

Process-Induced Monomer on a Medical-Grade Polymer and Its Effect on Short-Term Hydrolytic Degradation

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ABSTRACT: While melt-spinning biodegradable poly-(L/D)LA 96/4 lactides into fibers, we intentionally induced monomer into the material by thermal degradation. Elevated temperatures and variable residence times were used during processing. By increasing the residence time, the molecular weight decreased, and the amount of monomer increased exponentially. The studied processing parameters induced from 0.17 to 1.24% of monomer into PLA fibers. In short-term

(9-week) *in vitro* studies, the rate of degradation was significantly faster for fibers with higher amounts of monomer. After 9 weeks *in vitro*, the 0.17% monomer fiber lost 3% of its strength, whereas the 1.24% monomer fiber lost 65%. © 2010 Wiley Periodicals, Inc. *J Appl Polym Sci* 119: 2996–3003, 2011

Key words: biodegradable; biofibers; extrusion; monomers; retardation time

INTRODUCTION

Processing polylactides (PLA) is not a novel science, although papers on the thermal degradation and degradability of polymers are still few in number. The most important factors governing the melt processing of lactide-based polymers are the processing temperature, shear force, residence time, the moisture content of the polymer, and the ambient processing atmosphere.¹ The effect of moisture can be countered with sufficient drying, and the effect of atmospheric oxygen can be minimized by using an inert gas such as nitrogen. The importance of purified polymer on PLA degradation after processing has been reported.² By using a purified medical-grade polymer, the effects of residual monomer and catalyst remains on thermal stability can, to a certain extent, be avoided.^{3–6} The presence of monomers and oligomers created by thermal degradation has been noticed, and publications have appeared on the effect of monomers and oligomers on the properties of PLAs.^{3,5–8} Oligomers and monomers appear also as degradation products in a part of normal PLA hydrolysis, in which a random hydrolysis of ester bonds, i.e., chain scissioning, occurs and creates them.^{3,7,9–11} Acidic degradation products, when accumulating inside polymer specimens or devices, enhance the autocatalytic degradation of the polymer.^{12,13} The lack of existing references and results from our previous processing experiments^{2,6,14}

encouraged us to make a study about the effect of processing parameters on monomer appearance and the effects of melt-spinning parameters on degradation of PLA fibers. While processing biodegradable polylactide P(L/D)LA 96/4 into fibers, we intentionally induced monomer into the polymer by thermally degrading it during the melt process with elevated temperatures and prolonged processing times.

MATERIALS AND METHODS

Fiber production

A commercial medical-grade polymer, P(L/D)LA 96/4 (PURAC Biochem bv, Goringchem, the Netherlands) was used as raw material. The inherent viscosity of polymer was 5.48 dL/g, its residual monomer content <0.02% and catalyst content <50 ppm (all reported by the manufacturer). The polymer was melt-spun to four-filament fibers using a laboratory-scale extruder (Gimac microextruder, screw Ø 12 mm) and a hot drawing line consisting of three caterpillars and three IR-heating units. The temperatures of the heating units were 105/125/120°C. The four-filament nozzle had a single orifice diameter of 0.4 mm each. The draw ratio of 4.0 was kept constant in the orientation line. The screw speed and the temperature of the mixing unit and the extruder nozzle were varied during melt-spinning.

Melt-spun fiber samples

In melt-spinning, temperatures in the extruder barrel were 200, 215, and 230°C. The studied temperature range T1 for the mixing zone was 270°C and for the

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TABLE I
Melt-Spun Fiber Sample Information

Sample ID	Screw speed (rpm)	Nozzle temp (°C)	Ave ^a . single fiber Ø (µm)	Hot draw ratio	Total Ø draw ratio	Retention time (s)
T1-9	9	277	101	4.0	4.0	270
T1-8	8	277	95	4.0	4.2	300
T1-7	7	277	86	4.0	4.7	335
T1-6	6	277	82	4.0	4.9	360
T1-5	5	277	74	4.0	5.4	410
T1-4	4	277	65	4.0	6.2	500
T1-3	3	277	54	4.0	7.4	600
T2-9	9	282	93	4.0	4.3	270
T2-8	8	282	92	4.0	4.3	300
T2-7	7	282	84	4.0	4.7	335
T2-6	6	282	79	4.0	5.1	360
T2-5	5	282	73	4.0	5.5	410
T2-4	4	282	63	4.0	6.3	500
T3-9	9	287	105	4.0	3.8	270
T3-8	8	287	90	4.0	4.4	300

^a $N = 20$.

nozzle 277°C. The screw speed was set at 9 rpm and then lowered stepwise (1 rpm at a time), and samples were collected on the spool. A minimum screw speed of 3 rpm was obtained, when the fiber was still suitable for spinning. For temperature range T2 the mixing zone and nozzle temperature were increased by 5°C, the screw speed set at 9 rpm, and the experiment was restarted. The lowest screw speed obtained was 4 rpm. For maximum temperature T3, the mixing zone was set to 280°C, the nozzle to 287°C, and the corresponding minimum screw speed was 8 rpm. An overall draw ratio (relative to thickness) comprising melt drawing and cold drawing was calculated. The residence times for correlative screw speeds were measured using a color dye. Sample data is presented in Table I.

In vitro degradation

Prior to incubation *in vitro*, the fibers were sterilized by gamma irradiation 25 kGy (commercial set-up) and then incubated for 0, 1, 2, 3, 6 (or 7), and 9 weeks at 37°C in phosphate-buffered saline (PBS, 3.48 g/dm³; Na₂HPO₄, 0.755 g/dm³; NaH₂PO₄, 5.9 g/dm³ NaCl buffered saline) at pH 7.4. A fresh buffer solution was changed fortnightly.

Material characterization and analysis

The lactide monomer content of fibers was measured using a gas chromatograph (Thermo Finnigan, Trace GC, Autosampler 3000, MA), equipped with a 25 m × 0.32 mm i.d WCOT fused silica Cp-Sil 43 CB Varian chrompack capillary column. A Flame Ionisation Detector (FID) was used for detection. Two parallel

samples were used; averages and standard deviations were calculated.

Molecular weights (number average, M_n , and weight average, M_w), polydispersity (PD), and inherent viscosity (i.v.) were measured by gel permeation chromatography (GPC) relative to narrow polystyrene standards. The GPC consisted of a Waters 410 RI differential refractometer detector and a Waters 515 HPLC pump (Waters, Milford, MA). The GPC columns were a PLgel 5-µm Guard and a 2 PL gel 5-µm mixed-C. The injection volume was 150 µL, and the eluent flow rate was 1 mL/min. Calibration was performed using monodisperse polystyrene standards, applying Mark-Houwink parameters for PS ($K = 1.12 \times 10^{-4}$ and $\alpha = 0.73$). Samples were dissolved in 0.1% w/v solutions of chloroform at room temperature and measured after processing before gamma irradiation. Two parallel samples were used; averages and standard deviations were calculated.

A differential scanning calorimeter (DSC) Perkin-Elmer Pyris 1 (Perkin-Elmer, Norwalk, CT) was used for thermal characterization. Samples were heated from 20 to 220°C at a rate of 20°C/min, and after a rapid cooling, the heating procedure was repeated. Glass transition temperatures (T_g) were determined from the second heating cycle. Melting temperatures (T_m) were determined from the melting peak of the first heating cycle, and the crystallinity (X_c) of the samples was determined from the melting enthalpy using 93.7 J/g as the melting endotherm of 100% Poly(L-lactide).¹⁵ Indium was used as a standard calibration material. DSC analysis was performed before gamma irradiation. Two parallel samples were used; averages and standard deviations were calculated.

Tensile properties of the fibers were tested using an Instron 4411 Materials Testing Machine (Instron, High Wycombe, England). All four filaments formed a yarn and were clamped between hydraulic jaws and pulled at a crosshead speed of 30 mm/min and a gauge length of 50 mm. Strength (MPa, N/mm²) values were calculated against the cross section of all fibers (mm²) and using max force (N). All samples were tested wet. Five parallel samples were used; averages and standard deviations were calculated.

RESULTS

Extrusion

The temperature could only be increased twice in the feasible range of fiber spinning due to melt behavior of the polymer. When the screw speed at T3 was >8 rpm the polymer was too molten, thus it was impossible to obtain good quality fibers. The diameter of single fibers changed due to the fluctuating polymer through-put velocity at the nozzle

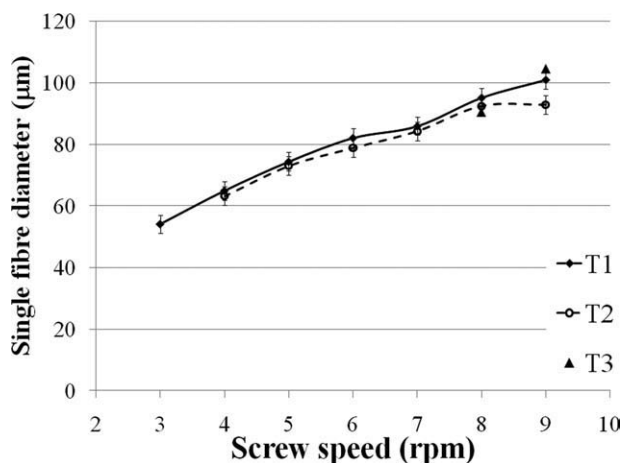


Figure 1 The change of single fiber diameter plotted against the screw speed for temperature ranges T1, T2, and T3 ($n = 20$).

(different screw speed) and due to fixed drawing parameters. There is a clear correlation between the screw speed and the fiber diameter (Fig. 1). Before *in vitro*, results showed a drop in tensile properties and an increase in strain properties between γ -irradiated and nonirradiated samples (Figs. 2 and 3). There was no correlation between monomer content and mechanical properties in the 0-week mechanical results.

Molecular weight and monomer content

Measured and calculated molecular weight values and monomer content results are listed in Table II. In the first temperature range T1, the molecular weight of the polymer decreased by 48–64% and the inherent viscosity by 35–50%, depending on the residence time, when compared to the raw material. The monomer content of the polymer increased at every step when residence time was increased; at the minimum T1 screw speed, the increase was $\sim 470\%$.

At temperature range T2, the molecular weight of the polymer decreased from 49 to 62%, and the inherent viscosity decreased from 31 to 48%, depending on the residence time, when compared to the raw material. For the longest T2 residence time (4 rpm), the fiber sample monomer increase, compared to T1-9 samples, was $\sim 620\%$. In comparison, the monomer increase due to the temperature rise from T1 to T2 was only 71 to 103% at comparative residence times. Plotting M_w against monomer content (Fig. 4), we can see that the relationship between the decrease of M_w and the increase of monomer content is almost linear. For the equipment relationships (Fig. 5) temperature and monomer were plotted against the screw speed. The increase of monomer has an exponential behavior within the measured screw speeds. The M_w and monomer content were plotted against the residence time, the actual time the polymer is affected by the temperature (Fig. 6), for this the values were picked from Tables I and II. From this graph, it is possible to state that the decrease in M_w at high processing temperatures is more heavily influenced by residence time, rather than the 5°C increase in temperature. On the other hand, the process-induced monomer is affected by both of the factors, temperature and residence time. We can clearly see that an increase in temperature has a stepwise effect on the monomer amount, and the step further increases with longer retention times. The residence time has an almost linear correlation to the monomer amount when higher than 300 s.

The changes in M_w had no significant change in polydispersity. Despite the maximum 30% reduction in T1-9 and T1-3 M_w and a 26% reduction in M_w between T2-9 and T2-4, there was no change in the PD.

We studied also the effect of gamma irradiation on monomer content, and found that though it decreased the molecular weight by random chain scission, gamma irradiation had no effect on the monomer content, whether monomer was present or not, prior the gamma irradiation.

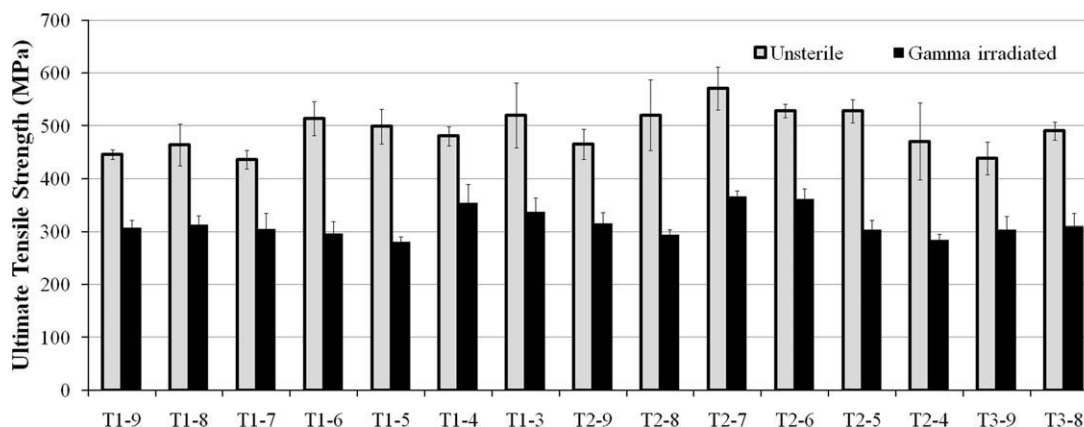


Figure 2 Ultimate tensile strength (MPa) of unsterile and γ -irradiated fiber batches; results are shown as averages with standard deviation ($n = 5$).

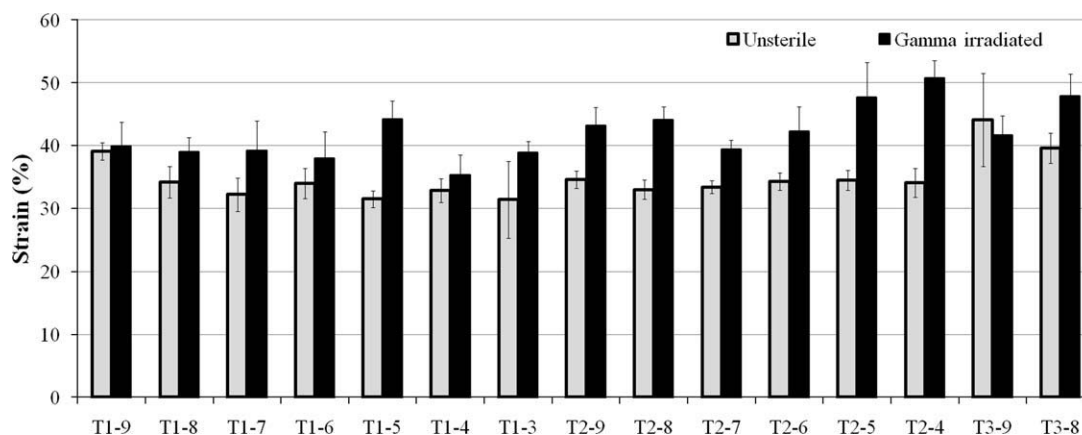


Figure 3 Strain at break (%) of unsterile and γ -irradiated fiber batches; results are shown as averages with standard deviation ($n = 5$).

Thermal measurement results

There was no change in T_m between the groups T1 and T2. The melting point for both of the groups for all residence times was 152°C. There was a slight increase in crystallinity when the residence time increased. The crystallinity increased from 29 to 33% between T1-9 and T1-3. Similar behavior was observed in the T2 group, where the crystallinity increased from 29 to 31% between T2-9 and T2-4. There was a slight decrease in T_g because of the increase in residence time. The T_g decreased from 62 to 58.5°C between T1-9 and T1-3. Similar behavior was observed in the T2 group, where the T_g decreased from 61 to 58°C between the T2-9 and T2-4. Increase in the processing temperature had neither significant effect on either T_g nor crystallinity.

In vitro degradation results

No significant difference occurred in mechanical properties between the groups of T1 and T2 at any time during the 9 weeks *in vitro*, when the screw speed was set to 9, 8, or 7 rpm. When the speed was set to 4 or 5 rpm, a noticeable difference in the mechanical properties was observed in groups T1 and T2 for the 7- and 9-week samples. A noticeable difference was also noticed when comparing the T3 group to T1 and T2 at correlative screw speeds of 9 and 8 for *in vitro* weeks 3, 7, and 9.

Remaining strength (%) was plotted against hydrolysis time (weeks). When fiber series were chosen according to correlative monomer contents of 0.2, 0.3, 0.5, and 0.8–1.2% [Fig. 7(A–D)], we discovered that the exponentially fitted curves of the correlative monomer content fibers had equal slopes. The slope

TABLE II
Mean Molecular Weight and Monomer Content Values of the Fiber Samples

Sample ID	M_n (dL/g)	M_w (dL/g)	i.v.	PD	M_w decrease (%)	i.v. decrease (%)	Monomer (%)	Monom. cont increase/T1-9 (%)
Polymer	211,600	346,000	5.5	1.60			<0.02	
T1-9	105,000	182,200	3.6	1.74	47	34	0.17	
T1-8	101,300	175,900	3.5	1.74	49	36	0.18	6
T1-7	96,000	170,900	3.6	1.78	51	35	0.23	35
T1-6	91,500	159,000	3.4	1.74	54	38	0.33	91
T1-5	86,400	153,700	3.4	1.78	56	38	0.47	172
T1-4	76,100	140,000	3.0	1.84	60	45	0.72	318
T1-3	68,500	125,200	2.8	1.83	64	49	0.98	472
T2-9	99,300	179,000	3.9	1.80	48	29	0.33	90
T2-8	99,000	176,000	3.7	1.78	49	33	0.34	98
T2-7	94,700	165,700	3.5	1.75	52	36	0.46	171
T2-6	87,500	156,600	3.2	1.79	55	41	0.67	289
T2-5	84,600	149,100	3.2	1.77	57	42	0.80	366
T2-4	73,500	132,700	2.9	1.81	62	48	1.24	621
T3-9	102,000	178,100	3.9	1.75	49	30	0.36	107
T3-8	90,800	156,900	3.4	1.73	55	39	0.52	204
	$n = 2$	$n = 2$	$n = 2$	$n = 2$			$n = 2$	

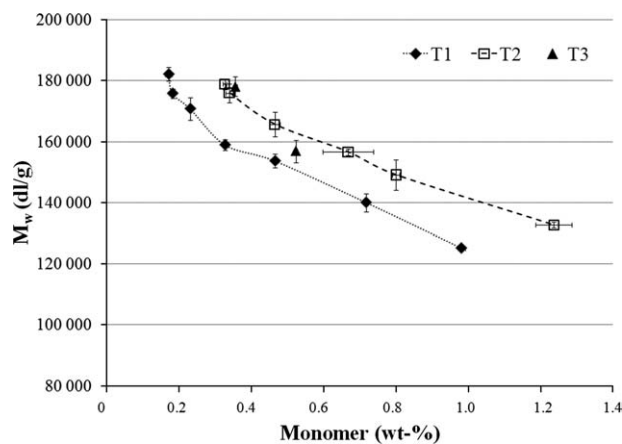


Figure 4 Correlation between a decrease in M_w and an increase in monomer content for temperature ranges T1, T2, and T3; results are shown as mean values ($n = 2$).

increased according to increasing monomer content, and degradation quickly occurred at a monomer content of about 1%. The amount of monomer correlates to a specific, unique degradation profile. The higher the monomer amount the faster the degradation. The effect of fiber thickness on strength reduction *in vitro* was less relevant in this study than monomer content and the remaining M_w . For example, when the fibers of similar thickness, are compared (Fig. 8), their degradation profiles are not the same. For example, during hydrolysis, T3-8 lost 40% of its strength, whereas T1-8 lost only 5%.

DISCUSSION

Melt-processing PLAs has been problematic due to the thermal and hydrolytical instability of the polymer. We have shown in this study that by controlling the polymer behavior with processing parameters,

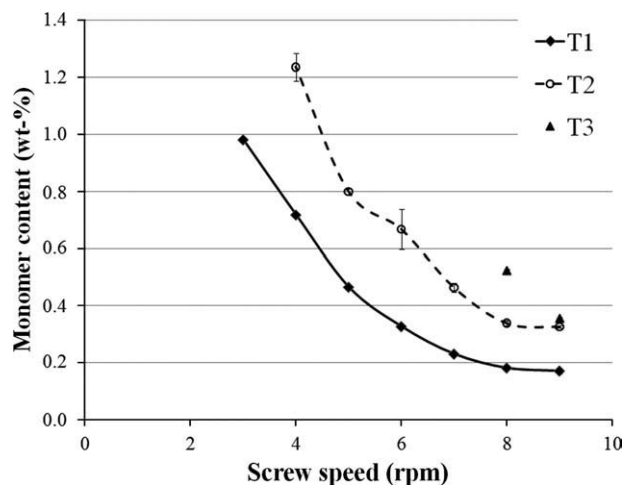


Figure 5 Correlation between the screw speed and monomer content for temperature ranges T1, T2, and T3; results are shown as mean values ($n = 2$).

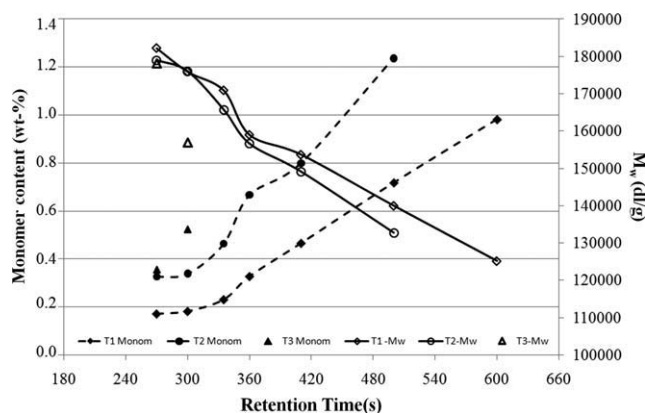


Figure 6 Decrease in M_w and the increase of monomer plotted against residence time for temperature range T1, T2, and T3; results are shown as mean values ($n = 2$).

we can minimize the undesired degradation during processing. Furthermore, we can predict and control the *in vitro* degradation that can be used to estimate the *in vivo* behavior. To measure and observe polymer degradation, researchers have used different indicators such as thermal properties, rheological properties, molecular weight, and mechanical properties of PLAs.^{12,16–20} Some studies have shown that monomer influences the degradation of melt-processed end-products,^{2,6} and our results corroborate that finding.

Successful processing starts by drying the raw materials, because many polymers, such as polyamides, absorb water during storage. The link between moist raw material and a melt-processed end-product with decreased molecular weight has been observed with PLAs.¹ Even sufficient drying does not necessarily remove the effect of thermal degradation during melt-spinning. Different melt-spinning studies have reported a minimum 27% and a maximum 69% decrease in molecular weight during the melt processing.^{17,19–21} Although we minimized the water content in the polymer prior to processing by drying and the polymer was processed carefully under nitrogen, we still measured a high (47–64%) drop in molecular weight (M_w). Therefore, we suspected that in this case the water was not the cause for the M_w drop, but that other factors were more heavily involved.

The suspected, processing-based factors were the processing temperature in specific extruder zones, the polymer residence time in the extruder (or machine-specific screw speed), and the shear stress exerted on the polymer. A correlation between processing temperature and monomer content can be immediately observed, and an increase in temperature can be seen as a phase shift in the increase of the induced monomer. The slope of the curve indicates that the residence time might have an optimum with

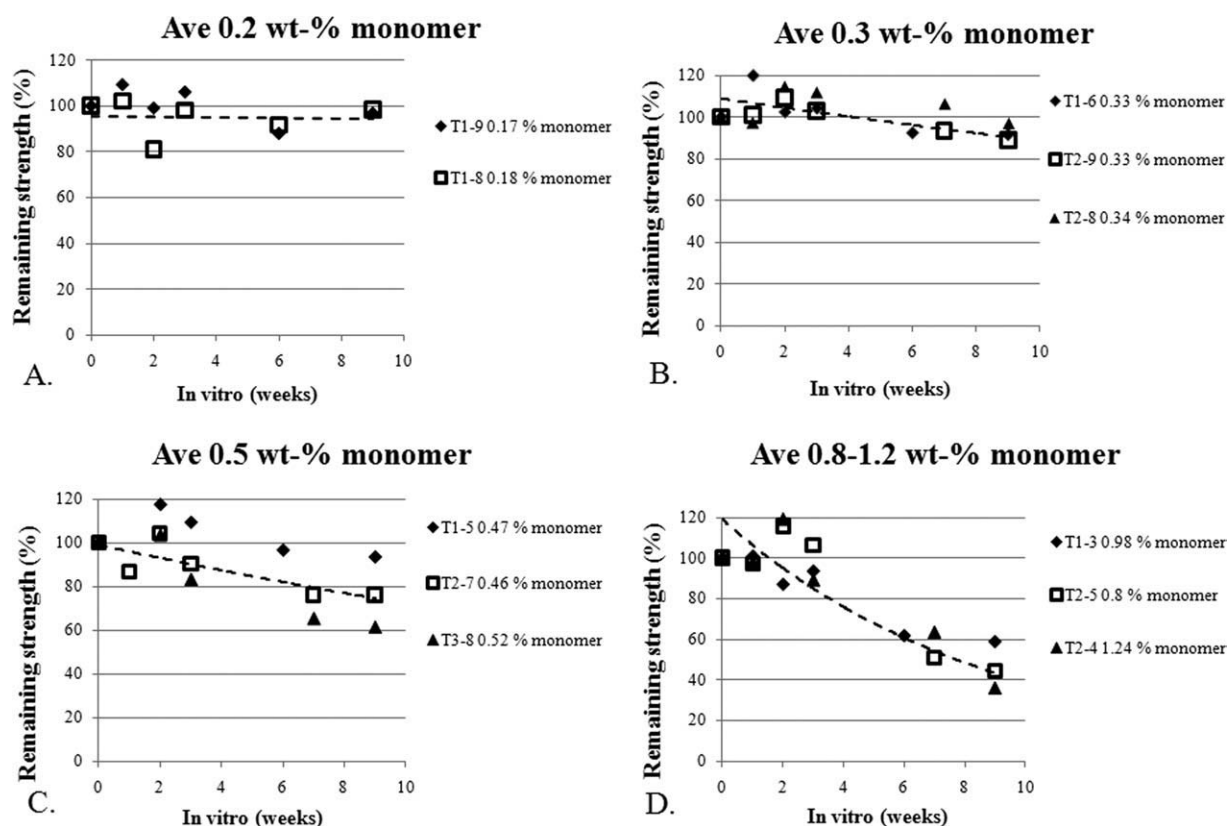


Figure 7 Mean values of cumulative strength retention of fibers during 9-week hydrolysis. At the start of hydrolysis, fiber monomer content was for (A) 0.2%, (B) 0.3%, (C) 0.5%, and (D) 0.8–1.2%; results are shown as mean values ($n = 5$).

this machine setup, when the screw speed is 8 rpm or higher. A close to linear increase in the monomer, as the residence time increases, also favors high screw speeds, when we are trying to reduce the monomer induced in the fiber. On the other hand, especially high-molecular-weight and thus highly viscous PLAs may show degradation due to high shear stress caused by high screw speed. Combined residence time and shear stress clearly affected the fibers, but the two are very difficult to separate from each other. At low screw speeds, shear stress is low but in contrast residence time is long, and vice versa. Thus, if shear stress has an effect, at the screw speeds used in this study, it cannot be detected and is overtaken by a more dominant factor, residence time. A similar effect on degradation due to a long residence time was also reported in Refs. 1 and 16; the authors also noticed that at low extrusion temperatures loss of molecular weight is less dependent on residence time.

On the basis of our latest studies,⁶ we predicted a correlation between molecular weight drop and increase in monomer content in PLA fibers after processing. We clearly witnessed this correlation and showed it in the current results. Because the raw polymer was highly purified medical-grade polymer with only traces of residual monomer and catalyst from polymerization, we had no such degradation problems as

in,^{2,4,7} and the monomer could only have been formed during processing. As mentioned earlier, it is difficult to verify whether the monomer was due either to prolonged residence time or shear stress or both. However, the greater slope of the higher temperature (T2) set, seen in Figure 6, may indicate a higher autocatalytic thermal degradation, caused by the monomers and oligomers occurred in extrusion. Liu et al.⁷ have suggested that degradation during processing is a result from a random chain scission in two or three stages, first dominated by oligomers containing

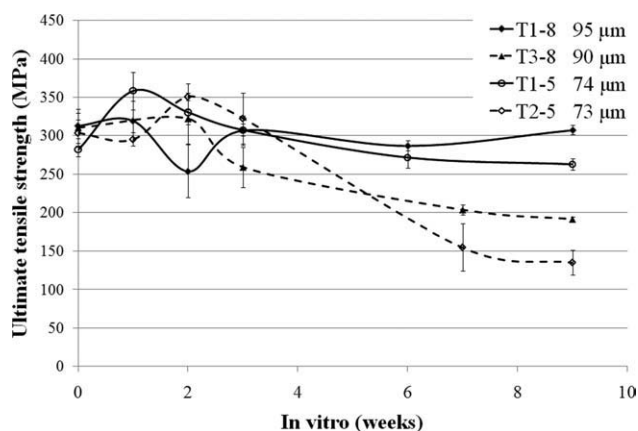


Figure 8 Ultimate tensile strength of T1-8, T1-5, T2-5, and T3-8 during the 9 week *in vitro* ($n = 5$).

carboxylic acid groups and hydroxyl groups. This may be relevant when processing high-viscosity lactides, since our group has shown, that whereas high-viscosity lactide polymers require high temperatures, low-viscosity polymers do allow processing at lower temperatures with less degradation and less induced monomer.⁶ Especially, for different branches of the industry where polylactide degradation is an issue, there is a need for a rapid and clear indicator to verify whether processing has been successful or not. Typically, a hydrolysis study of specific length is performed to prove the quality of the product lot, and even the standard for biodegradable polymers suggests that.²² Mechanical properties of spun fibers alone cannot be used as an indicator for successful or unsuccessful spinning because of no correlation between, the nonirradiated or γ -irradiated fiber tensile strength and the corresponding monomer content.

The postprocessing properties of biodegradable polymer end-products are important for the application. Equally important, are also the properties during the degradation period. When monomer was added in the plates,⁵ a correlation occurred between monomer content and strength retention, but not with degree of degradation (loss of M_w); furthermore, all monomer was eluted from the material upon immersion. Because fibers have a high surface area, it is easy to show a correlation between monomer content and degree of degradation. In the early stages of immersion, monomer elution may lead to a high water uptake in the polymer due to acidic degradation products that accelerate water penetration into the polymer. Weight increase from water penetrating the polymer due to the monomer content has been shown in Ref. 5 and suggested in Ref. 23.

In contrast to a study by Pegoretti et al.,¹⁸ our earlier data⁶ showed no difference in short-term degradation behavior *in vitro*, between thick or thin melt-spun fibers (made from the similar raw materials where i.v. was close to each other), if the monomer content was low in the fiber. Current paper reports fibers with equal thicknesses showing different degradation rates. We can conclude that the rapid degradation of the fibers in this study was not caused by the thickness of the produced fibers, though thickness may play a role in how easily the effect of the monomer can be seen. To sum up, the thinnest fibers (T1-3) in this study (54 μm) were close to the F22 fibers (45 μm),⁶ and T1-3 fibers (monomer 0.98 wt %) lost 60% of their strength in 9 weeks, whereas the F22 fibers (monomer < 0.02 wt %) lost only 25% of their strength during the same period. According to these results, we can rule out the effect of thickness, when considering it as a crucial factor affecting the degradation in short-term hydrolysis. In general, the fibers produced in this study had similar initial properties than the previously studied PLDLA

fibers.^{6,24,25} A minor decrease in T_g and a minor increase in crystallinity at increasing die temperature were also previously reported.²¹ Since the melt-spinning parameters had no significant impact on crystallinity, T_m , or T_g between the groups (T1, T2, and T3), they did not affect the rapid degradation reported in this study.

From the graphs it is possible to obtain equations on how the monomer is formed during the processing. Although these equations are considered to be machine dependent, it should be further studied how they hold on to different melt processing machines and set ups. The changes to it are more than likely, when other melt processing parameters, set-ups or a different polylactide polymer is used. However, based on this study, we propose that a clear correlation exists among parameters, equipment, and process-induced monomer.

This article shows that with less than 0.2 wt % of thermally induced monomer in the fiber, no rapid degradation can be observed, and that the degradation behavior of those fibers is typical for PLDLA polymer. The effect of this amount of thermally induced or residual monomer is noticeable at the later stages of hydrolytic degradation, where it further enhances autocatalytic degradation.^{6,26} We also believe that the monomer's location in the polymer affects the degree of degradation. Process-induced monomer may be more homogeneously distributed in the specimen than added monomer, thus accelerating hydrolysis compared to solution-added monomer.

In our own previously reported studies¹⁴ and in some publications,^{17,18} only one optimized setup was used for melt processing parameters. Therefore, one might assume that the effect of thermally-induced monomer on degradation was not of knowledge at the time because it has been overlooked. Although we used a purified medical-grade polymer, it is yet unclear what part the residual monomer, catalysts, and solvents played in this equation, uncertainty similar to that expressed in.^{4,5}

CONCLUSIONS

On the basis of melt-spinning and degradation tests, our experimental results lead to following conclusions. There is a direct correlation between the fiber diameter and the extrusion speed. The amount of monomer induced in processing can be predicted, and a model, dependent on the processing system, for estimating it can be calculated. More than 0.2 wt % of monomer will affect short-term degradation. About 1.0 wt % process-induced monomer has a devastating effect on short-term degradation behavior.

As for the biomedical industry, it is crucial to understand this phenomenon because it has everything to do when manufacturing products with

predictable and reliable behavior. These results can be also used to a certain extent to modify the degradation behavior of polylactides by inducing a desired amount of monomer into the polymer product. The phenomenon can be used for biomedical products and for additive-free, biodegradable consumer products. As for the scientist pondering on the explainable rapid degradation of their polymers *in vitro* or *in vivo*, the aspect of taking the monomer factor into consideration might explain better their results.

Although it has been previously shown that monomer has an effect on degradation,⁶ we clearly, for the first time, showed the direct dependency between the temperature, the residence time, and the induced monomer amount in a real processing. For the first time, we also clearly showed how the different monomer amount can be linked up to precise degradation profile at the very beginning of the degradation.

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