Miscibility and Mechanical Properties of Blends of (L)-Lactide Copolymers with Atactic Poly(3-hydroxybutyrate)

Maria Letizia Focarete and Mariastella Scandola*

University of Bologna, Department of Chemistry "G.Ciamician" and ISOF, Consiglio Nazionale delle Ricerche, via Selmi 2, 40126 Bologna, Italy

Piotr Dobrzynski and Marek Kowalczuk

Center for Polymer Chemistry, Polish Academy of Sciences, 41-800 Zabrze, Poland

Received June 17, 2002

ABSTRACT: Poly(L-lactide-*co*-glycolide) (PLLAGA) copolymers and poly(DL-lactide) (PDLLA) were synthesized using the low toxicity compound zirconium(IV) acetylacetonate. Blends with synthetic atactic poly(3-hydroxybutyrate) (a-PHB) were prepared in film form by solvent casting. The solid-state properties of the plain polymers and of the blends were investigated by thermogravimetric analysis coupled with mass spectrometry (TGA−MS), differential scanning calorimetry (DSC), wide-angle X-ray diffraction (WAXD) and stress−strain measurements. The a-PHB/PDLLA blends are miscible over the whole composition range. On the other hand, blends of a-PHB with PLLAGA copolymers containing 5 and 16 mol % of GA units show partial miscibility. The solubility limit of a-PHB in PLLAGA is around 20 wt % in both cases. In the blends, the a-PHB in excess to this value segregates as a pure phase. The mechanical properties of blend films of either PDLLA or PLLAGA containing up to 50 wt % of a-PHB can be modulated by changing blend composition. The tenacity progressively increases by the addition of a-PHB not only in the miscible amorphous a-PHB/PDLLA system but also in the partially miscible a-PHB/PLLAGA blends.

Introduction

Poly(glycolic acid) (PGA), poly(lactic acid) (PLA), and their copolymers are synthetic, bioerodible materials widely investigated and commonly used in the biomedical field.[1−4] They have been used for a variety of applications ranging from surgical sutures and drug release systems to osteosynthetic devices and vascular prostheses.

The synthesis of lactide−glycolide copolymers is commonly carried out using tin compounds as initiators. However, these compounds are known to be highly toxic,[5,6] and their complete removal from the polymers obtained is practically impossible.[7] A new method of copolymerization of glycolide with L-lactide has been previously reported using zirconium(IV) acetylacetonate ($Zr(acac)_4$) as initiator.[8] The toxicity of the latter compound is 10−20 times lower than that of comparable tin compounds.[5] The chain microstructure of lactide−glycolide copolymers obtained using zirconium-based initiators is more segmental as compared with that of copolymers obtained using tin compounds. The copolymer chains are composed of glycolidyl and lactidyl microblocks together with short alternate lactoyl/glycoloyl segments.[8]

One of the common strategies to tune the physical and mechanical properties of a polymer material is blending two or more polymer components. When the new material is to be used in the biomedical field, the blend components must be biocompatible, a property that must be maintained after blend formation. The aim of this work is to obtain new biomaterials for soft tissue temporary applications. For this purpose L-lactide copolymers, i.e., poly(DL-lactide) (PDLLA) stereo-copolymer and poly(L-lactide−glycolide) copolymers (PLLAGA), synthesized using $Zr(acac)_4$ initiator were blended with synthetic atactic poly(*R*,*S*-3-hydroxybutyrate) (a-PHB). An interesting feature of the latter polymer is that it is environmentally biodegradable[9] and biocompatible, i.e., the fact that its hydrolytic degradation products (*R*)- and (*S*)-3-hydroxybutyrate are nontoxic compounds.[10,11] Blends of a-PHB with natural PHB have been recently reported to perform satisfactorily in an in vivo study of gastrointestine defect closure in rats.[12]

Atactic PHB was selected as the second blend component in the L-lactide based systems investigated in this work with the aim to improve the flexibility and impact resistance of L-lactide copolymers. Indeed, both the amorphous PDLLA and semicrystalline PLLAGA copolymers are rigid materials that show very small elongation at break. The glass transition temperature of these materials is ca. 60 °C. a-PHB is a low glass transition (ca. 0 °C) amorphous polymer and behaves as an elastomer at room temperature. In a previous paper,[13] we reported that a-PHB was totally miscible with the isotactic poly(L-lactic acid), PLLA, homopolymer.

In this work we present the solid-state characterization of binary blends of a-PHB with the stereocopolymer PDLLA and with PLLAGA copolymers. The mechanical properties of the blend films obtained are discussed in terms of miscibility and phase behavior.

Experimental Section

Materials. Poly(*R*,*S*-3-hydroxybutyrate) (a-PHB) was synthesized by bulk polymerization of (*R*,*S*)-β-butyrolactone at room temperature, using KOH/18-crown-6 complex as the initiator.[14,15] The extent of the reaction was monitored by FT-IR spectrometry based on the intensities of the carbonyl stretching vibration bands of the lactone monomer (1815 cm^{-1}) and of the polyester formed (1760 cm^{-1}). After completion of the reaction the residual monomer was eliminated by vacuum treatment in an oven at 80 °C. ^{13}C NMR and ^{1}H NMR spectroscopy showed that the polymer obtained was atactic.[16] Poly(DL-lactide) (D/L = 50/50, PDLLA) and poly(L-lactide)

10.1021/ma020940z CCC: $22.00

Table 1. Molecular Weight and Thermal Properties of the Polyesters

	L-lactide content (mol %)	$M_n \times 10^{-3}$	PDI	T_{max}(TGA) (°C)	T_m[a] (°C)	ΔH_m[a] (J/g)	T_g[b] (°C)	ΔC_p[b] (J/g °C)
a-PHB		13	1.2	256			2	0.57
PDLLA	50	44	1.8	316			54	0.51
PLLA	100	40	1.8	317	187	91	61	0.53
PL5GA	95	64	2.4	328	177	68	62	0.52
PL16GA	84	53	2.1	339	155	47	60	0.51
PL52GA	48	n.d.[c]	n.d.[c]	352			51	0.51
PGA		n.d.[c]	n.d.[c]	380	225	105	41	0.49

[a] From first DSC scan. [b] From second DSC scan after melt quenching. [c] n.d.: not determined owing to sample insolubility.

(PLLA) were synthesized in bulk at 120−130 °C using zirconium(IV) acetylacetonate as the initiator (Zr(acac)$_4$ to monomer molar ratio = 1.2×10^{-3}), degassing by conventional methods with a vacuum line and sealing of the ampules. The time of reaction was 48 h. Polyglycolide (PGA) and poly(L-lactide−glycolide) copolymers, containing 5 (PL5GA), 16 (PL16GA), and 52 mol % (PL52GA) of glycolide, were synthesized similarly, and details of the copolymerization procedure were described previously.[8] The extent of the reaction was determined gravimetrically by weighing the washed and dried copolymers. The composition of the copolymers and their chain microstructure were defined by ^{1}H NMR and ^{13}C NMR spectroscopy.[8] The number-average molecular weight (M_n) and polydispersity index (PDI) of the polymers studied in this work are reported in Table 1. All samples were dried in an oven at 50 °C under vacuum overnight before use. Films for mechanical analysis were obtained by solvent casting at room temperature. The residual solvent (CH_2Cl_2) was evaporated at 65 °C under vacuum overnight.

Blend Preparation. For each blend appropriate amounts of the two polymers were solubilized in CH_2Cl_2 (5% w/v). The solutions were cast on Petri dishes, and the solvent was allowed to evaporate at room temperature. All films obtained were placed in an oven at 65 °C under vacuum overnight to eliminate residual solvent. Blends spanning the whole composition range were obtained.

Polymer Characterization Techniques. Number-average molecular weight (M_n) and polydispersity index (PDI) of a-PHB and copolymers soluble in chloroform were determined by GPC experiments (THF solution, 35 °C, flow rate 1 mL/min) using a Spectra-Physics 8800 solvent delivery system with two Mixed C Styragel columns in series and a Shodex SE 61 refractive index detector. A volume of 10 μL of copolymer sample solutions in $CHCl_3$ (concentration 2% w/v) was injected, as previously described.[17] Polystyrene standards with low polydispersity were used to generate a calibration curve.

^{1}H NMR spectra of the copolymers were recorded on a 300 MHz Varian multinuclear spectrometer using 5 mm sample tube. Dried dimethyl sulfoxide-d_6 was used as the solvent with TMS as the internal standard. The spectra were obtained at 80 °C with 32 scans, 3.74 s acquisition time, and 7 μs pulse width. The ^{13}C NMR spectra of the copolymers were recorded at 75 MHz with 25000−30000 scans, 1.8 s acquisition time, 7 μs pulse width, and delay of 4.7 s between pulses.

Thermogravimetric (TGA) measurements were performed using a TA TGA2950 (purge gas, helium; scan rate, 10 deg/min). The volatile products released were directly transferred to a quadrupole mass spectrometer (Balzers, ThermoStar GSD 300T; temperature setting of the interface was 200 °C; mass range, 10−300 amu; CH-tron detector, 1400 V) and analyzed after ionization by electron impact (70 eV).

Differential scanning calorimetry (DSC) was performed with a 2010 TA thermal analyzer at a heating rate of 20 °C/min. The temperature range explored was from −80 to +220 °C for PLLA and the PL5GA-based blends and from −80 to +180 °C for all other samples. The temperature scale was calibrated with high-purity standards. The melting temperature (T_m) was taken as the peak temperature of the melting endotherm, and the glass transition temperature (T_g) was taken as the midpoint of the stepwise increase of the specific heat associated with the transition.

Wide-angle X-ray diffraction spectra (WAXS) were collected with a Philips PW1050/81 powder diffractometer controlled by a PW1710 unit, using nickel filtered Cu Kα radiation (λ = 0.1542 nm, 40 kV, 30 mA).

Tensile mechanical measurements were performed with an Instron 4465 machine (gauge length = 20 mm, crosshead speed = 0.5 mm/min). Rectangular specimens (5 mm wide) die-cut from solvent cast films (0.15−0.25 mm thick) were used. Five replicate specimens were run for each sample.

Results and Discussion

Characterization of Blend Components. All L-lactide based copolymers used in this work to blend with a-PHB—i.e., PDLLA, PL5GA, PL16GA—were high molecular weight ((40−64)$M_n \times 10^{-3}$; Table 1) which is typical of copolymers synthesized using Zr(acac)$_4$ as initiator.[8,18] As previously reported,[8] due to the specific transesterification process, PLLAGA copolymers show glycolidyl (GG) and lactydyl (LL) microblocks linked by relatively short segments containing lactyl and glycolyl sequences (−GLG−, −LGL−, −GLGL−). Conversely, the stereocopolymers PDLLA and poly(*R*,*S*-3-hydroxybutyrate) have a totally random distribution of the enantiomeric units, as revealed by ^{13}C NMR spectroscopy, based on the tetrads and hexads intensities of the racemic polylactide−methine carbon and carbonyl carbon regions[19] for PDLLA and on the basis of diads and triads stereosequence distribution reported previously[16] for a-PHB.

Thermal stability of the polymers investigated in this work was evaluated by TGA. All polymers showed a single weight loss step at the temperatures (T_{max}) listed in Table 1. The polymer with the lowest thermal stability is a-PHB (T_{max} = 256 °C). PDLLA and PLLA degrade about 60 °C higher, whereas PLLAGA copolymers undergo thermal degradation at temperatures that increase with glycolide unit content, reaching 380 °C for pure PGA (Table 1). The thermal degradation products of polymers and copolymers were investigated by TGA−MS. Under the experimental conditions applied (standard electron impact source, 70 eV) primary thermal fragmentation products of PLA and PGA are not detected because high molecular mass fragments and cyclic oligomers that are initially formed undergo further fragmentation.[20−22] During thermal degradation of PLLAGA copolymers, TGA−MS reveals CO, CO_2, acetaldehyde, formaldehyde, and methyl ketene as the main volatile products, in agreement with earlier studies on degradation of PLA[20,22,23] and PGA.[24] The products released by a-PHB thermal degradation are fragments at m/z = 39 and 41. These substances are derived from decarboxylation of crotonic acid, which is known to be the main degradation product of poly(3-hydroxybutyrate).[25−28]

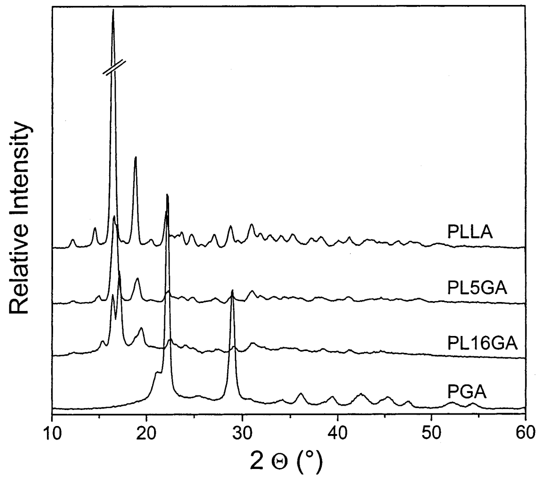

Figure 1. WAXS spectra of PLLA, PL5GA, PL16GA, and PGA.

The calorimetric (DSC) results of the polymers investigated are summarized in Table 1. The L-lactide stereocopolymer PDLLA and a-PHB were totally amorphous, whereas PLLA and PGA were highly crystalline polymers; PLLA melts about 40° lower than PGA. The L-lactide copolymers containing a small amount of glycolide units (i.e., PL5GA and PL16GA) were partially crystalline, while the high glycolide content in PL52GA completely prevented crystallization. All analyzed polymers and copolymers had a glass transition higher than room temperature, except the a-PHB that was used in this work as the low-T_g component of the blends. The T_g of the PLLAGA copolymers decreased with increasing glycolide content (Table 1). Also the melting temperature (T_m) and heat of fusion (ΔH_m) decrease with an increasing amount of foreign GA units along the polylactide chain. Similar changes of thermal properties with composition have been reported earlier for PLLAGA copolymers synthesized by stannous octanoate catalysis.[29] A broad range of melting enthalpy values are found in the literature for PLLA, spanning, for the totally crystalline polymer, from $\Delta H_m° = 93$ J/g[30] up to $\Delta H_m° = 203$ J/g.[31] The present enthalpy data indicate that the polyesters investigated are characterized by a very substantial crystalline fraction.

The powder X-ray diffractograms of the crystalline polymers and copolymers investigated are shown in Figure 1. The two homopolymers exhibit different X-ray profiles that reflect the well-known differences of PLLA[32,33] and PGA[34,35] unit cell parameters and chain conformation. The X-ray patterns of the two PLLAGA copolymers clearly indicate that the PLLA crystal phase develops when 5% and 16% glycolide units are incorporated in the copolymer. In PL5GA the main PLLA reflection at $2\theta = 16.7°$ is split. This feature becomes more evident in the copolymer richer in GA units (PL16GA) and is tentatively attributed to small PLLA unit cell distortions associated with the presence of the glycolide comonomer. The WAXS diffraction pattern of PL52GA (not shown) contains no crystalline reflections, in agreement with the DSC results that do not show any crystalline phase in this almost equimolar lactide–glycolide copolymer.

Blends. Thermal Degradation. The thermal stability of blends of a-PHB with PDLLA, PL5GA and PL16GA was investigated by TGA. As an example, Figure 2 reports the TGA curves of a-PHB/PL16GA blends with changing composition. All the blends in Figure 2 show two distinct weight loss steps whose intensity closely reflects blend composition. An analogous behavior is shown by the other blends investigated (a-PHB/PDLLA and a-PHB/PL5GA). In all cases, the step at lower temperature is attributed to a-PHB degradation, the higher one to decomposition of the second blend component. This attribution is confirmed by the mass spectra of the volatile thermal degradation products of the blends that show the presence of the molecular fragments expected at each step. A similar two-step degradation behavior was earlier found in graft copolymers[28] and blends of a-PHB with poly(methyl methacrylate).[36] The curves of Figure 2 show that only at either side of the composition interval the degradation step of the minor component tends to shift toward the T_{max} of the major component.

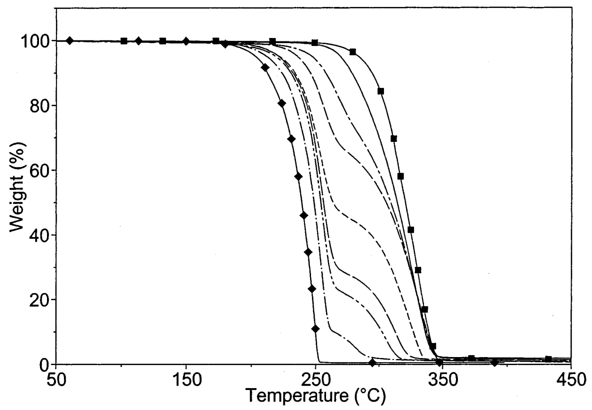

Figure 2. Thermogravimetric curves of a-PHB (–◆–) and PL16GA (–■–) and of a-PHB/PL16GA blends: 90/10 (—·—), 75/25 (— - - —), 70/30 (— —), 50/50 (- -), 35/65 (– –), 20/80 (— - —), and 10/90 (—).

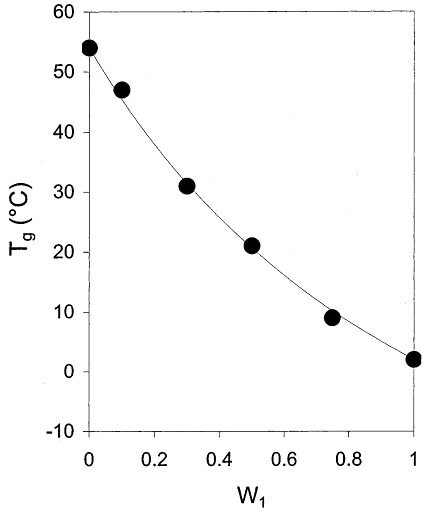

Figure 3. Glass transition temperature of a-PHB/PDLLA blends as a function of a-PHB weight fraction (w_1).

Miscibility. Miscibility and phase behavior of the different blend systems was investigated by DSC. Figure 3 shows the glass transition temperature of a-PHB/PDLLA blends as a function of composition. All blends show a single glass transition that regularly decreases with increasing a-PHB content. The curve drawn in Figure 3 represents the well-known relationship used by Wood[37] to describe the T_g–composition dependence of plasticized polymers and of miscible polymer blends:

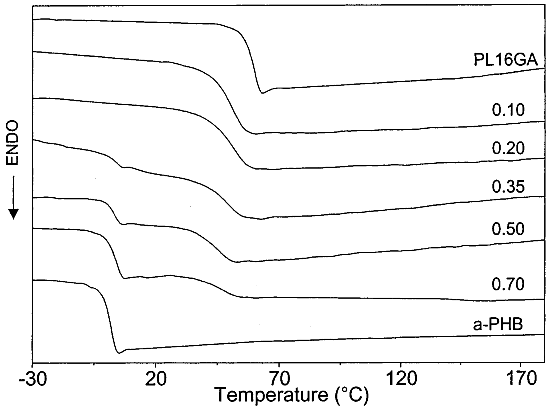

Figure 4. Calorimetric curves of melt quenched PL16GA, a-PHB, and a-PHB/PL16GA blends. Numbers on curves: a-PHB weight fraction (w_1).

$$T_g = (w_1 T_{g1} + k w_2 T_{g2})/(w_1 + k w_2) \tag{1}$$

where 1 and 2 indicate a-PHB and PDLLA, respectively, w is the weight fraction, and k is an adjustable parameter ($k = 0.56$ in this case). The very good fit of eq 1 to the experimental results demonstrates that PDLLA and a-PHB are miscible over the whole composition range. This result agrees with earlier data showing total miscibility of a-PHB with poly(L-lactic acid).[13]

In Figure 4 are some selected DSC curves (second scans after melt quenching) of a-PHB/PL16GA blends. The analyzed samples are completely amorphous and show a single glass transition in the range of a-PHB weight fraction 0−0.2, with T_g that regularly decreases with increasing amount of a-PHB. When the a-PHB content is $w_1 \geq 0.35$, two constant-temperature glass transitions appear in the DSC curve: the upper one at 47 °C and the lower T_g at 3 °C. The constancy of temperature indicates constancy of composition of the phases undergoing the glass-to-rubber transition. The higher T_g is that of a a-PHB/PL16GA mixture containing around 20% of a-PHB, a composition that represents the solubility limit of a-PHB in PL16GA. All a-PHB in excess to this limit phase-separates and gives rise to a pure a-PHB phase, identified by the low-temperature glass transition in Figure 4.

Shown in Figure 5 are some selected DSC curves (second scans after melt quenching) of a-PHB/PL5GA blends. The blend with 10% a-PHB shows a single glass transition, whereas two constant-temperature glass transitions are shown by blends richer in a-PHB. The limit of miscibility above which a-PHB phase-separates is the same as that of the other PLLAGA blend analyzed above, i.e., around 20% a-PHB content. The T_g that appears at 3 °C is due to phase separated a-PHB in excess to the solubility limit. The intensity of this glass transition clearly increases with the amount of a-PHB in the blend. Unlike the a-PHB/PL16GA blends (Figure 4), the curves of Figure 5 show crystallization and melting of the PLLAGA component. It is interesting to note that cold crystallization of PL5GA occurs in the blends but not in the plain copolymer (Figure 5). This observation is explained by the decrease of the blend glass transition temperature that widens the temperature window ($\Delta T = T_m - T_g$) where PL5GA can crystallyze.

The present results show that PDLLA is totally miscible with a-PHB, whereas the two investigated PLLAGA copolymers are only partially miscibile with a-PHB. The presence of the polar glycolide units along the chain reduces the miscibility compared with polymers containing only lactide units, i.e., PDLLA and PLLA.

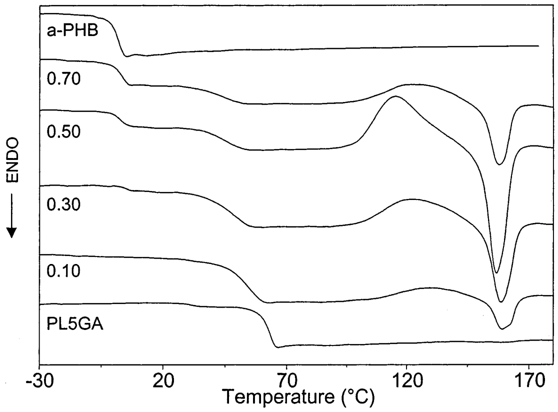

Figure 5. Calorimetric curves of melt quenched PL5GA, a-PHB, and a-PHB/PL5GA blends. Numbers on curves: a-PHB weight fraction (w_1).

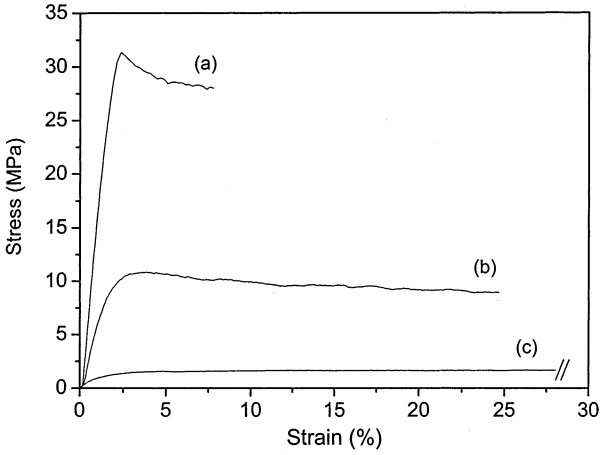

Figure 6. Stress-strain curves: (a) PDLLA; (b) a-PHB/PDLLA (25/75); (c) a-PHB/PDLLA (50/50).

Mechanical Properties. The mechanical properties of a-PHB/PDLLA and a-PHB/PL16GA blends are characterized in view of their potential application as membrane biomaterials. The results of stress−strain measurements on the two blend systems are shown in Figures 6 and 7, respectively. Two compositions are investigated: 25/75 and 50/50 by weight. Table 2 collects the relevant mechanical data together with the thermal properties of the film samples subjected to tensile measurements.

The two blends show a similar behavior with increasing a-PHB content (Figures 6 and 7): the elastic modulus (E) stress at yield (σ_y) and stress at break (σ_b) decrease, whereas the elongation at break (ϵ_b) increases. Both PDLLA and PL16GA are hard-tough fragile materials that become ductile upon blending with the low-T_g a-PHB component. The observed changes of mechanical properties can be correlated with the variation of the blend thermal properties with composition (Table 2).

Let's consider the a-PHB/PDLLA system. PDLLA is glassy at room temperature ($T_g = 50$ °C) and accordingly its stress−strain curve (Figure 6) is typical of a glassy, rigid material. As discussed above, PDLLA and a-PHB are totally miscible, and the blend T_g regularly de-

Table 2. Thermal and Mechanical Properties of Films of PDLLA and PL16GA and of Their Blends with a-PHB

	blend compn (wt %)	T_g[a] (°C)	T_m[a] (°C)	ΔH_m[a] (J/g)	σ_y[b] (MPa)	ϵ_y[b] (%)	σ_b[b] (MPa)	ϵ_b[b] (%)	E[b] (GPa)
PDLLA		50			28 ± 3	2.5 ± 0.2	26 ± 2	7 ± 3	1.8 ± 0.1
a-PHB/PDLLA	25/75	32			12 ± 2	3.9 ± 0.3	9 ± 1	26 ± 13	0.8 ± 0.1
a-PHB/PDLLA	50/50	23			1.6 ± 0.1	6 ± 1	n.d.[c]	>300	0.10 ± 0.01
PL16GA		56	132	18	43 ± 2	3.0 ± 0.1	39 ± 2	5 ± 3	1.9 ± 0.1
a-PHB/PL16GA	25/75	2; 48[d]	134	8	29 ± 1	5 ± 1	23 ± 1	23 ± 9	0.9 ± 0.1
a-PHB/PL16GA	50/50	0; 50[d]	134	0	12 ± 2	4 ± 1	11 ± 1	116 ± 75	0.51 ± 0.04

[a] From first DSC scan. [b] From stress–strain measurements (σ_y, stress at yield; ϵ_y, elongation at yield; σ_b, stress at break; ϵ_b, elongation at break; E, tensile modulus). The standard deviation is reported. [c] n.d. = not determined. [d] Two glass transitions.

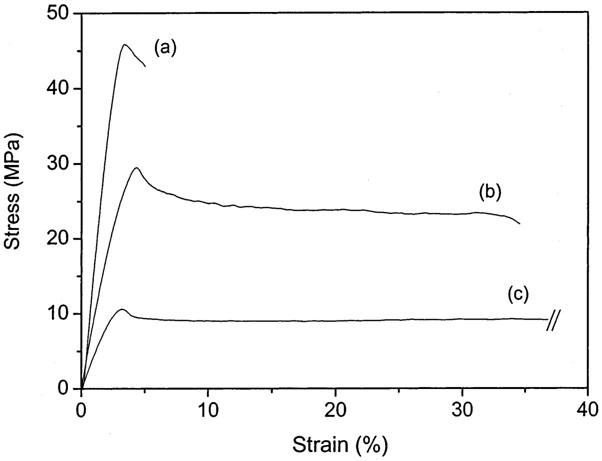

Figure 7. Stress-strain curves: (a) PL16GA; (b) a-PHB/PL16GA (25/75); (c) a-PHB/PL16GA (50/50).

creases with increasing a-PHB content (Figure 3). Taking into account that the T_g values in Table 2 are "midpoint" T_gs (see Experimental Section) and that the DSC glass transition of a-PHB/PDLLA blends is broad (11 °C in blend 25/75 and 26 °C in blend 50/50), it is clear that the glass-to-rubber transition of the two blends encompasses room temperature. The basis of the increase of polymer chain mobility at the test temperature easily explains the observed increase of ϵ_b and the decrease of both E and σ with increasing a-PHB content (Table 2).

PL16GA is a partially crystalline polymer. Besides the crystal phase, it contains an amorphous fraction that is glassy at room temperature (Table 2). As a consequence, PL16GA is quite rigid and fragile (Figure 7). As mentioned above a-PHB/PL16GA blends are miscible only up to about 20% a-PHB content. Above this composition limit, a-PHB separates as a pure amorphous phase, that is rubbery at room temperature (a-PHB $T_g = 3$ °C). The tensile properties of the two a-PHB/PL16GA blends investigated can be rationalized on account of the glass transition depression (Table 2) and of the presence of rubbery a-PHB in excess to the solubility limit. The latter amount is small in blend 25/75 but is consistent in blend 50/50. Both blends contain a mixed a-PHB/PL16GA (20/80) phase with T_g lower than that of PL16GA but still well above room temperature (Table 2). In addition to this glassy phase, the blend with 25% a-PHB also contains a small crystalline fraction that imparts strength to the sample. The stress–strain curve of blend 25/75 reflects the complex phase behavior of this sample. When the amount of a-PHB in the blend increases to 50%, the concomitant disappearance of the crystalline PL16GA phase and the increase of the elastomeric a-PHB phase lead to the change of mechanical properties observed in Figure 7.

It is concluded that films of both a-PHB/PDLLA and a-PHB/PL16GA blends show interesting mechanical properties that can be modulated by changing blend composition. The tenacity of both PDLLA and PL16GA progressively increases by the addition of proper amounts of the low-T_g polyester a-PHB. It is worthwhile to note that this is true not only for the miscible amorphous a-PHB/PDLLA system but also for partially miscible a-PHB/PL16GA blends. In the latter, the elastomeric a-PHB phase dispersed in the rigid glassy or glassy/crystalline matrix substantially contributes to the tunable mechanical properties shown by this system.

Acknowledgment. Thanks are due to D. Sbattella for experimental assistance. This work was partially supported by the Italian Ministry for Education, University and Research (M.I.U.R.) and by the Foundation for Polish Science (Grant TECHNO 25/2000).

References and Notes

(1) Vert, M.; Schwarch, G.; Coudane, J. *J. Macromol. Sci.—Pure Appl. Chem.* **1995**, *A32*, 787–796.
(2) Wu, X. S. In *Encyclopedic Handbook of Biomaterials and Bioengineering*; Wise, et al., Eds.; Marcel Dekker: New York, 1995.
(3) Khon, J.; Langer, R. In *Biomaterial Science*; Ratner, et al., Eds.; Academic Press: New York, 1996.
(4) Ikada, Y.; Tsuji, H. *Macromol. Rapid Commun.* **2000**, *21*, 117–132.
(5) Levis, R. J. *Sax's Dangerous Properties of Industrial Materials*, 8th ed.; Sr. Van Nostrand-Reinhold: New York, 1992.
(6) Salanki, Y.; D'eri, Y.; Platokhin, A. *Neurosci. Behav. Physiol.* **2000**, *30*, 63–73.
(7) Schwach, G.; Coudane, J.; Engel, R.; Vert, M. *J. Polym. Sci., Part A* **1997**, *35*, 3431–3440.
(8) Dobrzynski, P.; Kasperczyk, J.; Janeczek, H.; Bero, M. *Macromolecules* **2001**, *34*, 5090–5098.
(9) Focarete, M. L.; Scandola, M.; Jendrossek, D.; Adamus, G.; Sikorska, W.; Kowalczuk, M. *Macromolecules* **1999**, *32*, 4814–4818.
(10) Seebach, D.; Brunner, A.; Bachmann, B. M.; Hoffmann, T.; Kühnle, F. N. M.; Lengweiler, U. D. *Biopolymers and -oligomers of (R)-3-Hydroxyalkanoic Acids—Contributions of Synthetic Organic Chemists*; Ernst Schering Research Foundation: Berlin, 1995.
(11) Pawan, G. L. S.; Semple, S. J. G. *Lancet* **1983**, *Jan 1/8*, 15–17.
(12) Freier, T.; Kunze, C.; Nischan, C.; Kramer, S.; Sternberg, K.; Sass, M.; Hopt, U. T.; Schmitz, K.-P. *Biomaterials* **2002**, *23*, 2649–2657.
(13) Focarete, M. L.; Ceccorulli, G.; Scandola, M.; Kowalczuk, M. *Macromolecules* **1998**, *31*, 8485–8492.
(14) Jedlinski, Z.; Kowalczuk, M.; Glowkowski, W.; Grobelny, J.; Szwarc, M. *Macromolecules* **1991**, *24*, 349–352.
(15) Kurcok, P.; Kowalczuk, M.; Hennek, K.; Jedlinski, Z. *Macromolecules* **1992**, *25*, 2017–2020.
(16) Jedlinski, Z.; Kowalczuk, M.; Kurcok, P.; Adamus, G.; Matuszowicz, A.; Sikorska, W.; Gross, R.; Xu, J.; Lenz, R. W. *Macromolecules* **1996**, *29*, 3773–3777.
(17) Adamus, G.; Sikorska, W.; Kowalczuk, M.; Montaudo, M.; Scandola, M. *Macromolecules* **2000**, *33*, 5797–5802.
(18) Bero, M.; Dobrzynski, P.; Kasperczyk, J. *Polym. Bull. (Berlin)* **1999**, *42*, 131–139.
(19) Kasperczyk, J.; Bero, M. *Polymer* **2000**, *41*, 391–395.

(20) McNeill, I. C.; Leiper, H. A. *Polym. Degrad. Stab.* **1985**, *11*, 267−285.
(21) Garozzo, D.; Giuffrida, M.; Montaudo, G. *Macromolecules* **1986**, *19*, 1643−1649.
(22) Kopinke, F.-D.; Remmler, M.; Mackenzie, K.; Möder, M.; Wachsen, O. *Polym. Degrad. Stab.* **1996**, *53*, 329−342.
(23) McNeill, I. C.; Leiper, H. A. *Polym. Degrad. Stab.* **1985**, *11*, 309−326.
(24) McNeill, I. C.; Leiper, H. A. *Polym. Degrad. Stab.* **1985**, *12*, 373−385.
(25) Grassie, N.; Murray, E. J.; Holmes, P. A. *Polym. Degrad. Stab.* **1984**, *6*, 47−61.
(26) Grassie, N.; Murray, E. J.; Holmes, P. A. *Polym. Degrad. Stab.* **1984**, *6*, 127−134.
(27) Aoyagi, Y.; Yamashita, K.; Doi, Y. *Polym. Degrad. Stab.* **2002**, *76*, 53−59.
(28) Adamus, G.; Kowalczuk, M.; Jedliński, Z.; Ballistreri, A.; Scherer, T.; Lenz, R. W. *Polym. Deg. Stab.* **1995**, *50*, 269−276.
(29) Grijpma, D. W.; Nijenhuis, A. J.; Pennings, A. J. *Polymer* **1990**, *31*, 2201−2206.
(30) Fischer, E. W.; Sterzel, H. J.; Wegner, G. *Kolloid Z. Z. Polym.* **1972**, *251*, 980−990.
(31) Jamshidi, K.; Hyon, S.-H.; Ikada, Y. *Polymer* **1988**, *29*, 2229−2234.
(32) De Santis, P.; Kovacs, A. J. *Biopolymers* **1968**, *6*, 299−306.
(33) Hoogsteen, W.; Postema, A. R.; Pennings, A. J.; ten Brinke, G.; Zugenmaier, P. *Macromolecules* **1990**, *23*, 634−642.
(34) Chatani, Y.; Suehiro, K.; Okita, Y.; Tadokoro, H.; Chujo, K. *Makromol. Chem.* **1968**, *113*, 215−229.
(35) Marega, C.; Marigo, A.; Zannetti, R.; Paganetto, G. *Eur. Polym. J.* **1992**, *28*, 1485−1486.
(36) Ceccorulli, G.; Scandola, M. *J. Macromol. Sci.—Pure Appl. Chem.* **1999**, *A36*, 327−337.
(37) Wood, L. A. *J. Polym. Sci.* **1958**, *28*, 319−330.

MA020940Z