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Biodegradable Fibers of Poly-L,DL-lactide 70/30 Produced by Melt Spinning

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Summary: Melt spinning of poly-L,DL-lactide 70/30 has been studied. Fiber having diameter lower than 120 micron exhibited tensile modulus and strength in the range of 3–4 GPa and 130–180 MPa, respectively. Maximum attainable modulus and strength of 4.7 GPa and 205 MPa were predicted, according to a proposed equation in dependence on the draw ratio. *In vitro* degradation performed in PBS solution at 37 °C, showed that after 4 weeks fibers maintained adequate properties for tissue engineering applications.

Keywords: drawing; fibers; *in vitro* degradation; mechanical properties; processing

Introduction

Biodegradable polymers and copolymers have been widely used in various biomedical fields for more than forty years. Recent applications consist in biodegradable scaffolds useful for cell seeding in order to promote biological tissue formation.[1] Typical scaffolds are based on films, sponges and fibrous materials that progressively degrade after implantation. The resorption rate depends on many factors, such as the type of polymer and its molecular weight and crystallinity.[2] In particular, polyglycolide fibers degrade in about 10–15 days, whereas poly-L-lactide or polycaprolactone last for more than one year, due to the slower degradation kinetics of the more hydrophobic and crystalline structure. On the other hand amorphous type materials are mainly used for applications and products where higher degradation rate and/or lower mechanical properties are requested. Poly-L,DL-lactide 70-30 is an amorphous copolymer of L-lactide and DL-lactide more hydrophobic than polyglycolide; it has been variously processed to obtain pins,[3] plates,[4] screws,[4–6] both hydroxyapatite filled and self-reinforced ones,[6] for small bones fixation, or to produce films to prevent the adhesion between tissues after surgery.[7] The degradation kinetics of this copolymer results in between that of polyglycolide and poly-L-lactide, hence poly-L,DL-lactide 70-30 fibers appear promising for production of biodegradable scaffolds where the maintenance of properties for some weeks is required. Object of this research was to study the melt spinnability of poly-L,DL-lactide 70-30.

Experimental

Poly-L,DL-lactide 70-30 (P-L,DL-LA) with the tradename of Resomer RL708 and inherent viscosity of 5.4 dl/g (25 °C 0.1% chloroform) was purchased by Boeringer Ingelheim, Germany.

Melt flow of copolymer was characterized by using a Melt Flow Index LMI 4000 instrument by Dynisco, according to ASTM D1238–98. Temperatures of 210–220–230 °C, and loads of 2.16 and 5.0 Kg were used.

The extrusion of monofilament was performed at temperatures between 120 and 195 °C with different draw ratios by using a commercial extruder Estru13

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(Friulfiliere, Buia-UD, Italy) with a screw of 14 mm diameter (L/D 20 and RC 2.5) and a single-hole spinnerette having diameter of 1.0 mm. The draw ratio λ is defined as the ratio between the section of the die, S_d, and the section of the fiber, S_f, according to eq. (1)

$$\lambda = S_d/S_f = (D_d/D_f)^2 \quad (1)$$

where D_d and D_f are the diameter of the die and the fiber, respectively.

Gel permeation chromatography (GPC) was performed with the aid of an apparatus consisting of an isocratic pump (Spectra Physics, P1500), refraction index detector (Shodex RI71) and a chromatography column (Shodex K 405). Analyses were carried out in chloroform solutions (polymer concentration 0.25% by wt.) at 1 ml/min, with polystyrene standards having molar masses in the range from 20 to 400 kDa. GPC analysis of P-L,DL-LA 70/30 revealed a weight average molecular weight Mw of 292 kDa and a polydispersity index PDI of 1.25.

Differential scanning calorimetry (DSC) was carried out on samples weighing 15 mg by using a Mettler DSC 30 calorimeter, from 0 °C to 230 °C with a heating rate of 10 °C/min in nitrogen flushing at 100 ml/min. A second scan was also performed under the same conditions on samples quenched at the end of the first run with a cooling rate of about −100 °C/min.

Mechanical properties of fibers were measured at room temperature by using an Instron tensile dynamometer mod. 4502, at a cross-head speed of 5 mm/min. Specimens with a gage length of 20 mm were prepared using a thin paper test specimen mounting tab as recommended in standard ASTM D 3379. All the reported tensile properties represent average values of at least five tests.

Tensile dynamic mechanical tests were conducted on 20 mm long single fibers with a dynamic mechanical thermal analyzer (DMTA Mk II by Polymer Laboratories) at a frequency of 5 Hz with 16 μm of dynamic deformation and static stress of 7.5 MPa, from −20 to 150 °C at a heating rate of 3 °C/min. Storage modulus and loss factor (tan delta) were evaluated.

Hydrolytic degradation of fibers was performed at 37 °C in phosphate buffer solution PBS (Sigma) up to 8 weeks. At each follow-up time part of the fibers (70–80 mg) were removed from the degradation bath, quickly wiped and weighed to assess the weight change.

Processing and Characterization

Poly-L,DL-lactide 70/30 is a semicrystalline copolymer with the glass transition at 59 °C and an endothermal melting peak of about 15 J/g in the range 80–130 °C, as shown in Figure 1.

A simplified rheological study was done by means of melt flow analysis. Following the approach proposed by Shenoy et al.,[8] melt flow was measured at different temperatures and loads in order to evaluate the activation energy , E_{act}, according

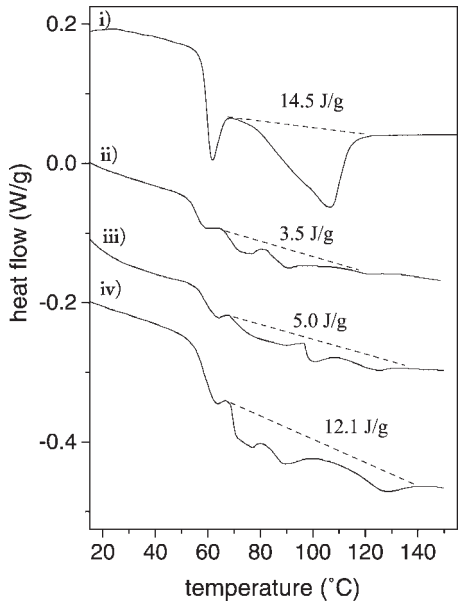

Figure 1.
DSC thermograms of P-L,DL-LA 70/30 pellets (i) and fibers collected at 25 m/min (ii), 50 m/min (iii) and 70 m/min (iv), with draw ratios of 64, 123 and 297 respectively. The dotted lines delimit the integration area of the endothermal peak.

to eq. (2)

$$\text{Log MFI} = K - E_{act}/(2.303 \times R) \times 1/T \quad (2)$$

where K formally represents the Log of MFI (Melt Flow Index) at infinite temperature, and R = 1.98 cal/(mol K). Both K and E_{act} depend on the applied load. From the slope of the line fitting the experimental data reported in Figure 2, activation energies of 49.7 ± 1.5 and 43.1 ± 0.1 Kcal/mol were evaluated for loads of 2.16 and 5.0 Kg, respectively. The higher the load, the lower the activation energy of the chain mobility in the flow.

A preliminary spinning was performed in a two-stage process (melt-extrusion and hot-drawing) according the procedure previously described for PLLA.[9–10] P-L,DL-LA was precautionally desiccated in vacuum at 70 °C for 24 hours. After extrusion in the range 125–195 °C and following drawing at 75 °C, fibers with diameter ranging 180–250 microns were obtained; they had a brittle mechanical behavior with modulus of 2–4 GPa and strength 50–70 MPa.

In order to produce fibers with lower diameter and higher tensile properties, a single extrusion-drawing process was applied. Fibers were produced with a die temperature of 170 °C and a constant output of 0.30 ± 0.05 cm^3/min, and various collection winding speeds between 5 and 70 m/min (with draw ratios of $4 < \lambda < 300$), as shown in Figure 3.

The diameter D of fibers can be approximately predicted by the equation:

$$D = 2 \times 1000(Q/(\pi WS))^{0.5} \quad (3)$$

where WS is the winding speed and Q the output (0.30 ± 0.05 cm^3/min). At winding speeds lower than 15 m/min, the die-swelling is not neglectable, where as at 70 m/min the diameter of the resulting fiber is lower than expected one due to partial crystallization of the fiber. In fact the higher the winding speed, the higher the crystallinity that the fiber developed, as detected by the DSC measurements reported in Figure 1. After heating up to 150 °C and fast cooled, crystallinity was lost and all the samples in the second DSC scan appeared amorphous with Tg at 59–60 °C.

Tensile modulus, deformation at break, yield stress and strength are reported in Figures 4A and 4B as function of the draw ratio λ.

Mechanical properties change with the draw ratio λ, but the effect is evident above a somewhat critical draw ratio λ_c. In fact below a draw ratio of about 50 (or above $1/\lambda = 0.02$), fibers properties (tensile modulus of 2.5 GPa, strength of 60–80 MPa, deformation at break around 200%) are independent of draw ratio. Above λ_c

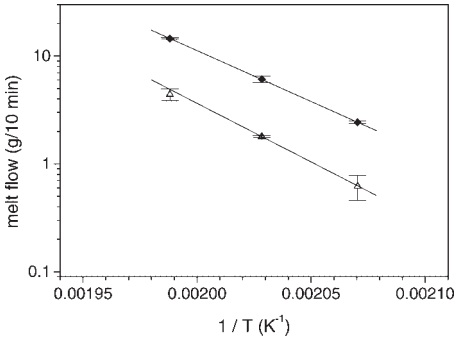

Figure 2.
Melt flow of poly-L,DL-lactide with i.v. of 5.4 dl/g (25 °C, 0.1% chloroform) at loads of 2.16 Kg (△) and 5.0 Kg (◆). The straight lines represent the best fit according to eq. (2).

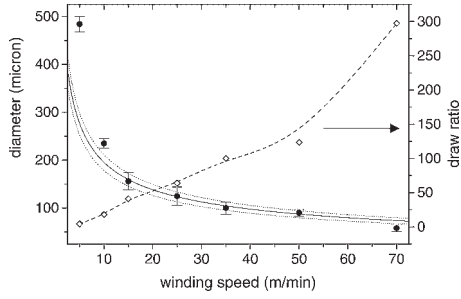

Figure 3.
Effect of winding speed on the diameter of P-L,DL-LA fibers (●) and on the draw ratio (◇). The continuous line represent the predicted value according to eq. (1) with an output of 0.30 cm^3/min, whereas the dotted line refers to outputs of 0.35 and 0.25 cm^3/min.

modulus and stress increase, and deformation at break decreases. Fibers produced at draw ratio $\lambda > 70$, showed modulus of 3–4 GPa, yield stress of 80–100 MPa, strength of 140–180 MPa and deformation at break of 100–150%.

Theoretical maximum attainable mechanical properties P_∞ could be predicted by the intercept of the straight lines fitting the experimental values of modulus or stress in Figs. 4A and 4B with the y axis, according to equation:

$$P = P_\infty - k_p\, 1/\lambda \qquad (4)$$

k_P being a proportionality constant taking into account the sensitivity of the property to the drawing. Following eq. (4) maximum attainable modulus, yield stress and strength of 4.7 ± 0.2 GPa, 111 ± 5 MPa and 205 ± 8 MPa could be respectively predicted, as shown in Figures 4A and 4B.

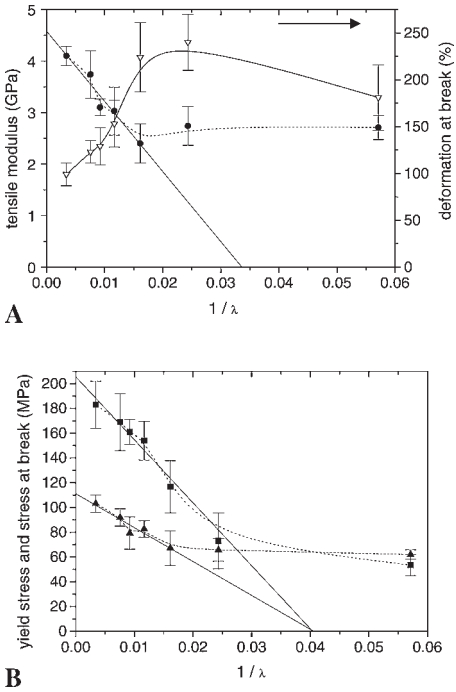

Figure 4.
A. Tensile modulus (●) and deformation at break (▽) as function of draw ratio (λ).The straight lines represent the best fit according to eq. (4). B. Yield stress (▲) and stress at break (■) as function of the inverse of the draw ratio (λ). The straight lines represent the best fit according to eq. (4).

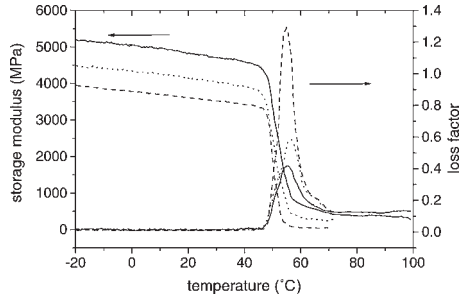

Figure 5.
Storage modulus and loss factor of fibers collected at winding speed of 10 m/min with $\lambda = 18$ (----), 25 m/min with $\lambda = 64$ (· · · · ·) and 70 m/min with $\lambda = 297$ (—).

Dynamical mechanical analysis confirmed the effect of drawing on fibers properties. As shown in Figure 5, the higher the drawing the higher the storage modulus in all range of tested temperatures, both above and below the glass transition temperature. At 37 °C, storage moduli of fibers obtained collected at 10 and 70 m/min (and with correspondent draw ratio of 18-297), range between 3.4 and 4.5 GPa, in good agreement with the tensile modulus values reported in Figure 4A.

The peak of the loss factor (i.e. the ratio between the loss modulus and the storage modulus[11]) is centered around 55 °C for all fibers. The peak temperature is related to the glass transition temperature while its height is proportional to the amorphous/crystalline-ordered phases content, i.e. the higher the crystallinity and/or the higher the orientation, the lower the peak. Fiber collected at 10 m/min ($1/\lambda = 0.056$) showed tan delta values of 1.27, that is typical of amorphous polymers such as polymethylmethacrylate or polystyrene.[12] Spinning performed for this fibers at a draw ratio below the critical one ($\lambda_c = 50$) did not produce in this case effective orientation-crystallization. On the other hand, fibers collected with higher winding speed, 25 and 70 m/min ($1/\lambda = 1.20 \times 10^{-3}$ and 0.34×10^{-3}) exhibited a peak of lower intensity (0.57 and 0.45), that indicates a higher level

of orientation and confirm the effectiveness of the spinning conditions. In the rubbery region above the glass transition temperature, storage moduli of fibers dramatically decline reaching values directly dependent on the draw ratio. Moreover, Figure 5 shows that storage modulus at 70 °C of fibers drawn at $\lambda = 18$, $\lambda = 83$ and $\lambda = 297$, decreases to 60, 250 and 450 MPa, respectively.

At the authors knowledge, no data on poly-L,DL-lactide 70/30 fibers have been reported in literature yet. On the other hand, P-L,DL-LA 70/30 has been used for the production of films 20–200 micron thick, proposed for adhesion reduction [7] and surgical mesh applications. These films exhibited tensile strength of about 55 Mpa,[13] these properties being appropriate for the specific clinical requirements. Higher mechanical properties were reported by Claes et al. for pins having bending strength up to 180 MPa after injection moulding of a high molecular weight copolymer (830 kDa).[3] Similar data were found for injection moulded screws showing a flexural strength of 119 MPa (Mw = 266 kDa) decreasing to 63 MPa after introduction of hydroxylapatite.[5] By using the self-reinforcing technique developed by Tormala,[14] screws with shear strength of 185 MPa and flexural modulus and strength of 4.5 GPa and 171 MPa[6] were produced from P-L,DL-LA weighing 910 kDa. Plates and screws produced by compression and injection moulding of P-L,DL-LA 165 kDa Mw, exhibited tensile strength and shear strength of 33 MPa and 30 MPa, respectively.[4]

The mechanical properties of P-L, DL-LA fibers spun at high draw ratio resulted much higher than those of films and very close to those of injection molded pins and self-reinforced screws.

In vitro Degradation

Degradation kinetics depend on many factors [2] that are related to the polymer characteristics and to the process. Produced fibers exhibited a molar mass decrease of about 35% after processing as a consequence of thermal degradation. The higher the degradation during the process, the higher the resulting *in vitro* hydrolysis due the larger amount of terminal groups. A sample of fiber with diameter of 108 micron obtained after drawing with $\lambda = 86$, was undergone to *in vitro* degradation in PBS solution at 37 °C for more than 8 weeks. The weight average molecular weight and the polydispersity index PDI showed an almost linear change with time of about −30% and +20% respectively, after the follow-up time, as reported in Table 1. At the same time, an almost negligible weight change was detected after 4 weeks ($0.3 \pm 0.1\%$), and a small weight decrease, $6.1 \pm 0.3\%$, was found after 8 weeks. Correspondently, fiber lost mechanical properties, showing modulus (−17% and −33%), yield stress (−12% and −31%) and strength (−24% and −68%) drops after 4 and 8 weeks.

Table 1.
Properties of fiber drawn with $\lambda = 86$ during *in vitro* degradation in PBS at 37 °C.

	initial	4 weeks	8 weeks
Mw (kDa)	188.4	154.9	145.2
PDI	1.92	2.15	2.37
Tensile modulus (GPa)	3.1 ± 0.5	2.6 ± 0.3	2.1 ± 0.2
Yield stress (MPa)	83 ± 6	73 ± 10	57 ± 6
Deformation at break (%)	123 ± 20	128 ± 13	14 ± 3
Stress at break (MPa)	154 ± 15	117 ± 25	49 ± 3

Conclusion

Melt spinnability of poly-L,DL-lactide 70-30 has been studied. Fibers were produced by melt spinning in a single step process, where orientation and drawing occur simultaneously. The effect of drawing appeared evident above a certain critical draw ratio, experimentally determined as $\lambda_c = 50$. The properties of fibers were found dependent on the draw ratio, and an empirical equation has been proposed in order to predict the mechanical properties as function of drawing. Fiber drawn with $\lambda = 297$, exhibited modulus and strength of 4.1 GPa and 183 MPa respectively. Maximum attainable values about 1.1 times higher were also predicted. *In vitro* degra-

dation showed the maintenance of adequate mechanical properties up to 4 weeks, and a significant decrease of strength associated to water sorption and molar mass decrease at longer time.

In conclusion, these P-L,DL-LA 70/30 fibers may be suitable for weaving meshes and/or fabrics for the production of biodegradable scaffold.

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