Biodegradable Studies of Poly(trimethylenecarbonate-ε-caprolactone)-*block*-poly(*p*-dioxanone), Poly(dioxanone), and Poly(glycolide-ε-caprolactone) (Monocryl®) Monofilaments

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ABSTRACT: The aim of the study was to investigate the mechanical properties and biodegradability of poly(trimethylenecarbonate-ε-caprolactone)-*block*-poly(*p*-dioxanone) [P(TMC-ε-CL)-*block*-PDO] in comparison with poly(*p*-dioxanone) and poly(glycolide-ε-caprolactone) (Monocryl®) monofilaments *in vivo* and *in vitro*. P(TMC-ε-CL)-*block*-PDO copolymer and poly(*p*-dioxanone) were prepared by using ring-opening polymerization reaction. The monofilament fibers were obtained using conventional melt spun methods. The physicochemical and mechanical properties, such as viscosity, molecular weight, crystallinity, and knot security, were studied. Tensile strength, breaking strength retention, and surface morphology of P(TMC-ε-CL)-*block*-PDO, poly(*p*-dioxanone), and Monocryl monofilament fibers were studied by immersion in phosphate-buffered distilled water (pH 7.2) at 37°C and *in vivo*. The implantation studies of absorbable suture strands were performed in gluteal muscle of rats. The polymers, P(TMC-ε-CL)-*block*-PDO, poly(*p*-dioxanone), and Monocryl, were semicrystalline and showed 27, 32, and 34% crystallinity, respectively. Those mechanical properties of P(TMC-ε-CL)-*block*-PDO were comparatively lower than other polymers. The biodegradability of poly(dioxanone) homopolymer is much slower compared with that of two copolymers. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 102: 737–743, 2006

Key words: biodegradable; absorbable suture; poly(trimethylenecarbonate); poly(ε-caprolactone); poly(*p*-dioxanone); block copolymer; monofilament; surface morphology

INTRODUCTION

Recently, it is known that the monofilament fiber evokes less contamination problem in suturing site than that of multifilament fibers due to its physical configuration. The degradation rate of monofilament fibers are studied extensively because their degradation rates could be controlled by using various comonomer or comonomer ratio. There are many kind of monofilament suture in suture market with different raw material to control degradation rate. Sutures used in operations on tiny body parts, such as blood vessels, require good flexibility to handle easily during surgical operations.[1–4] Although homopolyester monofilaments are limited by its inherent brittleness, their properties can be significantly enhanced and broadened by modification via copolymerization. In particular, block copolymerization may offer a broader spectrum of mechanical and degradation properties to meet demands of various applications. Copolymers of glycolide, lactide, and caprolactone can be obtained by modulation of their ratio in the polymers, such as poly(lactide-*co*-glycolide), poly(lactide-*co*-caprolactone), poly(glycolide-*co*-caprolactone), and poly(lactide-*co*-glycolide-*co*-caprolactone).[5–7] Copolymers of poly(trimethylenecarbonate), poly(ε-caprolactone), and poly(*p*-dioxanone) began to attract considerable interest only in recent years.[8–11] Although the copolymers based on trimethylenecarbonate (TMC), caprolactones, and *p*-dioxanone (PDO) have been disclosed, they have not been studied because of either poor flexibility or low knot-security. In previous publication, we have reported on the synthesis of poly(trimethylenecarbonate)(ε-caprolactone)/poly(*p*-dioxanone) [P(TMC-ε-CL)-*block*-PDO] copolymers and their physical and mechanical properties.[12] It was demonstrated that poly(*p*-dioxanone) was used as a main block because it has good flexibility and tensile strength useful for the monofilament,[11,13] and the other block was designed by the random copolymer of ε-caprolactone (CL) and TMC. The CL has low stiffness and provides excellent handling characteristics, and TMC shows rubbery state at room tempera-

ture and acts as a soft segment.[11,13] In the results, it appeared that P(TMC-ε-CL)-*block*-PDO (5/5/90) copolymer has excellent properties to be used in suture.

In the present study, we describe recent efforts to extend this work to investigate the mechanical properties and biodegradability of P(TMC-ε-CL)-*block*-PDO (5/5/90) monofilament fiber in comparison with commonly used absorbable poly(*p*-dioxanone) and Monocryl® monofilament fibers *in vitro* and *in vivo*.

EXPERIMENTAL

Materials

Poly(glycolide-ε-caprolactone) (Monocryl) were obtained from Ethicon (Someville, NJ). Trimethylenecarbonate (TMC) was supplied from Sam Yang (Taejeon, Korea). ε-Caprolactone (CL) was purchased from Acros (Geel, Belgium), dried over calcium hydride at room temperature for 24 h and purified by vacuum distillation in a nitrogen atmosphere. *p*-Dioxanone (PDO), stanneous ethylhexanoate, lauryl alcohol, hexafluoroisopropanol, ethylene oxide, phosphate-buffered saline (pH 7.4), ketamine hydrochloride, and xylazine hydrochloride were purchased from Aldrich Chemical. Common reagents, such as chloroform, hexane, and methanol, were used without further purification.

Measurements

Molecular weights of polymers were determined relative to polystyrene standards by gel permeation chromatography in CH_2Cl_2 as the eluent on a Waters 510 HPLC equipped with a set of four μstyragel columns (500, 10^4, 10^5, and 100 Å) in series and a UV detector. The degree of crystallinity was measured with X-ray diffraction Rigaku Tenki RAD/B. The inherent viscosity of the polymers was 2.3 dL/g as measured in a 0.1 g/dL solution of hexafluoroisopropanol at 25°C. The diameter of monofilaments was measured by Digital Thickness Gauge Mitutoyo DP-1 HS.

Monofilament preparation

Melt spin was through a centered single orifice spinneret of 1.8 mm capillary hole diameter (L/D 6), and maximum melt pressure should not exceed about 8000 psi with monofilament spinning machine FET. While extrusion temperatures depended both on the polymer T_m and on the melt viscosity of the polymer at a given temperature, extrusion of these block copolymers at temperatures of about 10–40°C above their melting point was often found satisfactory. The prepared block copolymers were extruded at a temperature of about 160°C. The extrudates were generally taken up through an ice water bath at 5 m/min, al-

though other bath temperatures and take-up speeds were occasionally used. The extrudate filaments were subsequently drawn about ×5 to ×6 in multistage drawing processes to achieve molecular orientation and improved tensile properties. The fibers were then wound, put into folders, and placed in aluminum foil-laminated packages. The fibers were sterilized with ethylene oxide, thoroughly degassed, and sealed in a dry atmosphere.

Knot-pull strength test

Knot-pull strength was determined with Universal Tensile Tester Instron 4465. Using a suitable tesilometer, the breaking load over a simple knot in the strand formed by passing one end, held in the right hand, over that in the left hand and drawing the free end through the loop so formed and pulling the knot tight was determined. The apparatus had two clamps for holding the strand, one of which was mobile, and was driven at a constant speed of 25–30 cm/min. The clamps were designed so that the strand being tested can be attached without any possibility of slipping. At the beginning of the test, the length of strand between the clamps was 12.5–20 cm and the knot was midway between the clamps. While the mobile clamp was set in motion, the load was recorded at which the strand was broken. If the strand broke in or within 1 cm of a clamp, the test on another strand was repeated.

Knot security test method

Knot security was measured in terms of the knot slippage ratio. A surgeon's knot (2 = 1 = 1) was selected for the knot tying method.[1,14] The length of sample was prepared 5 mm and tested 500 mm/min measuring rate. The knotted sutures were placed on a tensile strength tester and pulled apart until knot breakage occurred or the knot slipped. After the measurements for ten times, the ratio of the number of knots slipped to the total number of knots tied indicates the knot slippage ratio.

In vitro breaking strength retention test

Breaking strength retention (BSR) was performed by using a universal tensile testing instrument, Instron 4465 as recommended in standard ASTM D 337. Sample length was 20 mm and the crosshead speed was 20 mm/min. The displacement of the sample and the load was recorded until the load passed through a peak and then declined again, indicating failure of the sample. All the reported tensile strength represented average values of at least five tests. The original straight pull tensile strength was measured at room temperature before immersion, and the five monofilament fibers were immersed in each vials filled with

pH 7.4 phosphate-buffered solution in a shaking water bath, maintained at 37°C for 1, 2, 3, and 4 weeks. The monofilament fibers were removed from the vials, washed with deionized water, and dried in a vacuum oven at 40°C for 24 h.

$$\text{BSR (\%)} = \frac{\text{tensile strength after immersion}}{\text{original tensile strength}} \times 100$$

In vivo BSR test

The test articles were implanted through the dorsal subcutis of rats and specimens of each type of sutures were retrieved at 1, 2, 3, 4, 5, and 6 weeks after implantation. The recovered samples were used as tensile testing samples at each time period. Tensile strength tests of sutures were carried out using a universal tensile testing instrument, Instron 4465. In the suture tensile strength test, sample length was 20 mm and the crosshead speed was 20 mm/min.

Absorbable test of monofilament suture in rats

Implantation studies of absorbable suture strands, poly(trimethylenecarbonate-ε-caprolactone)-*block*-poly(p-dioxanone) [P(TMC-ε-CL)-*block*-PDO], Monocryl, and poly(dioxanone) monofilament fibers were performed in gluteal muscle of rats. Male Sprague–Dawley rats weighing between 160 and 170 g were utilized to evaluate the *in vivo* degradation of block copolymer suture. Optical Microscope BX-51 (Olympus Optical, Japan), Embedding Center Leica EG1140H (Leica, Germany), and Microtome Leica RM 2155 (Leica, Germany) were used. Rats were acclimatized for a few days before the study anesthetized with an intramuscular injection of a mixture of ketamine hydrochloride (60 mg/kg) and xylazine hydrochloride (10 mg/kg) and prepared for surgery by clipping the hair of the dorsal sacral area. A midline incision was made on the skin over the sacral spine parallel to the vertebral column. Following retraction of the skin laterally, sterile suture strands were drawn into the right and left gluteal muscles. Two suture segments, each ~3 cm long, were implanted per both sides of muscle. For preventing secession of suture strand, both ends of suture were tied a knot with a little space. The skin incisions were then closed and the rats were retained. At the predetermined periods of *in vivo* residence, predesignated rats were killed by carbon dioxide asphyxiation. Gluteal muscles containing the implanted suture samples were excised and preserved in 10% neutral formalin fixative. A transverse section of each formalin-fixed sample was trimmed and processed for paraffin embedding, sectioning, and staining with hematoxylin and eosin. Histological examination of the implant sites was conducted using cross sections of 6
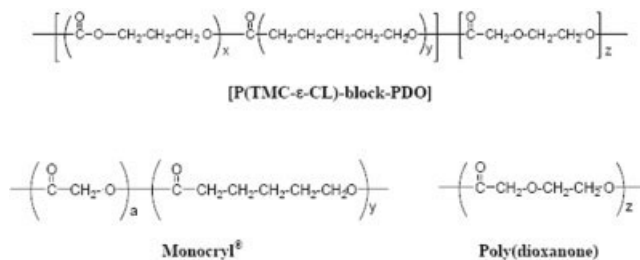

Figure 1 Chemical structures of three synthetic absorbable sutures.

μm in thickness. The behaviors of suture strands were obtained at 3–240 days after implantation. Test was carried out in accordance with the requirements of the international organization for standardization 10,993: biological evaluation of Medical Devices. Part 6: Tests for Local Effect after Implantation.[14–18]

RESULTS AND DISCUSSION

Polymer properties

Three different polymers, P(TMC-ε-CL)-*block*-PDO, poly(p-dioxanone), and Monocryl, are shown in Figure 1. P(TMC-ε-CL)-*block*-PDO (5/5/90 mol %) and poly(p-dioxanone) polymers were prepared by using ring-opening polymerization reactions as follows our literature.[12] In our previous article, we described that a higher molar ratio of trimethylene carbonate in the segmented copolymer correlates to higher flexibility, while a higher molar ratio of CL in the segmented copolymer correlates to a longer period of strength retention. Therefore, the molar ratio of CL/trimethylene carbonate can be controlled to provide various degrees of flexibility, strength retention, or absorption rate. Preferably, the content of PDO in the copolymers is to 90 mol %. Monocryl is block copolymer of glycolide 75 mol % and CL 25 mol %. The general properties of polymers are shown in Table I. The viscosities of polymers shown are within the range of 1.7–2.3 dL/g. The molecular characteristics of the polymers were in the range of M_n of 31,000–56,000 g/mol, and M_w of 110,000–152,000 g/mol, respectively, in given reactions that is useful for commercial applications. The polydispersities of polymers were about 2.71–3.51, indicating relatively broad distribution of the molecular weight. The polymers were semicrystalline and showed 27, 32, and 34% crystallinity, respectively.

The polymers were melting spun into monofilament using conventional methods of melt extruding, quenching, drawing, and relaxing continuous thermoplastic monofilaments with monofilament spinning machine FET. The properties of monofilament fibers are listed in Table II. The knot-pull strengths and tensile strengths of the monofilament fibers showed

TABLE I
Results of Physical Properties of [P(TMC-ε-CL)-*block*-PDO], Poly(dioxanone), and Monocryl

	Inherent viscosity (g/dL)	M_n	M_w	M_w/M_n	Crystallinity (%)
[P(TMC-ε-CL)-*block*-PDO]	2.3	56,000	152,000	2.71	27
Poly(dioxanone)	2.2	54,000	150,000	2.78	32
Monocryl	1.7	31,000	110,000	3.55	34

3.06–5.30 kg f and 4.41–8.80 kg, respectively. The elongation of polymers decreased as the crystallinity increased. Those mechanical properties of the prepared P(TMC-ε-CL)-*block*-PDO were comparatively lower than other polymers because the total crystalline domains were reduced, which thereby provide for low degree of crystallinity. In other words, the increased noncrystalline domains of block copolymers had a low tensile strength in comparison to the tensile strength of Monocryl and poly(dioxanone) polymers. Knot security (%) was measured in terms of the knot slippage ratio, which is (sliding knotted sample no./10 knotted samples) × 100. Thus, the less the ratio, the better is the knot security of the suture. P(TMC-ε-CL)-*block*-PDO and Monocryl block copolymers showed better knot-security (3–4 out of 10 knots failed) than the comparative homopolymer. The low tensile strength of the block copolymers correlates with higher flexibility and more stable knot-security. We assumed that the stable knot-security of Monocryl is affected by chemical structure and physical crosslinking between noncrystalline domains formed by copolymerization of glycolide and CL. It has been reported that the mechanical properties of polymer are enhanced by a microphase-separated morphology in which soft segment gives flexibility, whereas the rigid phase provides mechanical strength.[19–21] The relationship of tensile strength and weight loss has reported that the loss of monofilaments mass is mainly due to the destruction of crystalline domains, while the loss of tensile strength is chiefly due to the scission of tie-chain segments strength.[22]

Biodegradation

Figures 2 and 3 presented the tensile strength and *in vitro* BSRs (%) of [P(TMC-ε-CL)-*block*-PDO], poly(dioxanone), and Monocryl during hydrolysis with phosphate-buffered saline (pH 7.4) for 6 weeks. Monofilament fibers were used here to examine the relative biodegradation of polymers. Panayiotou et al. have studied this system because it is strongest enzymatic activity in copolymers.[23] Measurements were only taken up to 6 weeks of hydrolysis, because samples degraded longer were too fragile to handle to be tested. The degradation of polymer is highly dependent, not only on the chemical structure but also morphology of the polymer, such as degree of crystallinity and microstructure.[20] The relationship of biodegradability and tensile strength of homopolymer from PDO and copolymer from PDO and morpholine-2,5-dione has been studied by Shalaby.[21] This ability to break the inherent fiber structure–property relationship through copolymerization is a major improvement in the biodegradation properties of absorbable sutures. It is interesting to recognize that a small percent of morpholine-2,5-dione (3%) in the copolymer is sufficient to result in a faster mass loss profile without detriment to its tensile strength loss profile. The ability to achieve this ideal biodegradation property might be attributed to both an increasing hydrophilicity of the copolymer and the disruption of crystalline domain due to the morpholine-2,5-dione moiety. The degree of crystallinity influences the rate of hydrolytic degradation as the crystal segments slow down the water permeation in the matrix. Hydrophilic and amorphous regions of the polymers allow better access to water molecules than the crystalline regions because of the higher rate of water uptake.[24–26] In this work, the tensile strength of the polymers as a function of the hydrolysis time has been performed to classify how changes in degradation rate can be related to monomers. The biodegradability of poly(dioxanone) homopolymer is much slower compared with that of two

TABLE II
Results of Mechanical Properties of [P(TMC-ε-CL)-*block*-PDO], Poly(dioxanone), and Monocryl

	Diameter (mm)	Knot-pull strength (kg f)	Knot security (%)	Tensile strength (kg)	Elongation (%)
[P(TMC-ε-CL)-*block*-PDO]	0.383	3.06	30	4.41	64
Poly(dioxanone)	0.358	3.31	80	5.72	62
Monocryl	0.378	5.30	30	8.80	55

Figure 2 Tensile strength (kg) as a function of hydrolysis time [P(TMC-ε-CL)-*block*-PDO], ♦; poly(dioxanone), ■; and Monocryl, ▲.
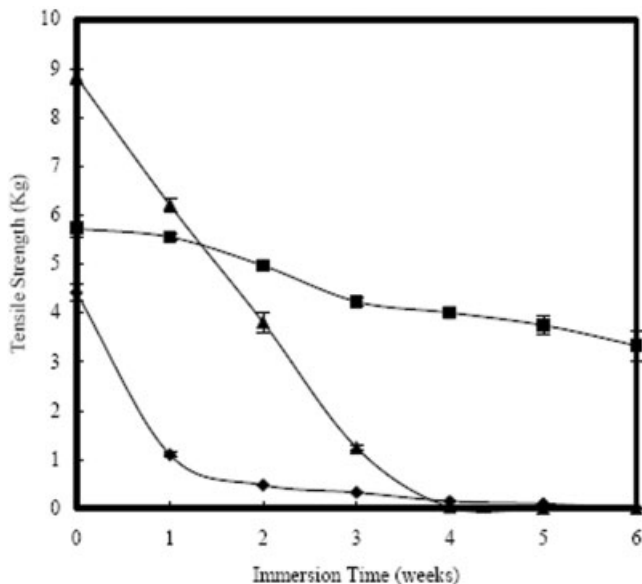

Figure 4 *In vivo* breaking strength retension (%) as a function of hydrolysis time for [P(TMC-ε-CL)-*block*-PDO], ♦; poly(dioxanone), ■; and Monocryl, ▲.

copolymers. Monocryl showed faster absorption rate than polymers based on high contents of PDO even though it had little high crystallinity. The main explanation for this behavior can be attributed to chemical structure of polymers and crystallinity. The terms of biodegradability could be classified by two meanings as the strength loss of polymer and absorption. Generally, the rate of strength loss is affected by the chemical structure of polymer and the rate of absorption is mainly affected by the crystallinity of polymer. The strength loss of polymer occurred at earlier stage of
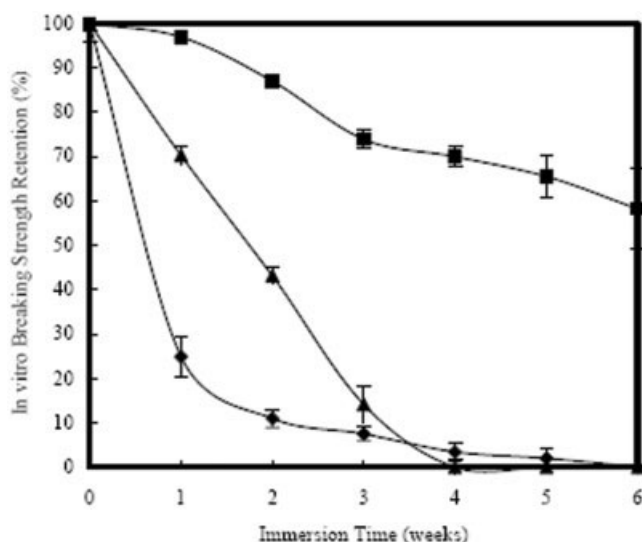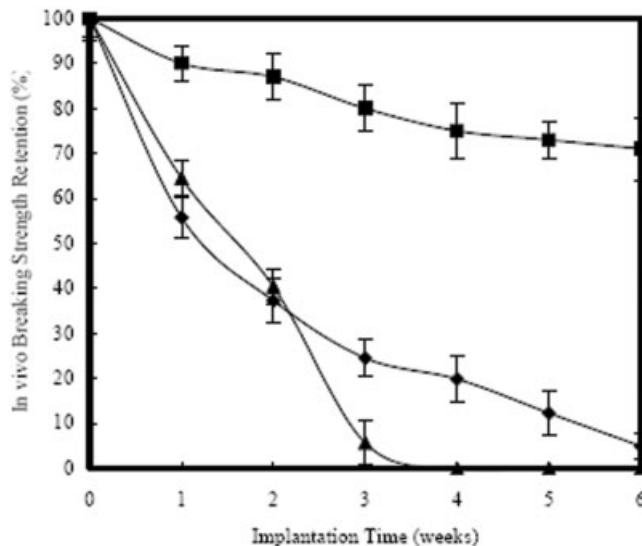
biodegradation and absorption occurred after complete strength loss. Therefore, biodegradation process is affected by both the factors.[27,28] *In vivo* BSRs (%) monitored the degradation process of monofilament (Fig. 4). It showed that *in vitro* condition promoted faster hydrolytic degradation than *in vivo* because of more severe and constant environmental conditions. The rate of BSRs (%) of P(TMC-ε-CL)-*block*-PDO *in vivo* was improved rather than *in vitro* condition compared with poly(dioxanone) and Monocryl.

We studied surface morphology of monofilament fibers *in vitro*. Figure 5 displayed the SEM photographs of three polymers hydrolyzed with phosphate-buffered saline (pH 7.4) for 8 and 12 weeks. The surface erosion appeared perpendicular to the drawing direction. Sabino et al. have reported that parallel
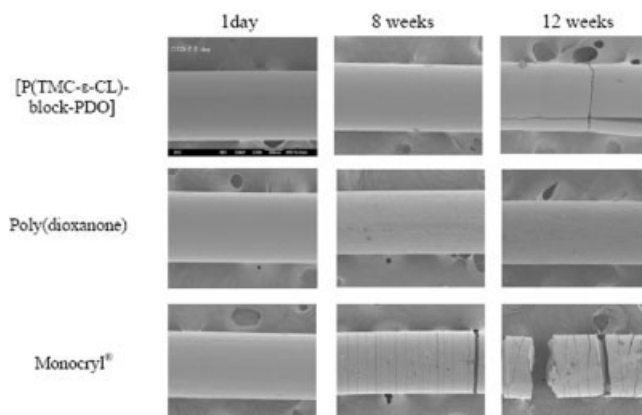

Figure 3 *In vitro* BSR (%) as a function of hydrolysis time for [P(TMC-ε-CL)-*block*-PDO], ♦; poly(dioxanone), ■; and Monocryl, ▲.

Figure 5 SEM microphotographs of [P(TMC-ε-CL)-*block*-PDO], poly(dioxanone), and Monocryl monofilament fibers after 8 and 12 weeks of enzymatic degradation *in vitro*.
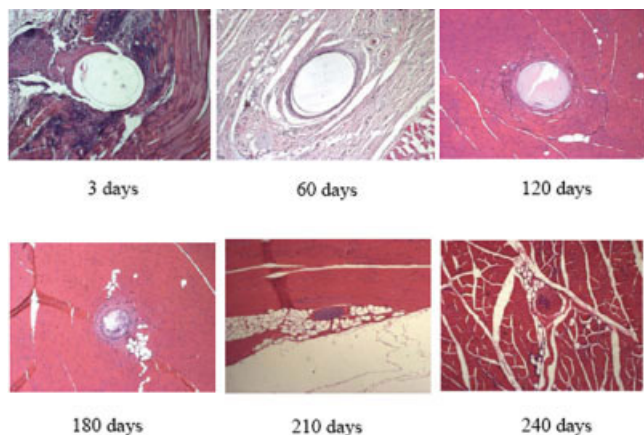
Figure 6 Microscopic observation of [P(TMC-ε-CL)-*block*-PDO] suture strands on rat tissue after 3, 60, 120, 180, 210, and 240 days. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
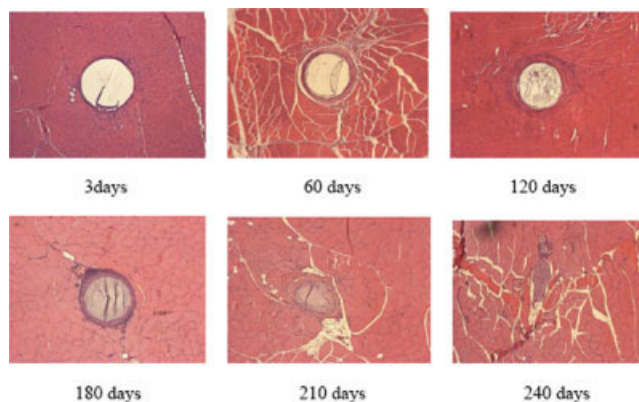

Figure 7 Microscopic observation of Poly(dioxanone) suture strands on rat tissue after 3, 60, 120, 180, 210, and 240 days. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

grooves or cracks are arranged perpendicular to the machine direction.[26] Monocryl showed a considerably eroded surface that contained a number of stripe cracks at 8 weeks and broke at 12 weeks. Poly(dioxanone) maintained the initial surface morphology after 8 and 12 weeks, and P(TMC-ε-CL)-*block*-PDO showed minute perpendicular cracks after 12 weeks. This behavior can be attributed to differences in crystallinity, chemical structure, and concentration of ester of the polymers. The long chain alkyl groups and degree of crystallinity of the polymer dictate hydrophobicity and influence the rate of hydrolysis by affecting the diffusion of water into the materials. Hydophilic and amorphous regions of the polymers allow better access to water molecules.[26]

Absorbable test

Microscopic observation on tissue reaction was performed on all slides of the implant site. Macrophages and fibroblasts have been seen throughout all study periods as shown in Figures 6–8. All of the three suture strands were surrounded by an irregular zone of acute inflammatory cells, consisting primarily of macrophages, fibroblasts, and leukocytes at initial stage of 3-days postimplantation. At 60 days, leukocytes disappeared and macrophages and fibroblasts prevailed. P(TMC-ε-CL)-*block*-PDO suture strand was fragmented at 180 while it was intact at 120 days (Fig. 6). Then, P(TMC-ε-CL)-*block*-PDO suture strand was almost degraded with only a few small detectable fragments at 210 days and has undergone absorption at 240 days, indicating that P(TMC-ε-CL)-*block*-PDO suture strand was completely absorbed between 210 and 240 days. The tissue reactions to P(TMC-ε-CL)-*block*-PDO suture strand were marked by the irregular zone of acute inflammatory cells, primarily macro-

phages and fibroblasts, surrounding the suture at early phase. After 60 days, narrow tissue reaction zone encircled the suture strand, and the numbers of surrounding macrophages and fibroblasts in the reaction zone were gradually diminished during the 240 days. Figure 7 showed absorbable behaviors of suture strands after postimplantation in gluteal muscles of rats. Poly(dioxanone) suture strand retained an intact form at implant site, and was surrounded by irregular zone of inflammatory cells at 3 days. At 60 days, the suture strand was surrounded by well-organized collagenous capsule. The suture strand was surrounded by thick collagenous capsule, with fibroblasts and macrophages at 120 days. At 180 days, the suture strand kept its original shape, yet extensive fissures were observed. The suture strand showed a substantial amount of absorption and a small portion of poly-(dioxanone) suture strand still remained at 210 and
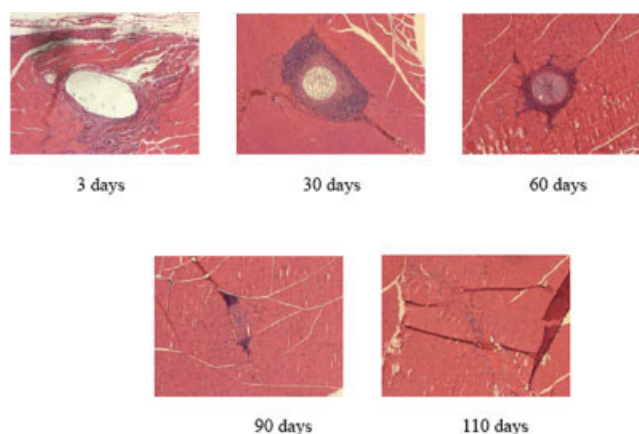

Figure 8 Microscopic observation of Monocryl suture strands on rat tissue after 3, 30, 60, 90, and 110 days. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

240 days. Figure 8 showed Monocryl suture absorption behaviors. Suture strands have fragmented at 30-days postimplantation in gluteal muscles of rats, indicating that degradation is undergoing with minimal tissue reaction. The suture strand is surrounded by band of collagen containing macrophages and fibroblasts and outer zone of collagen band was surrounded by a large mass of macrophages. At 60 days, the suture strand was surrounded by fibroblasts, macrophages, and scattering lymphocytes. Extensive fissuring of the suture has occurred and a substantial amount of the strands has absorbed. At 90 days, Monocryl suture strand has been completely absorbed. No fragment of suture strands was observed. The inflammatory reaction zone was composed of large macrophages, fibroblasts, and lymphocytes. At 110 days, the implant site was replaced with collagen and there were a few inflammatory cells.

On the basis of the results of this study, P(TMC-ε-CL)-*block*-PDO, Monocryl, and poly(dioxanone) were absorbed with different time postimplantation. There were significant differences in absorption rate between P(TMC-ε-CL)-*block*-PDO and Monocryl sutures during the whole test period *in vivo* system. P(TMC-ε-CL)-*block*-PDO suture had much slower absorption than Monocryl, and poly(dioxanone) suture showed latest absorption rate as can be expected. The macroscopic tissue scores of both P(TMC-ε-CL)-*block*-PDO and Monocryl were zero throughout the study periods, indicating that there was no capsule formation or sign of tissue contact irritation. Therefore, P(TMC-ε-CL)-*block*-PDO does not cause significant contact irritation. The tissue reactions to the P(TMC-ε-CL)-*block*-PDO were minimal and comparable with that of Monocryl throughout the same study period. P(TMC-ε-CL)-*block*-PDO is considered to have comparable biocompatibility to Monocryl in terms of absorption rate and local irritant response.

CONCLUSIONS

P(TMC-ε-CL)-*block*-PDO copolymer was synthesized by using two step polymerization reactions. P(TMC-ε-CL)-*block*-PDO monofilament fiber was studied in comparison with poly(dioxanone) and Monocryl monofilament fibers *in vivo* and *in vitro*. The hydrolytic degradation of polymers was studied in a phosphate buffer solution, pH = 7.2, at 37°C and biological absorbable test was performed in rats. It appeared that *in vitro* condition promoted a faster hydrolytic degradation than the *in vivo* because of more severe and constant environmental conditions. Monocryl containing ester group degraded faster than other polymers based on high contents of PDO. The main explanations for this behavior can be attributed not only to the chemical structure but also to the morphology of the polymer, such as degree of crystallinity and micro-

structure. P(TMC-ε-CL)-*block*-PDO suture strand was almost degraded with only a few small detectable fragments at 210 days and has undergone complete absorption at 240 days. From these results, P(TMC-ε-CL)-*block*-PDO has excellent properties to be used in suture.

References

1. Im, J. N.; Seo, J. I.; Hong, J. T.; Pai, C. M.; Yoon, H. S. Eur. Pat. 1,348,449 (2003).
2. Charuchinda, A.; Molloy, R.; Siripitayananon, J.; Molloy, N.; Sriyai, M. Polym Int 2003, 52, 1175.
3. Uddin, A. J.; Katayama, N.; Ohkoshi, Y.; Gotoh, Y.; Nagura, M. J Polym Sci Part B: Polym Phys 2002, 40, 2449.
4. Nelson, K. D.; Romero, A.; Waggoner, P.; Crow, B.; Borneman, A.; Smith, G. M. Tissue Eng 2003, 9, 1323.
5. Tracy, M. A.; Ward, K. L.; Firouzabadian, L.; Wang, Y.; Dong, N.; Qian, R.; Zhang, Y. Biomaterials 1999, 20, 1057.
6. Perego, G.; Vercellio, T. Makromol Chem 1993, 194, 2463.
7. Yuan, W.; Tang, X.; Huang, X.; Zheng, S. Polymer 2005, 46, 1701.
8. Raquez, J.-M.; Degee, P.; Narayan, R.; Dubois, P. Macromol Rapid Commun 2001, 22, 126.
9. Fabre, T.; Schappacher, M.; Bareille, R.; Dupuy, B.; Soum, A.; Bertrand-Barat, J.; Baquey, C. Biomaterials 2001, 22, 2951.
10. Albuerne, J.; Marquez, L.; Mueller, A. J.; Raquez, J. M.; Degee, P. H.; Dubois, P. H.; Castelletto, V.; Hamley, I. W. Macromolecules 2003, 36, 1633.
11. Bhattarai, N.; Cha, D. I.; Bhattarai, S. R.; Khil, M. S.; Kim, H. Y. J Polym Sci Part B: Polym Phys 2003, 41, 1955.
12. Hong, J. T.; Cho, N. S.; Yoon, H. S.; Kim, T. H.; Lee, D. H.; Kim, W. G. J Polym Sci Part A: Polym Chem 2005, 43, 2790.
13. Von Fraunhofer, J. A.; Von Storey, R. S.; Stone, I. K.; Masterson, B. J. J Biomed Mater Res 1985, 19, 595.
14. Pineros-Fernandez, A.; Drake, D. B.; Rodeheaver, P.; Moody, D. L.; Edlich, R. F.; Rodeheaver, G. T. J Long Term Eff Med Implants 2004, 14, 359.
15. Bezwada, R. S.; Jamiolkowski, D. D.; Lee, I. Y.; Agarwal, V.; Persivale, J.; Trenka-Benthin, S.; Erneta, M.; Suryadevara, J.; Yang, A.; Liu, S. Biomaterials 1995, 16, 1141.
16. Molea, G.; Schonauer, F.; Bifulco, G.; D'Angelo, D. Br J Plast Surg 2000, 53, 137.
17. Niessen, F. B.; Spauwen, P. H.; Kon, M. Ann Plast Surg 1997, 39, 254.
18. Ray, J. A.; Doddi, N.; Regula, D.; Williams, J. A.; Melveger, A. Surg Gynecol Obstet 1981, 153, 497.
19. Stone, I. K.; Masterson, B. J.; Von Fraunhofer, J. A. Surf Coat Technol 1986, 27, 287.
20. Nishida, H.; Konno, M.; Ikeda, A.; Tokiwa, Y. Polym Degrad Stab 2000, 68, 205.
21. Lele, B. S.; Leroux, J. C. Polymer 2002, 43, 5595.
22. Shakaby, S. W.; Koelmel, D. F. Eur. Pat. 86,613 (1983).
23. Seretoudi, G.; Bikiaris, D.; Panayiotou, C. Polymer 2002, 43, 5405.
24. Pezzin, A. P. T.; Duek, E. A. R. Polym Degrad Stab 2002, 78, 405.
25. Jarrett, P.; Cook, W. J.; Bell, J. P.; Huang, S. J.; Cameron J. A. Polym Prepr 1981, 22, 351.
26. Sabino, M. A.; Gonzalez, S.; Marquez, L.; Feijoo, J. L. Polym Degrad Stab 2000, 69, 209.
27. Kuwabara, K.; Gan, Z.; Nakamura, T.; Abe, H.; Doi, Y. Biomacromolecules 2002, 3, 390.
28. Chu, C. C. Polymer 1985, 25, 591.