis, R. *Surg. Gynecol. Obstet.* 1972, **135**, 525
2   Rubin, R. M., Marshall, J. L. and Wang. *J. Clin. Orthop.* 1975, **113**, 212
3   Chu, C. C. *J. Appl. Polym. Sci.* 1981, **26**, 1727
4   Chu, C. C. and Campbell, N. D. *J. Biomed. Mater. Res.* 1982, **16**, 417
5   Chu, C. C. and Williams, D. F. *J. Biomed. Mater. Res.* 1983, **17**, 1029
6   Chu, C. C. *Polymer* 1980, **215**, 1480
7   Chu, C. C. and Moncrief, G. *Ann. Surg.* 1983, **198**, 223
8   Chu, C. C. in 'CRC Critical Review in Biocompatibility', (Editor-in-Chief, D. F. Williams), CRC Press, Boca Raton, Florida, to be published
9   Reed, A. M. and Gilding, D. K. *Polymer* 1981, **22**, 494
10   Williams, D. F. and Mort, E. *J. Bioeng.* 1977, **1**, 231
11   Sharma, C. P. and Williams, D. F. *Eng. Med.* 1981, **10**, 8
12   Ravens, D. A. S. and Ward, I. M. *Trans. Faraday Soc.* 1961, **57**, 150
13   Chu, C. C. *Ann. Surg.* 1982, **195**, 55