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Self-reinforcement and hydrolytic degradation of amorphous lactic acid based poly(ester-amide), and of its composite with sol-gel derived fibers

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The self-reinforcing and hydrolytic degradation of an amorphous poly(ester-amide) (PEA) based on lactic acid have been studied and compared with those of poly-L-lactide (PLLA). The studied PEA-rods were self-reinforced (SR) by solid-state die drawing resulting double shear strength. The hydrolytic degradation of PEA was studied during exposure to phosphate buffered saline at pH 7.4 and at 37 °C for 18 weeks. The degradation and mechanical properties of PEA were also followed in a self-reinforced composite structure consisting of PEA and sol-gel derived SiO_2-fibers (SGF, 8 wt %). The hydrolytic degradation of the SR-PEA-rods with and without SG-fibers was significantly faster than that of SR-PLLA-rods. The weight average molecular weight (M_w) of PEA decreased by 90% from the initial M_w during the first 6 weeks in hydrolysis, when the M_w of the PLLA decreased by 10%.

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1. Introduction

A demand to find and develop new bioabsorbable materials, which have both high initial strength and controlled strength and modulus retention, grows further with new biomedical applications. Aliphatic polyesters of α-hydroxy acid derivatives, such as polylactides (PLA) and polyglycolide (PGA), are some of the most well-known and important bioabsorbable polymers, which are used, e.g., in biomedical, pharmaceutical and ecologically feasible applications [1–7]. For some of these applications shorter degradation times and lower processing temperatures are required. For example, the total resorption time of highly crystalline poly-L-lactide (PLLA) is more than five years [8, 9], and the processing temperature required in melt extrusion is over 180 °C [10], which can be unsuitable, e.g. in drug delivery applications. The degradation of polylactides can be accelerated by changing the stereoisomerism of PLA and thus by decreasing the crystallinity of the polymer [11–13], but even in this way a sufficient improvement in degradability is not always achieved. So amorphous poly(ester-amides) with highly hydrolyzable ester and amide groups have recently aroused great interest [14].

Bioabsorbable polymers, when processed with traditional techniques of plastics technology, are often mechanically unsuitable (too brittle or flexible) for clinical use [1, 2]. Therefore, different kinds of reinforcing techniques have been developed for bioabsorbable polymers, whereupon materials with improved strength, ductility and elastic modulus have been obtained [15–17]. Ultra-strong, bioabsorbable materials are achieved with the self-reinforcing technique introduced by Törmälä *et al.* [18, 19]. By self-reinforcing the bioabsorbable polymer matrix is reinforced with orientated, fibrous reinforcement elements, and these elements have the same chemical composition as the matrix polymer. The high degree of molecular orientation, achieved by self-reinforcing, makes reinforcement elements both stiff and strong in the direction of their long axis. The bending strength of PLLA has been improved with this method from the initial strength of 110–140 to 300 MPa [7, 16].

There is also a high demand for bioactive composites.

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The sol-gel derived silica gel is biodegradable and bioactive forming interfacial bonding with tissues [20–25]. Due to the low processing temperature of silica gel it can also be doped with medicines and other temperature sensitive compounds without the decomposition of the added compounds [26]. For this reason, polymer/sol-gel derived SiO_2 based fiber composite can be made, which acts as an active agent delivery system with controlled and prolonged release [27].

Lactic acid based polymers have traditionally been synthesized by a ring-opening polymerization of lactide [5, 28]. An alternative way to high molecular weight poly(lactic acid) is to treat condensation polymers with chain extenders. Previously, we have widely studied the synthesis and characterization of lactic acid based poly(ester-urethanes) (PEU) and poly(ester-amide) (PEA) [29–32]. These biodegradable polymers are synthesized using a two-step synthesis including condensation polymerization of lactic acid with butanediol or succinic anhydride to low molecular weight prepolymer and the molecular weights were increased by using 1,6-hexamethylene diisocyanate or 2,2′-bis(2-oxazoline) as the chain extender forming PEU and PEA, respectively. Although these polymers are amorphous by nature, their mechanical properties are comparable with PLLA. In addition, the degradation rate of PEU is considerably faster than PLLA [31].

The purpose of this work was to investigate the self-reinforcing and hydrolytic degradation of poly(ester-amide), and its behavior with SiO_2-based fibers in the composite structure. The studied PEA- and PLLA-rods were reinforced by solid-state die drawing, creating orientation of polymer chains. In order to combine beneficial properties of PEA, and the bioactivity of sol-gel derived fibers, the composite structure (PEA-SGF) was also formed. The effect of SG-fibers on the self-reinforced PEA-SGF composite was investigated, and the properties of pure SR-PEA and SR-PEA-SGF composite were compared with those of pure SR-PLLA and SR-PLLA-SGF composite.

2. Materials and methods

2.1. Preparation of poly(ester-amide)

Poly(ester-amide) was prepared by using a two-step synthesis including polycondensation and chain linking [32]. The prepolymer was condensation polymerized from L-Lactic acid (88% L-lactic acid in water, ADM) with 2 mol % succinic anhydride (used as received, Fluka) and Sn(II)octoate (0.01 mol %, used as received, Aldrich) in a rotation evaporator to produce carboxyl-terminated oligomer. The flask was purged with nitrogen and placed in an oil bath. The reaction mixture was polymerized at 200 °C for 24 h, with a continuous nitrogen stream fed below the surface of the melt, at a reduced pressure of 20 mbar. Chain extending polymerizations were carried out in a batch reactor under nitrogen. Carboxyl-terminated lactic acid based prepolymer (1000 g) was dry-blended with the chain extender 2,2′-bis(2-oxazoline) (Tokyo Kasei) and the mixture was fed to the heated reactor. The polymerizations were carried out at 200 °C for 20 min.

2.2. Manufacturing of self-reinforced PEA and PLLA rods

The biodegradable rods from PEA with and without (8 wt %) sol-gel derived silica fibers were made using the self-reinforcing (SR) technique. As a reference, PLLA rods with and without (8 wt %) sol-gel derived silica fibers were also made in the same way. The SiO_2-based fibers were prepared from tetraethyl orthosilicate (TEOS) by using the sol-gel method and dry spinning technique. The sol was compounded of TEOS, ethanol, deionized water and HNO_3 in a molar ratio of 1/1/2/0.036. The preparation process of the studied fibers has been presented earlier by Jokinen *et al.* [23] and Peltola *et al.* [24]. Poly-L-lactide is the product of Purac Biochem BV.

In the manufacturing of SR-PEA and SR-PLLA rods, the polymer was granulated, dried in a vacuum oven and melt-extruded (Brabender) to cylindrical billets of 4 mm diameter. After which, the billets were self-reinforced using the solid-state deformation technique, with die drawing at a temperature of 52–58 °C for PEA and 124 °C for PLLA through a conical die to the draw ratio of 4 to accomplish the self-reinforced fibrillated structure.

In the preparation of the composite rods, SR-PEA-SGF and SR-PLLA-SGF, the polymer matrices were dissolved in chloroform and the cut fibers ($l = 10$–15 mm) were compounded with the dissolved polymer solution. After compounding, the solvent was evaporated, and the mixtures were granulated and dried in a vacuum oven. The materials were melt-extruded and self-reinforced in the same way as the SR-PEA and SR-PLLA rods, except that the die drawing temperatures were 50–56 °C for the PEA-SGF material and 115 °C for the PLLA-SGF material. The diameter of all finished SR-rods was 2 mm.

2.3. Degradation *in vitro*

The SR-rods for *in vitro* exposure testing were immersed in phosphate buffered saline (PBS, 3.48 g/dm^3 Na_2HPO_4, 0.755 g/dm^3 NaH_2PO_4, 5.9 g/dm^3 NaCl buffered saline) at pH 7.4, and maintained at 37 °C. The PBS solution was changed at two-week intervals. The samples were removed from the solution at weeks 1, 3, 6, 9, 12, 15 and 18, and the changes in mechanical properties, thermal behaviors and molecular weights were examined. The morphologies of the rods were studied using SEM.

2.4. Strength measurements

A tool consisting of two sections, which were joined together by the rod, measured the shear strengths of the intact rods and rods after *in vitro* exposure (Fig. 1). During the test, the sections were pulled apart using an Instron 4411 Materials Testing Machine operating at a crosshead speed of 10 mm min^{-1}. After PBS exposure, the shear strength of four parallel samples were tested at room temperature in a wet state.

The bending strengths and modulus of the rods were measured with a three-point bending test using an Instron 4411 Materials Testing Machine at room temperature.

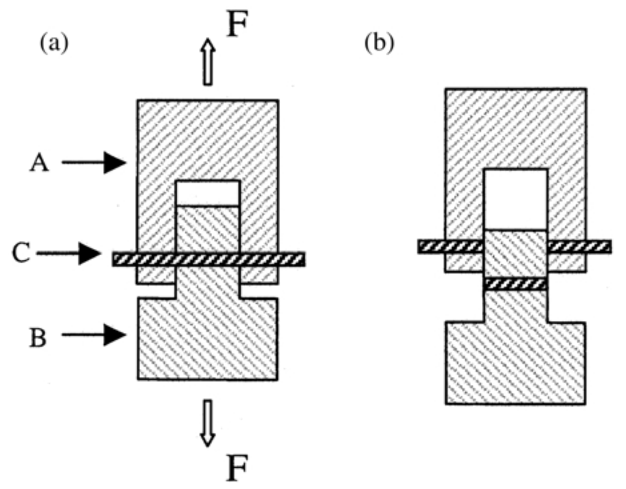

Figure 1 The schematic cross-sectional drawing of the shear strength measurement arrangement. (a) The test rod (C) were placed through the drill holes of two test tool parts (A and B). (b) In the test two tool parts were pulled apart, when the test rod was cut into three pieces perpendicular to the longitudinal direction of the rod.

The test rod rested on the two rigid supports with a span of 32 mm, the rod was then loaded with its striking edge at the mid-point between the supports at a crosshead speed of 5 mm min^{-1}.

2.5. Characterization

The thermal behavior of intact SR-rods and *in vitro* exposed rods were measured using a Perkin-Elmer Pyris 1 differential scanning calorimeter (DSC) (Perkin-Elmer Co., USA), calibrated with indium standard. The samples were heated from 30 to 200 °C at a rate of 20 °C min^{-1}. After which the samples were cooled to 30 °C and heated again to 200 °C. The glass transition temperatures and crystallinities were measured during the second heating period.

Molecular weights (M_n and M_w) and molecular weight distributions (MVD) were determined relative to polystyrene standards by gel permeation chromatography (GPC). The Waters Associates system was equipped with a Waters 700 Satellite wisp injector, a Waters 510 HPLC solvent pump, four linear PL gel columns (10^4, 10^5, 10^3 and 100 Å) connected in series, and a Waters 410 differential refractometer. All the samples were analyzed at room temperature. Chloroform (Riedel-de Haen Ag, stabilized with 1% ethanol) was used as eluent and was delivered at a flow rate of 1.0 ml min^{-1}. The samples were dissolved in chloroform at a concentration of 1.0% (w/v). The injection volume was 200 µl.

The surface and internal morphologies of the SR-rods were characterized with a JEOL JSM-T100 (JEOL LTD, Tokyo, Japan) scanning electron microscopy (SEM) at 15 kV. Samples were vacuum-dried, mounted on the metal stubs with an adhesive, and then coated with gold.

Specimens (125, 625 and 1250 mg) from SR-PEA-SGF and SR-PLLA-SGF composite rods, containing 8 wt % SG-fibers, were placed into six bottles, and each sample was immersed in 50 ml of PBS. The temperature of the closed bottles were maintained at 37 °C. The 5 ml of PBS-fluid were removed from these bottles and the 5 ml of pure PBS-fluid was substituted at two-week intervals. Silicon concentrations in the PBS-samples were monitored with a UV-vis spectrophotometer (Hitachi Model 100-60) at Institute of Dentistry, University of Turku.

The pH measurements of PBS were performed with a pH-meter (GWB 761 Calimatic) during the PBS exposure to the specimens.

3. Results and discussion

Significant differences occur in the structure and properties of PEA and PLLA, although their chemical structures are very similar. The oxamide bonds are able to form hydrogen bonds, and the irregularities in the structure of PEA, caused by the chain extender and racemization of L-lactic acid units during the polymer synthesis, inhibit crystallization. Because of the absence of the crystallinity, PEA can be processed at temperatures lower than that for crystalline PLLA. The processing temperature of the PEA was 120–140 °C in the extrusion and that of the PLLA was 180–220 °C. During the die drawing, the temperature was 50–58 °C for PEA and 115–124 °C for PLLA. The initial molecular weight of PEA was considerably lower and the polydispersity wider than those of PLLA (Table I). During the extrusion and orientation the molecular weights of both the polymers reduced due to thermal degradation to 55–75% of their initial molecular weights.

The mechanical properties of PEA without self-reinforcement were reported to be comparable to the properties of PLLA [32], despite the fact that the molecular weights of PEA are often considerably lower. Because of the increase in the molecular orientation accompanied by self-reinforcing, the mechanical properties of both the polymers in the direction of the orientation improved considerably (Table II). After self-reinforcement, the mechanical properties of PEA corresponded to the cortical bone

TABLE I Molecular weight of the polymers

Polymer	M_n	M_w	MWD
PEA	66 000	204 000	3.10
SR-PEA	50 000	157 000	3.16
SR-PEA-SGF	50 000	149 000	2.99
PLLA	1 100 000	1 800 000	1.64
SR-PLLA	830 000	1 160 000	1.40
SR-PLLA-SGF	620 000	940 000	1.52

TABLE II Initial mechanical properties of the self-reinforced polymer rods

Polymer	Bending modulus (GPa)	Bending strength (MPa)	Shear strength (MPa)
PEA	2.8	116	47
PEA-SGF	2.1	81	32
PLLA	2.6	138	47
PLLA-SGF	2.7	121	46
SR-PEA	4.4	185	85
SR-PEA-SGF	3.1	122	65
SR-PLLA	5.6	210	143
SR-PLLA-SGF	4.7	180	123

properties. The bending and shear strength values of the cortical bone are 180–195 and 68 MPa respectively [7]. This improving of mechanical properties by self-reinforcing is known for PLLA in which the crystallinity is also increased [33], but with amorphous polymers this notable increase in mechanical strength opens up new possibilities.

The sol-gel derived fibers indicated no reinforcing effect on the properties of the PEA and PLLA composites, which were partly derived from the brittle nature of the SiO_2-fibers. The sol-gel derived fibers acted as a bioactive filler in the composite, which was discovered from shear strengths in Table II. The properties of the SR-PEA-SGF and SR-PLLA-SGF rods were lower compared with those of the SR-PEA and SR-PLLA rods.

The significant degradation of PEA occurred during the first weeks of the hydrolysis. The molecular weight of both the PEA-type rods decreased considerably faster than the molecular weight of the PLLA rods, as expected. The M_w of the SR-PEA and SR-PEA-SGF rods decreased from the initial molecular weight to 10% during the first six weeks and the M_w of PLLA rods decreased to 90% in corresponding time (Figs. 2 and 3). The mechanical strength of the PEA rods also decreased considerably after the first week of *in vitro* exposure. The shear strength of SR-PEA rods was decreased to 10% from the initial strength and that of SR-PEA-SGF composite rods to 30% of the initial strength after one week in PBS (Fig. 4). After nine weeks the PEA-rods became too brittle to test, whereas hardly any changes were noticed in the shear strength of the PLLA rods, predictably. The M_w of the SR-PLLA-SGF rods diminished to half of its initial molecular weight during 42 hydrolysis weeks (not shown), but this decrease did not significantly affect their mechanical properties. The dissimilarity of degradation rate between polymers was a consequence of differences in their chemical composition, crystallinity, impurities, monomer content, thermal history, molecular orientation, matrix/reinforcement morphology and molecular weight distribution [2, 3, 7, 34]. The degradation time of PEA could be extended by minimizing the monomer content and by optimizing molecular orientation and its relaxation in PEA.

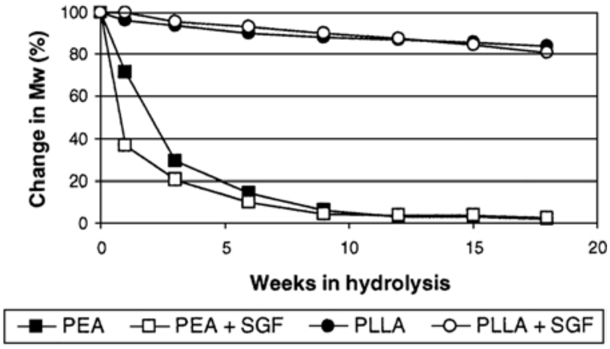

Figure 3 Changes of M_w during hydrolysis.

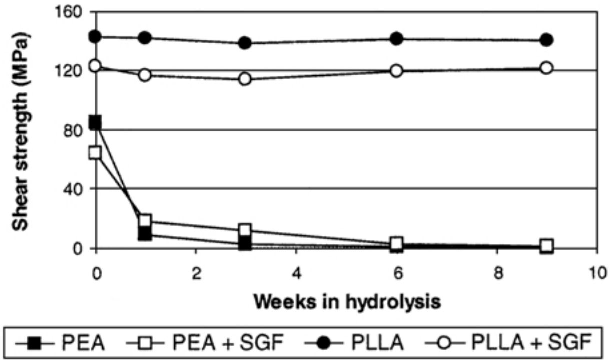

Figure 4 Changes of shear strength during hydrolysis.

The effect of PBS exposure to the dimensions of self-reinforced native poly(ester-amide) and composite was remarkable. During the PBS exposure the SR-PEA and SR-PEA-SGF rods shrank longitudinally and simultaneously their diameters increased (Figs. 5 and 6), but the shrinkage of PLLA rods was not observed. The shrinkage of the rods made impossible to test the bending strength of the PEA rods after the first week in hydrolysis. This shrinkage probably arose from the relaxation of orientated structure. The increase in the rod diameter was more pronounced with PEA than with PEA-SGF composite, which indicates that the SG-fibers support the macroscopic structure. In addition to dimension changes, the physical appearance of the PEA rods changed during the hydrolysis. The PEA rods whitened in hydrolysis, which indicated the partial crystallization of the polymer chains and the absorption of water in the structure. This has also been observed to take place with PLLA during the degradation at 37 °C [34]. The whitening of SR-PEA-SGF rods was not so distinct.

According to earlier investigation, the crystallinity of PLLA increased during the self-reinforcement [33], but the PEA remained totally amorphous after the mechanical orientation, i.e. solid-state die drawing. Although the molecules were oriented parallel, no crystallinity was

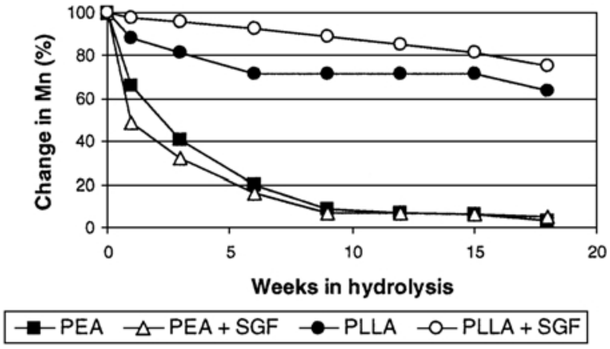

Figure 2 Changes of M_n during hydrolysis.

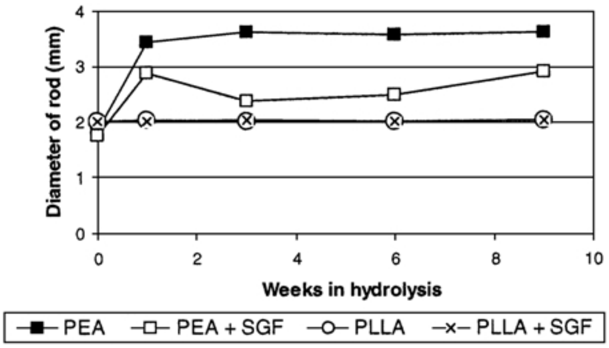

Figure 5 Changes of rod diameter during hydrolysis.

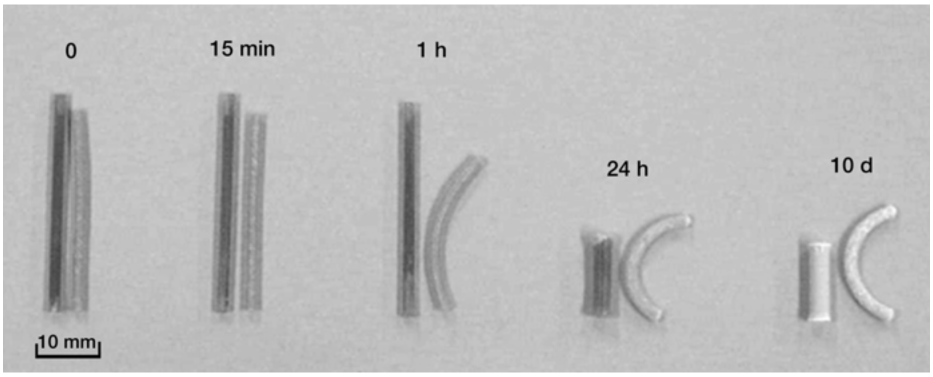

Figure 6 Shrinkage of SR-PEA (left-hand) and SR-PEA-SGF rods during the PBS exposure.

detected. However, after one-week immersion a melting peak was detected in the DSC curves of the PEA (Figs. 7 and 8). As the hydrolysis proceeded this melting endotherm became more pronounced and ΔH_m increased. This was a direct indication of the partial crystallization of the PEA. Similar changes have been observed with polylactides earlier, and the increase of the crystallinity has been suggested to result from the re-crystallization of the degraded polymer chains [11, 12, 35–38].

Sol-gel derived fibers affected the degradation of the poly(ester-amide). SG-fibers did not reinforce the polymer composite prior to exposure to PBS, but after the first week in hydrolysis the SR-PEA rods containing the SG-fibers had a higher shear strength than the rods without the SG-fibers (Fig. 4). However, the molecular weight of the PEA decreased faster with the SG-fibers during the first week (Figs. 2 and 3). Smaller changes of shear strength and rod length in hydrolysis arose from the fibers, which prevented the relaxation of orientated structure. Figs. 9 and 10 show PEA separated from the SG-fibers during one-week of PBS-exposure, in other words, the degradation was faster at the interface of the polymer and the SG-fibers in the exposure. The diffusion of the PBS-fluid into the polymer structure along the interface of fibers and polymer presumably accelerated the degradation of the PEA at the beginning of the hydrolysis, and it was also seen as a faster decrease of molecular weight. Jiang and Hinrichsen [39], and Törmälä *et al.* [19] have adduced this type of phenomenon in the biodegradable composites.

SEM-analysis showed that, small cracks and bubbles appeared on the surface of the PEA-specimens in hydrolysis (Figs. 11–13). The PEA-rods appeared to be whole in the external appearance after the exposure to PBS, but they disintegrated when handled at the 12, 15 and 18 weeks of immersion. This indicates that the degradation of the rods proceeded faster in the center than on the surface of the rods. A phenomenon of this kind has also been reported earlier with polylactides and lactide-glycolide copolymers [34, 35, 37, 40, 41]. It was suggested that this surface/center differentiation results from the increased number of carboxylic end-groups in the rod center during the degradation and from the

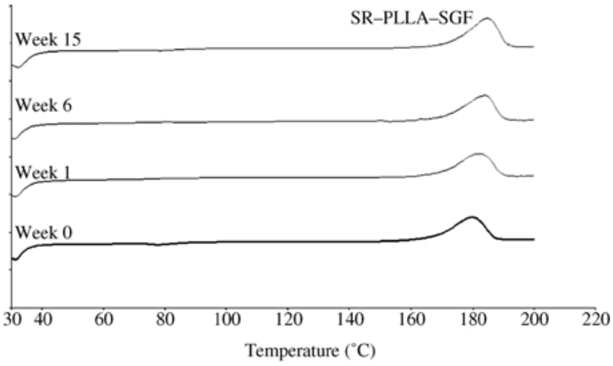

Figure 8 DSC thermograms of SR-PLLA-SGF rod at different degradation times after the PBS exposure.

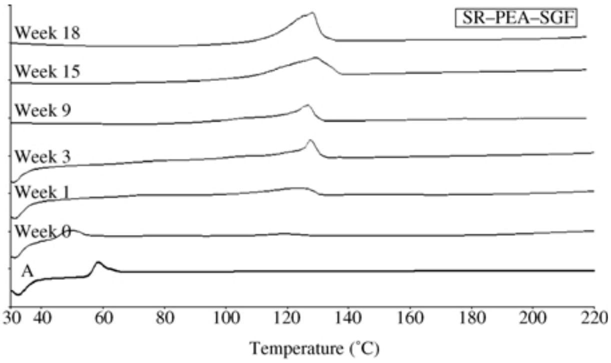

Figure 7 DSC thermograms of SR-PEA-SGF rod at different degradation times after the PBS exposure (A = cylindrical billet).

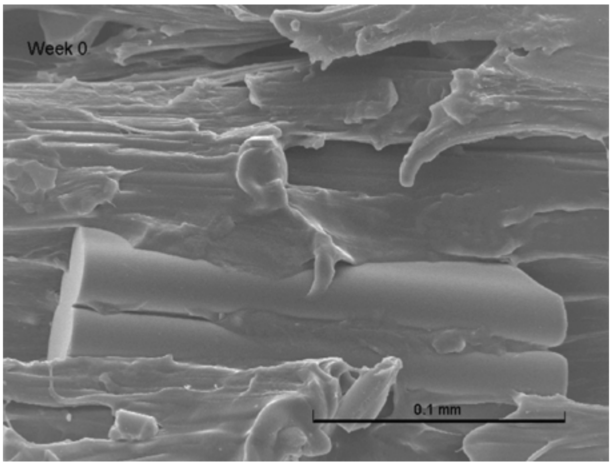

Figure 9 Interface of PEA and SG-fibers before PBS-exposure (SEM, 500 ×).

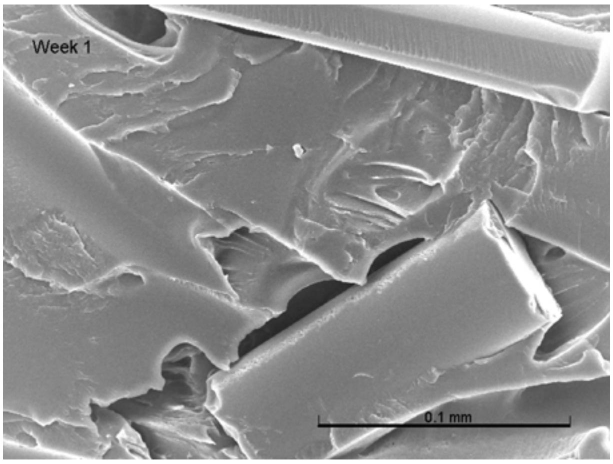

Figure 10 Interface of PEA and SG-fibers after one-week PBS exposure (SEM, 500 ×).

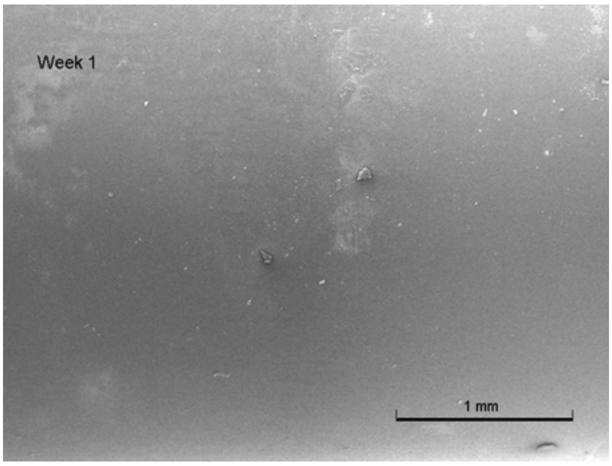

Figure 11 Changes in surface of SR-PEA rods (SEM, 35 ×).

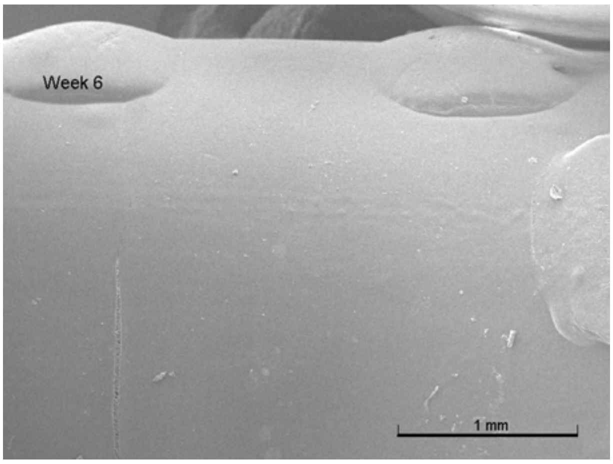

Figure 12 Changes in surface of SR-PEA rods (SEM, 35 ×).

catalytic effect of these groups in the ester degradation (inner autocatalytic mechanism) [35, 40, 41]. The formed degradation products dissolved more easily at the surface of the specimen than from the center, which leads to the different concentrations of the carboxylic groups through the rod, to a bimodal degradation and finally to hollow rods. In the present study the formation of the acidic compounds was seen as a decreasing of the pH of the buffered saline solution from 7.4 to 6.5 during hydrolysis.

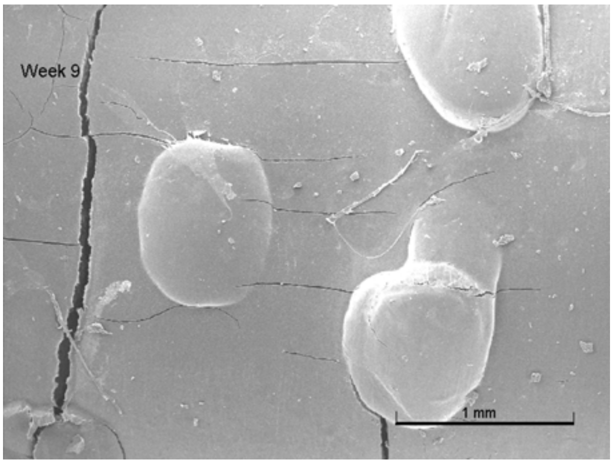

Figure 13 Changes in surface of SR-PEA rods (SEM, 35 ×).

In this study the release of silica from the fibers of composite rods, or the degradation of the SiO_2-fibers, was not observed with UV-vis spectroscopy during 18 weeks in hydrolysis. The acidic degradation product of PEA and PLLA has probably disturbed the determination of silicon [42].

4. Conclusions

The study showed that the self-reinforcing of amorphous poly(ester-amide) succeeded in solid-state die drawing. The initial mechanical properties of the amorphous PEA are equal to those of PLLA-polymer, and with self-reinforcing the properties can be improved considerably. For example, the shear strength of PEA improved with self-reinforcing from 47 to 85 MPa. In the aqueous media considerably faster degradation was reached with PEA than with PLLA, which was probably due to the chemical composition and amorphous characteristic of PEA. The amorphous structure accelerated the access of water molecules into the polymer, and thus the degradation of PEA proceeded faster than that of crystalline PLLA.

The studied sol-gel derived SiO_2-fibers did not appear to have a reinforcing effect in the composite structures prior to PBS exposure, which resulted from the poor quality of fibers. But during PBS exposure the fibers hindered the relaxation of orientation, which appeared as smaller changes of shear strength and as lesser shrinkage in the composite rods.

Acknowledgments

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