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Biocompatible Polymer Blends of Poly(D,L-lactic acid-*co*-glycolic acid) and Triblock PCL-PDMS-PCL Copolymers: Their Characterizations and Degradations

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Polymer blends of poly(D,L-lactic-*co*-glycolic acid), PDLLGA, and triblock polycaprolactone-poly(dimethylsiloxane)-polycaprolactone (PCL-PDMS-PCL) copolymer, TEGOMER, were obtained by coprecipitation from their chloroform mixed solutions into methanol and were characterized by differential scanning calorimetry (DSC), Fourier transform infrared (FTIR), degradation tests and scanning electron microscopy (SEM). Binary blends of PDLLGA/TEGOMER were found to be partially miscible according to DSC measurements and FTIR analysis. Stress-strain results showed that addition of TEGOMER improved significantly the overall toughness of PDLLGA. Degradation of PDLLGA/TEGOMER blends was investigated in phosphate buffered saline at pH = 7.4 and 37 °C, and the morphology of the blends during degradation was examined by scanning electron microscopy.

Key words
• poly(D,L-lactic acid-*co*-glycolic acid)
• polycaprolactone-poly(dimethylsiloxane)-polycaprolactone
• degradation
• blends

INTRODUCTION

Biodegradable polymers are natural or synthetic in origin and are degraded *in vivo*, either hydrolytically or enzymatically to produce biocompatible, toxicologically safe by-products that are further eliminated by the normal metabolic pathways. Since the last two decades, synthetic biodegradable polymers have been increasingly used as scaffolds in tissue engineering to direct specific cell growth and also to deliver drugs.[1–5] Among them, poly(D,L-lactic acid-*co*-glycolic acid) (PDLLGA) copolymers have been approved by the US Food and Drug Administration for human clinical uses. Depending on the molar ratio of individual monomer components (lactide or glycolide) in the copolymer chain, it is possible to prepare PLGAs with desired degradative properties.[6–9] PLGA is biocompatible, has a high tensile strength, and a high elastic modulus. However, a drawback of PLGA is its low elongation at break due to the brittle fracture while under tensile stress. Poly(lactic acid) (PLA) shows similar

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mechanical behavior. The elongation at break of PLA is typically 3–5 %.[10] One of the reasons for this brittle behavior is physical aging that occurs during storage at room temperature and which has been studied extensively.[11] Blend preparation is a common technique used to increase the ductility of a brittle polymer.

Poly(ε-caprolactone) (PCL) is another well-known biocompatible polyester. It has been utilized as drug carrier because of its excellent drug permeability. However, its high crystallinity and low degradation rate make it suitable only for long-term drug delivery systems. The biodegradability can be enhanced by copolymerization or blending of this compound with a variety of hydrophobic polymers.[12]

Blending with other biodegradable polymers has become the most versatile way of achieving materials with new, desirable properties. However, manifestation of superior properties depends upon the miscibility of polymers at the molecular level. Thus far, several blend systems have been investigated, such as PLA / Poly(ethylene glycol) (PEG),[13] Poly(L-lactic acid) (PLLA)/Poly(D,L-lactic acid) (PDLLA),[14–16] PLLA/PCL,[17,18] PDLLA/PCL.[19] However, most of the blends were found to be immiscible or partly miscible depending on their composition.[13] Recently, Rusa and Tonelli studied the miscibility of the PLLA/PCL blends using α-cyclodextrin as inclusion compound.[20] They reported that α-cyclodextrin may represent a unique means to achieve intimately compatible blends from normally immiscible polymers.

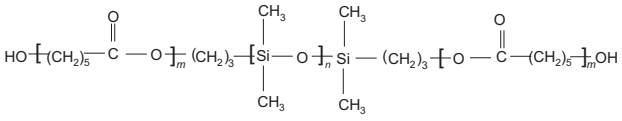
Modification of polymers through the addition of small amounts of siloxane polymers received increasing attention in the last decade as well.[21–23] While its surface properties render PDMS very attractive for modification of other surfaces and interfaces, its low solubility parameters cause it to be highly immiscible with other materials. An effective way of achieving compatibility in PDMS blends is through the use of siloxane containing carbon-based copolymers.

In this work, we studied PDLLGA and triblock polycaprolactone-poly(dimethylsiloxane)-polycaprolactone (TEGOMER) blends to develop a biocompatible and biodegradable blend with variable physical and mechanical properties, depending upon the requirements of a particular application. The characterization and miscibility of the blends were investigated by the FTIR spectroscopy, differential scanning calorimetry (DSC), stress-strain measurement and scanning electron microscopy (SEM) techniques. Hydrolytic degradation of blends was also studied.

EXPERIMENTAL

Materials

Triblock PCL-PDMS-PCL copolymer was supplied by Th. Goldschmidt A.G., Germany, under the name TEGOMER (TEGOMER H-Si 6440). The molecular weight (M_n) of TEGOMER is 6500 ± 600 g mol^{-1} and it has PCL end blocks, $M_n \cong 2000$ g mol^{-1}. TEGOMER has the following molecular structure:

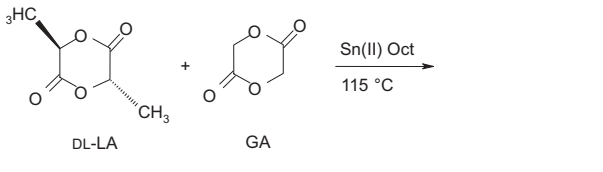


n / *m* = 30 / 18

D,L-lactide (DLLA) and glycolide (GA) were obtained from Polysciences, Inc. D,L-lactide was recrystallized from dry benzene and dried under vacuum at room temperature before use. Glycolide and stannous octoate (Sigma Corp.) were used as received.

Synthesis of Poly(D,L-lactic acid-co-glycolic acid) Copolymer

PDLLGA copolymer was prepared by the ring-opening polymerization of D,L-lactide and glycolide in the presence of stannous octoate as catalyst. A representative polymerization reaction is given in Scheme 1. A solution of stannous octoate in dry chloroform and 10.48 g of monomer mixture (9.18 g LA + 1.30 g GA) were added to a reaction tube (mole ratio, monomer to catalyst, M/C = 1000). The molar ratio of the feed D,L-lactide/glycolide was 85/15. The solvent was removed *in vacuo*, and the tube was sealed and immersed in a silicone oil bath at 115 °C. At the end of polymerization (24 h), the product was dissolved in a small amount of chloroform and precipitated in an excess of methanol. The conversion to copolymer was 98.5 %. The molecular weight M_n of the copolymer was 26×10^3 g mol^{-1} and the polydispersity index, determined from the GPC measurement, was 1.68. The copolymer composition (PDLLA:PGA) (molar ratio) was found from ^{1}H-NMR as 80:20.



Scheme 1. PDLLGA copolymer synthesis.

Preparation of Polymer Blends

PDLLGA/TEGOMER blends were prepared by the coprecipitation method in four different compositions (95/5; 90/10; 85/15; and 50/50). Both PDLLGA and TEGOMER were separately dissolved in chloroform. The solutions were then mixed at room temperature and stirred for 24 h, followed by precipitation into a large excess of methanol. The resulting blends were then dried in a vacuum oven at room temperature until the weight was constant.

Characterization

The copolymer molecular weight was determined by gel permeation chromatography (GPC) using the Waters styragel column HT6F and Waters 410 differential refractometer detector. THF was used as the eluting solvent at a flow rate of 1 ml min^{-1} and polystyrene standards were used to calibrate the molecular weights.

^{1}H NMR spectrum of the copolymer was obtained on a Bruker AC 200L spectrometer at 200 MHz. The spectrum was taken in deuterated chloroform at 20 °C. The copolymer composition was calculated from the ratios of absorbance at 4.77 and 5.18 ppm.

^{1}H NMR ($CDCl_3$) δ/ ppm: 1.56 (3H, CH_3), 4.77 (2H, CH_2), 5.18 (H, $OC\underline{H}CH_3$).

The infrared spectra of polymers and polymer blends were recorded on a Perkin Elmer 983 IR spectrometer at room temperature.

IR ν_{max}/cm^{-1}: (PDLLGA) 2997–2965 (CH_2&CH_3), 1759 (C=O), 1360–1450 (CH_3);

(TEGOMER) 3500 (OH), 1720 (C=O), 1260–800 (Si-CH_3), 1026 (Si-O-Si).

Thermal characterization of the PDLLGA copolymer, TEGOMER and their blends were performed using a DuPont DSC 910 Model device. The samples were scanned from –140 °C to +140 °C, at a heating rate of 10 °C min^{-1}. DSC samples were first heated under a nitrogen atmosphere to +140 °C, then quenched to –140 °C using liquid nitrogen. This heating/cooling cycle was repeated twice. Reported thermograms were always taken from the second heating run.

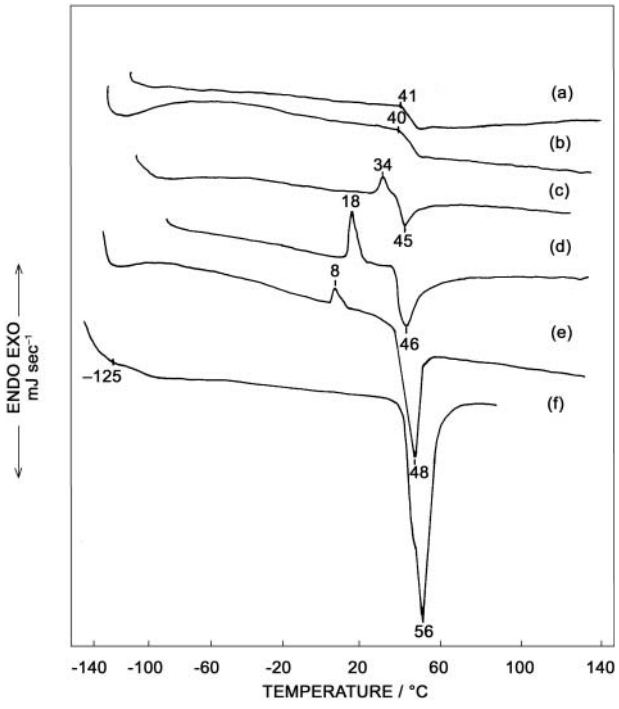


Figure 1. DSC thermograms for PDLLGA/TEGOMER blends of different compositions: (a) pure PDLLGA; (b) 5 % TEGOMER; (c) 10 % TEGOMER; (d) 15 % TEGOMER; (e) 50 % TEGOMER; (f) pure TEGOMER.

Mechanical properties of blended samples were determined by standard tensile stress-strain tests to measure the modulus (E), ultimate tensile strength (σ) and elongation at break (ε). Standard tensile stress-strain experiments were performed at room temperature on a Tensilon tester, Toyo Measuring Instruments Co. Ltd. (UTM II), using a crosshead speed of 20 mm min^{-1}.

Scanning electron microscopy was performed using a JEOL-JXA 840 Å scanning electron microscope (SEM). The specimens were prepared for SEM by freeze-fracturing in liquid nitrogen and applying a gold coating of approximately 300 Å on an Edwards S 150 B sputter coater.

The *in vitro* degradation studies of PDLLGA and PDLLGA/TEGOMER (85/15) blend were performed at 37 °C in phosphate buffer saline (pH = 7.4, PBS). Polymer films were prepared by solvent casting from chloroform with a total polymer concentration of 5 % (*w*/*v*). Solutions were poured into Teflon moulds (diameter = 22 mm, height = 10 mm). Following solvent evaporation, polymer films were dried to a constant weight in a vacuum oven at room temperature. Dry films were placed in vials containing 15 ml PBS. The vials were incubated at 37 °C for various periods of time. The buffer solution was replaced every 60 hours. After incubation, the film was washed extensively with water and dried at 30 °C *in vacuo* until a constant weight was reached. The degree of degradation was estimated from the mass loss and molecular weight loss by GPC.

RESULTS AND DISCUSSION

Thermal Analysis

Differential scanning calorimetry (DSC) scans of all samples were performed in order to characterize the thermal properties of the blends. Figure 1 summarizes the DSC results of PDLLGA/TEGOMER blends for four different compositions (95/5, 90/10, 85/15, 50/50). The T_g (glass transition temperature) was taken at the onset of the corresponding heat capacity jump and the melting points are the peak temperatures of the melting endotherms.

DSC analysis of pure TEGOMER clearly indicated the formation of two-phase morphology[24] with the siloxane T_g around –125 °C and polycaprolactone melting point T_m around +56 °C, as shown in Figure 1.

For pure PDLLGA, the T_g was observed at approximately 41 °C. At a 5 % TEGOMER concentration, a single T_g was seen at 40 °C. For blend compositions having higher TEGOMER concentrations, the T_g could not be observed by DSC due to the screening effect of the melting endotherm. For pure PDLLGA and PDLLGA/TEGOMER (95/5), no melting endotherm and no crystallization exotherm were observed. As far as T_c (crystallization temperature) and T_m of the quenched samples, as a function of the blend composition, are concerned (Figure 1), it can be seen that T_c increases with the amount of PDLLGA for the blends with 50 to 90 % PDLLGA. This fact indicates that the crystallization of TEGOMER in the blends

is progressively hindered with an increase of the amount of PDLLGA.

Simultaneously, the TEGOMER T_m in the blends decreases with an increase of the amount of PDLLGA. T_m depression is a common phenomenon for miscible blends having one crystallizable component.

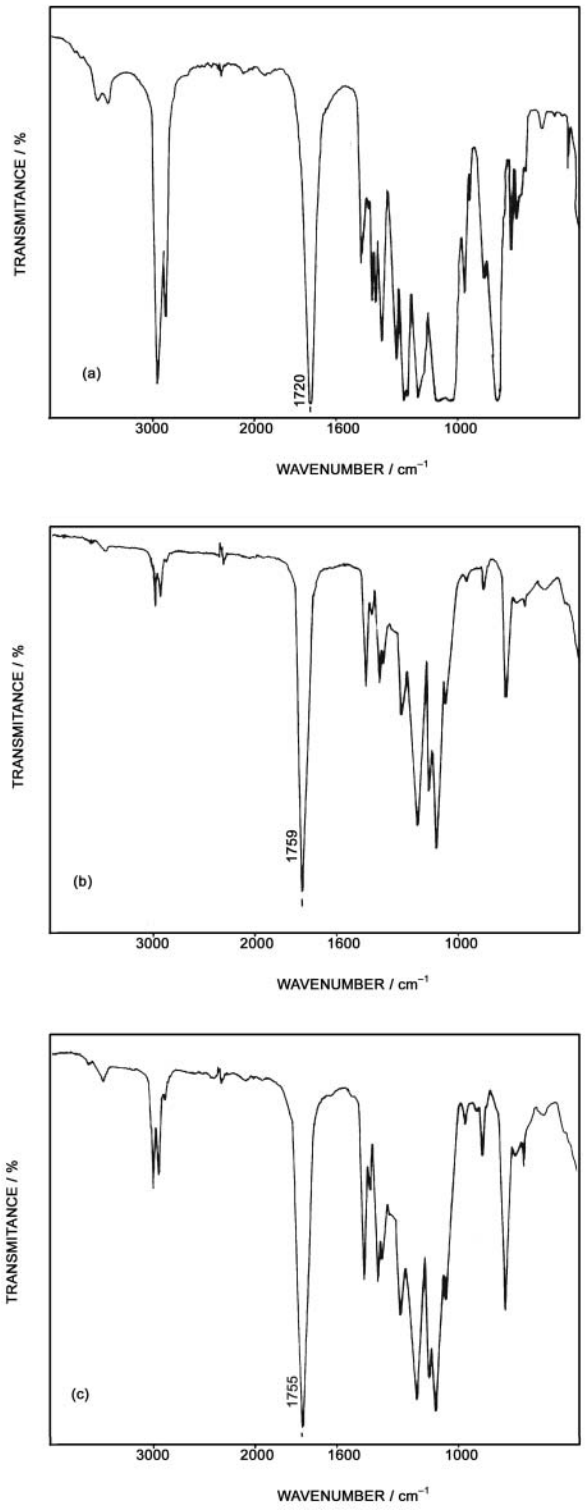


Figure 2. FTIR spectra of TEGOMER (a); PDLLGA (b); PDLLGA/TEGOMER (85/15) blend (c).

FTIR Analysis

Figure 2a–c shows the FTIR spectra of the TEGOMER, PDLLGA and PDLLGA/TEGOMER (85/15) blend, respectively. The specific interactions determined by FTIR showed a slight decrease in the absorption frequency of the carbonyl (C=O) group for the PDLLGA/TEGOMER system, as seen in Figure 2a–c. Carbonyl absorptions of the samples were observed at 1720 cm^{-1}, 1759 cm^{-1} and 1755 cm^{-1} for TEGOMER (Figure 2a), PDLLGA (Figure 2b) and the blend (Figure 2c), respectively. Carbonyl absorption was the same (1755 cm^{-1}) for the binary blends at all investigated compositions (95/5; 90/10; 85/15; 50/50). This shift to lower frequencies can be indicative of the hydrogen bonding interaction between the hydroxyl end groups of TEGOMER and the carbonyl groups of PDLLGA.

Other characteristic peaks of TEGOMER were observed at 3500 cm^{-1} for –OH stretching vibration, at 1260–800 cm^{-1} for Si-CH_3 deformation, at 1026 cm^{-1} for Si-O-Si asymmetric vibration. In the FTIR spectrum of PDLLGA, we observed a peak at 1360–1450 cm^{-1} for symmetric and asymmetric CH_3 vibrations and at 1190 cm^{-1} for C(C=O)-O stretching. FTIR spectra of PDLLGA/TEGOMER blends (Figure 2c) have characteristic peaks of these two components.

Tensile Properties

Mechanical properties of PDLLGA and PDLLGA/TEGOMER blends are given in Table I. The data are the averages of three runs for the ultimate tensile strength (σ), Young's modulus (E) and the elongation at break (ε). Addition of TEGOMER improved significantly the overall toughness of PDLLGA. As illustrated in the stress-strain curves (Figure 3), the PDLLGA was fairly rigid but very brittle with very low break strain and no yield point. Only 5 % of TEGOMER sufficed to increase the elongation at break to 1400 %. The range of the blend modulus (95/5) decreased to the range typical of elastomers. Higher TEGOMER concentration tremendously increased the elastomeric properties, which could not be measured with acceptable accuracy with our tensilon equipment.

Degradation

The hydrolytic degradation study was carried out on the PDLLGA and PDLLGA/TEGOMER 85/15 blend for 60

TABLE I. Tensile properties of PDLLGA/TEGOMER blends

Blend composition (w)	Ultimate elongation (ε)	Ultimate strength (σ)	Young's modulus (E)
%	%	MPa	MPa
100/0	8.1	11.2	244
99/1	21.9	4.4	63.8
95/5	1410	2.0	0.8

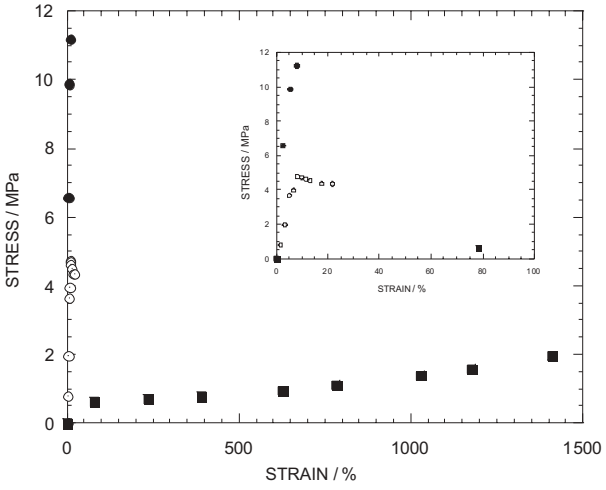


Figure 3. Stress-strain curves for PDLLGA (●); PDLLGA/TEGOMER (99/1) blend (o); PDLLGA/TEGOMER (95/5) blend (■).

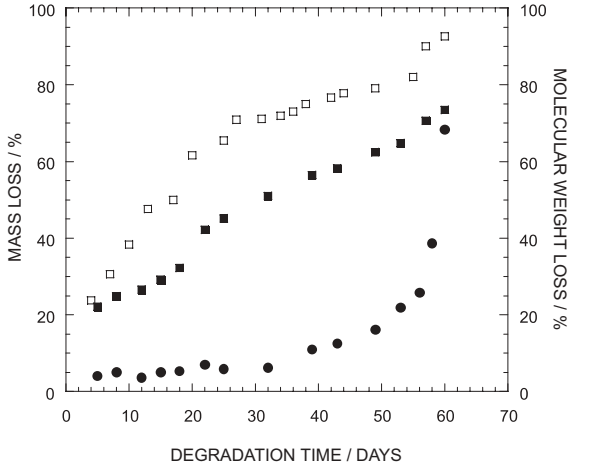


Figure 4. Mass loss for PDLLGA (o); PDLLGA / TEGOMER (85 / 15) blend (●); and molecular weight (M_w) loss for PDLLGA (□); PDLLGA / TEGOMER (85 / 15) blend (■).

days. The 85/15 blend is the sample where the influence of TEGOMER can be clearly seen (see DSC results) and the amount of PCL is not too high to prolong significantly the degradation process. The molecular weight and mass losses for both samples are shown in Figure 4. These results indicate that degradation occurs in the bulk by random chain scission. Once the average molecular weight of the sample decreases to a certain level, chains become soluble and mass loss is observed.[22,25,26] For the PDLLGA sample, about 23 % of the mass of the material was left in 60 days, while the mass loss of PDLLGA/ TEGOMER blend was 68 % in the same time interval. This small difference observed in mass loss may be a result of a more difficult penetration of water molecules within the sample composed of the PDLLGA/TEGOMER blend due to its higher hydrophobicity. The molecular weight loss determined from GPC measurements is also shown as a function of degradation time for both PDLLGA and the PDLLGA/TEGOMER (85/15) blend. The overall trend to a decrease in molecular weight of the PDLLGA/ TEGOMER blend is similar to that of the PDLLGA copolymer. The molecular weight kept going down with the degradation and the molecular weight loss for the 85/15 blend was 74 % after 60 days. The appearance of the PDLLGA and PDLLGA/TEGOMER blend samples changed from a slightly translucent material to a white brittle material within 60 days.

Morphology Studies

Figure 5 shows the SEM images of PDLLGA/TEGOMER blends (85/15) during degradation. Secondary electron images (SEIs) were applied in SEMs. Figure 5a,b shows the fractured surface morphology of the PDLLGA/ TEGOMER blend at two different magnifications prior to degradation (×500 and ×5000). The homogeneity of the fractured surface is very high and phase separation is not observed. Consequently, we can claim that the PDLLGA/ TEGOMER blend (85/15) is a one phase system. After 5 days of degradation, a well-defined erosion zone was observed (Figure 5c). The erosion zone showed longitudinal cracks and voids. Spherical structure was observed at ×5000 magnification (Figure 5d). These spheres had a very small size, close to 1 μm in diameter. Twelve days after the start of the degradation experiment, the number and also the size of the voids seemed to increase (Figure 5e,f). After 22 days of degradation, the morphology of the film became more brittle. The size of the holes increased. Finally, after that time, we were not able to continue the SEM measurements due to technical difficulties in sample preparation with these fragile films.

CONCLUSION

The spectroscopic, thermal, mechanical, morphological properties and degradation kinetics of PDLLGA/ TEGOMER binary blends have been investigated by several techniques. The results of DSC and FTIR showed that the binary PDLLGA/TEGOMER blends are partially miscible for compositions containing small amounts of PCL. The effect of the siloxane component in the tensile properties of blends can be clearly observed.

Degradation studies of PDLLGA and PDLLGA/ TEGOMER blends were performed at 37 °C in phosphate buffered saline. The results indicated that the degradation occurred in the bulk by random chain scission. The weight loss of PDLLGA/TEGOMER (85/15) blend was 68 % in 60 days. The SEM micrograph of this blend system showed a rather homogeneous structure. After degradation in several days, some voids and cracks were seen at the fractured surface. The size of these voids increased with the degradation time.

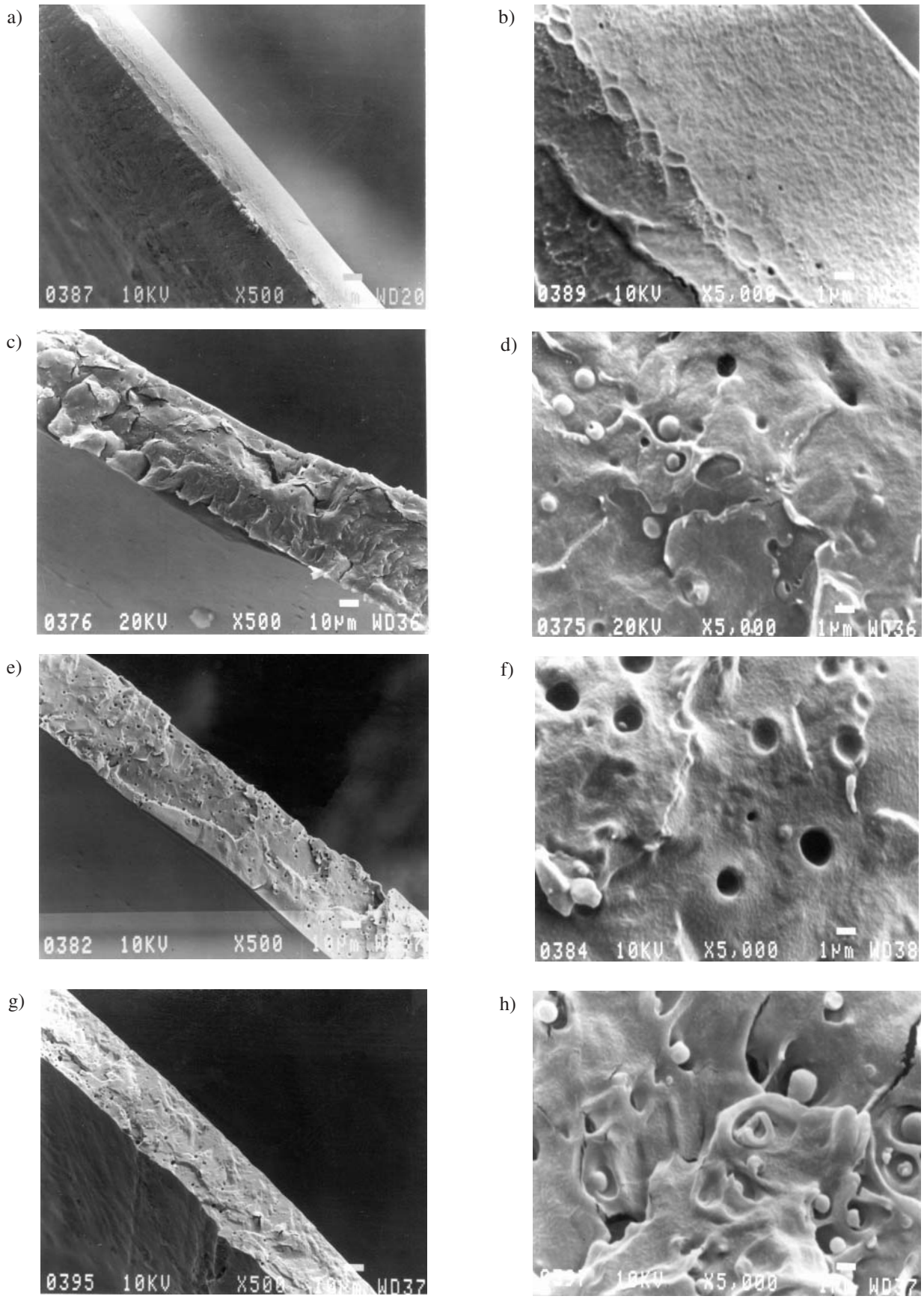


Figure 5. SEM micrographs of PDLLGA/TEGOMER (85/15) blend: after synthesis ×500 (a), ×5000 (b); 5 days after degradation ×500 (c), ×5000 (d); 12 days after degradation ×500 (e), ×5000 (f); 22 days after degradation ×500 (g), ×5000 (h).

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SAŽETAK

Biokompatiblne polimerne smjese poli(D,L-mliječna kiselina-*co*-glikolna kiselina) i triblok PCL-PDMS-PCL kopolimera: karakterizacija i degradacija

Alexandra Porjazoska, Oksan Karal-Yilmaz, Nilhan Kayaman-Apohan, Maja Cvetkovska i Bahattin M. Baysal

Polimerne smjese poli(D,L-mliječna kiselina-*co*-glikolna kiselina), PDLLGA i triblok kopolimer polikaprolakton-poli(dimetilsiloksan)-polikaprolakton (PCL-PDMS-PCL) pripravljene su koprecipitacijom miješanih kopolimernih kloroformnih otopina u metanolu i ispitane diferencijalnom pretražnom kalorimetrijom (DSC) i infracrvenom spektroskopijom s Fourierovom transformacijom (FTIR), degradacijskim testovima i pretražnom elektronskom mikroskopijom (SEM). Na temelju DSC mjerenja i FTIR analize utvrđeno je da su binarne smjese PDLLGA/TEGOMER djelomično mješljive. Rezultati naprezanje-istezanje pokazuju da se dodatkom TEGOMER-a znatno poboljšava ukupna žilavost PDLLGA. Degradacija PDLLGA/TEGOMER istraživana je u fosfatnom puferu pri pH = 7,4 i 37 °C, a morfologija smjesa ispitana je pretražnom elektronskom mikroskopijom.