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Thermal, morphologic and mechanical characterization of poly (L-lactic acid) / poly (hydroxybutyrate-co-hydroxyvalerate) blends

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Abstract
The development of bioabsorbable polymers can be considered one of the major advances in biomedical material research. Bioabsorbable materials have numerous applications in medicine. The purpose of this work was to study the Poly(L-lactic acid) and Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) PLLA/PHBV blends in different compositions (100/0, 60/40, 50/50, 40/60, and 0/100), obtained by melting in a mini-injector Mini Max Molder making samples with 3.1 mm diameter and 90 mm length. The blends were characterized by Differential Scanning Calorimetry (DSC), Dynamical Mechanical Analysis (DMA), Scanning Electron Microscopy (SEM) and Mechanical Tests. DSC and DMA data showed that the PLLA/PHBV blends presented two distinct glass transition temperatures, crystallization temperatures and melting temperature, respectively, for the pure polymers, indicating that the blends are immiscible in all compositions. It was possible to observe, by SEM analysis, that the pure polymers and the blends presented dense morphology. The blends showed phase separation, confirming the DSC and DMA data. The flexural mechanical tests indicated that PLLA improves mechanical stress and flexibility in the system. Due to their good thermal and mechanical compatibility, the PLLA/PHBV blends, have proven to be an interesting alternative for the orthopedic area. **Keywords**: Biomaterial, Bioabsorbable polymer, Blend, Poly(L-lactic acid), Poly(hydroxybutyrate-co-hydroxyvalerate).

Resumo
O desenvolvimento de polímeros bioabsorvíveis pode ser considerado como um avanço no desenvolvimento de materiais biomédicos. Materiais bioabsorvíveis apresentam numerosas aplicações na medicina. A proposta deste trabalho foi estudar blendas de Poli(L-ácido láctico) e Poli(3-hidroxibutirato-co-3-hidroxivalerato) PLLA/PHBV em diferentes composições (100/0, 60/40, 50/50, 40/60, e 0/100), obtidas através da fusão dos polímeros em uma mini injetora Mini Max Molder, obtendo pinos de 31x90 mm. As blendas foram caracterizadas através das análises de Calorimetria Diferencial de Varredura (DSC), Análise Dinâmico-Mecânica (DMA), Microscopia Eletrônica de Varredura (SEM) e ensaios mecânicos. As análises de DSC e DMA mostraram que as blendas de PLLA/PHBV apresentaram duas temperaturas de transição vítrea, cristalização e fusão distintas, respectivas aos polímeros puros, indicando a imiscibilidade das blendas em todas as composições. Através do SEM foi possível observar que tanto os polímeros puros como as blendas apresentaram uma morfologia densa, sendo que nas blendas verificou-se a presença de duas fases, confirmando os dados de DSC e DMA. Os testes de ensaio mecânico de flexão mostraram que o PLLA impõe maior resistência mecânica e flexibilidade ao sistema. Devido à sua boa compatibilização térmica e mecânica, as blendas de PLLA/PHBV, mostraram ser uma boa alternativa para aplicação na área ortopédica. ***Palavras-chave:*** *Biomaterial, Blenda, Polímero bioabsorvível, Poli(L-ácido láctico), Poli(hidroxibutirato-co-hidroxivalerato).*

Introduction

The application of polymeric materials in medicine has been growing considerably in these last decades, especially in the field of artificial organs. It is not surprising that synthetic substances with structures similar to these organs should be used as substitutes (Giusti, 1987; Penning *et al.*, 1993).

Generally, for such materials, several properties must be fulfilled. These requirements are mostly biological ones that all implanted biodegradable materials must carry out, especially mechanical properties and biodegradation kinetics. However, only some polymers are able to attend all of these requirements (Zhang *et al.*, 1995).

The blending of polymers is a good way of obtaining material with the desirable properties. Blends exhibit advantageous physical and mechanical properties, which each individual polymer does not possess. Depending on the thermodynamic compatibility of the two chosen polymers, phase-separated polymers can be obtained, imposing different morphologies and matrix characteristics (Park *et al.*, 1992).

The properties of the blends depend mainly on the thermodynamic miscibility. If the polymers are immiscible, the properties will depend not only on each component, but also on the morphology and adhesion of the phases (Ultracki, 1989).

Polymer blends containing biodegradable components or hydrolytically unstable components, are of great interest, because of the way in which their physical properties and degradation characteristic can be tailored. These materials have attracted quite a lot of attention, especially in relation to applications in devices and biomedical uses (Nijenhuis *et al.*, 1996). Studies have been focusing more on the development of biodegradable polymers for fracture fixation (Reis and Cunha, 1995; Elst *et al.*, 1995; Elst *et al.*, 1996).

Aliphatic polyesters such as glicolic acid; D,L- and L-lactic acid; β-hydroxybutyrate, and e-caprolactan, are the most important biodegradable polymers, which have frequent application as biodegradable products in prosthesis and controlled drug releases (Elst *et al.*, 1996; Zhang *et al.*, 1995; Ignatius and Claes, 1996).

Among bioabsorbable fixation device materials, poly (L-lactic acid) (PLLA) tends to be used more frequently than poly (glicolic acid) (PGA) because its slow degradation is believed to result in a lower rate of inflammatory tissue reaction. However, several complications have been reported, including late aseptic swelling, osteolytic change at the implant site, incomplete restitution of normal bone architecture in the medullary canal after implant resorption, and early micromovement of the implant (Furukawa *et al.*, 2000).

Williams in a recent paper clearly showed that PHB and PHBV copolymers, processed to form monofilament fibres, do not undergo any significant loss of mechanical properties even after six months (Vert *et al.*, 1992). Holland *et al.* (1990) report that even if they found evidence of degradation for low molecular mass compounds with poor mechanical properties, high molecular mass copolymers with good mechanical properties exhibited 1% weight loss after 200 days at pH 7.4 and 37°C for melt press discs (Holland *et al.*, 1990).

Duek *et al.* and Suming *et al.* report that the PLLA crystalline started to decrease its Storage Modulus after 2 weeks, whereas the PLLA amorphous retained its initial value for almost 10 weeks (Duek *et al.*, 1999; Suming *et al.*, 1990).

At temperatures above Tg, a polymer behaves in a rubber like manner and at temperatures below Tg, in a glass like manner. A polymer with a Tg around body temperature may be much more ductile when implanted than it appears to be at room temperature. These properties can affect both the mechanical properties as well as the degradation time of the implant. For the polyesters, the presence of water can act as a plasticizer lowering the Tg and consequently affecting the degradation and mechanical properties (Middleton and Tipton, 2000).

Due to the great interest demonstrated in the development of biodegradable polymers, by modifying the characteristics of these and by increasing their applicability in biomedical uses, the decision to study the poly(L-lactic acid)/poly(hydroxybutyrate-co-hydroxyvalerate) (PLLA/PHBV) blend was therefore made. With this premise, the objective of this work was the study of the miscibility, physicochemical, thermal and mechanical properties of these blends, varying the composition of the pure polymers, for application in the medical area.

Materials and Methods

Poly(L-lactic acid), molecular weight Mw = 100.000 Daltons (Medisorb - Dupont), and poly(3-hydroxybutyrate-co-3-hydroxyvalerate), with 12% of hydroxyvalerate (Aldrich), were used in this research.

The PLLA/PHBV blends were prepared by melting the polymers, using a Mini Max Molder model LMM - 2017. The final compositions were 100/0, 60/40, 50/50, 40/60, and 0/100 (w/w). The blends were heated in a container up to 200°C. After that, the blends

were sheared by rotation of a piston to obtain homogeneity during the melting process. The material was injected into the desired mold (heated at 120°C) to give a pin-shaped specimen of 3.1 mm diameter and 90 mm length. After cooling at room temperature, the pins were stored under vacuum. The samples were characterized by Differential Scanning Calorimetry (DSC), Dynamical Mechanical Analysis (DMA), Scanning Electron Microscopy (SEM), and Three-point mechanical bending tests.

Thermal transitions of the blends were measured by means of differential scanning calorimetry (DSC) using a STA 409C of NETZSCH - Gerätebau GmbH Thermal Analysis, at a heating rate of 10 °C/min in helium atmosphere. Samples were first heated from 25 to 200 °C and maintained at this temperature for 5min, until completely melted, thus eliminating thermal history. They were then cooled to -20 °C for 5 min and heated again to 200 °C. The melting temperatures of the two phases and the enthalpy associated to the melting and/or crystallization process were determined.

Dynamical mechanical analysis (DMA) was performed using a NETZSCH - Dynamic Mechanical Analysis - 242. The samples were cooled to -20 °C and soon after heated up to 200 °C, with a heating rate of 5°C/min, under air, with a maximum force of 1 N, frequency of 1 Hz and amplitude of 15 μm using a dual cantilever system.

SEM photomicrographs were obtained in a JSM-5900LV ARP microscope (10 keV) after sputter coating with gold to observe the cross section of the pins, that were previously fractured in liquid N_2.

The blends obtained from the melting were submitted to three-point mechanical bending tests, according to the ASTM D 790-95a, in a MT TestStar II, using a 20 kgf load cell and 2 mm/min speed. The distance between the points was 18 mm. The stress (σ) and strain (ε) below were obtained considering the pins as cylindrical systems (Nielsen, 1974):

$$\sigma = \frac{8.F.Lo}{\pi.D^3} \quad (1)$$

$$\varepsilon = \frac{6.D.Y}{Lo^2} \quad (2)$$

where F is the force (N); Lo is the separation between the points (mm); ε is the elongation (%); σ is the tension (MPa); Y is the deformation (mm); and D is the diameter (mm).

Results and Discussion

Differential Scanning Calorimetry

Figure 1 and Table 1 show the DSC behavior for the PLLA/PHBV blends in different compositions. Glass Transition Temperature (Tg) was observed around 0°C for PHBV and 54°C for PLLA. It was possible to obtain the Tg of PHBV in the second heating only because it does not appear in the first heating. According to Zhang about a study of PHB, this fact can be explained by the very fast crystallization and also by the fact that the amorphous areas do not present enough mobility to characterize Tg (Zhang *et al.*, 1995). Tg of PLLA, when mixed to PHBV, was only possible to obtain in the first heating, because in the second heating the Tg of PLLA was overloaded by the crystallization peak of PHBV. No variation in the Tg values was verified when comparing pure polymers in relation to blend composition.

The Crystallization Temperatures (Tc) were around 69°C and 104°C, for PHBV and PLLA, respectively. PLLA/PHBV blends presented small crystallization peaks in the first heating, due to having a fast cooling rate. It was also observed that there was no variation in the crystallization temperatures for both polymers in the blend, compared to pure polymers. According to Penning and Manley, the crystallization of each blend component represents a phase separa-

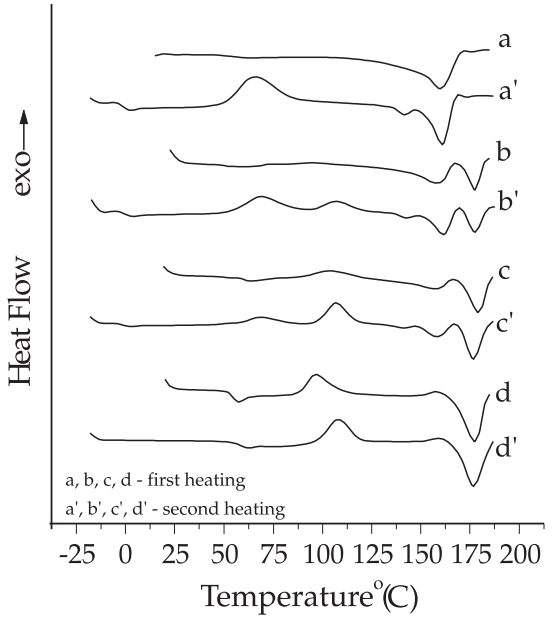

Figure 1. DSC thermograms of PLLA/PHBV blends in different compositions: (a) 0/100, (b) 40/60, (c) 60/40 and (d) 100/0, first and second heating.

Table 1: Differential scanning calorimetry of PLLA/PHBV blends in different compositions

PLLA/PHBV	Heating	Tg (°C)		Tc (°C)		ΔHc (J/g)		Tm (°C)		ΔHf (J/g)	
		PHBV	PLLA	PHBV	PLLA	PHBV	PLLA	PHBV	PLLA	PHBV	PLLA
100/0	1°		54		97		17		177		36
	2°		58		108		21		178		34
60/40	1°		52		104		9	157	180	10	20
	2°	-1		69	107	5	16	141-159	178	11	22
50/50	1		50		104		8	159	180	11	15
	2°	-1		70	108	11	14	142-160	178	11	17
40/60	1°		50				2	158	178	20	13
	2°	1		69	107	19	8	144-162	179	20	2
0/100	1							162		42	
	2°	0		66		37		142-162		43	

Tg = Glass Transition Temperature, Tc = Crystallization Temperature, Tm = Melting Temperature, DHc = Crystallization Enthalpie and DHf = Melting Enthalpie.

tion process in which the polymers partially segregate from the mixture to form a pure phase (Penning and Manley, 1996).

The Melting Temperatures (Tm) (Table 1) were around 143°C-160°C (in the second heating) and 178°C for PHBV and PLLA, respectively. The melting temperature of PLLA and PHBV also did not present variation, due to the composition of the blend. Although Tm of PHBV showed a small variation in the first heating, it was not possible to observe two distinct melting peaks, as observed in the second heating. There is an enlargement of the curve (Figure 1), not only for pure PHBV, but also for PHBV in the blend. This can be explained due to the fast cooling rate.

According to Verhoogt, the presence of two (or more) melting transitions for PHBV may be due to crystal thickening and/or recrystallization, which occurred during the heating in DSC. Usually the lower-temperature peak is considered as the 'true' melting point since it represents the behavior of the original, unannealed crystals (Verghoogt *et al.*, 1996).

For the first heating, the polymer chains were basically organized in a random form and they reached the crystallization temperature quickly (Tc). However, in the second heating the crystallization enthalpy (DHc) increased, due to some crystals formed during the cooling, which requests great energy for crystallization (Iannace *et al.*, 1994). This explains why the crystallization enthalpy (DHc) increased in the second heating in relation to the first.

Variations on the crystallization and melting enthalpies for the blends can be observed in Table 1. As expected, as the composition of one polymer in the blend was reduced, its crystallization and melting enthalpy decreased and almost disappeared when the polymer composition was very small. Iannace *et al.* (Iannace *et al.*, 1994) also showed this variation for the PLLA/PHBV blends obtained by casting and concluded that these results suggest that the crystallization process does not take place in totally pure polymer domains.

Dynamical Mechanical Analysis

Figure 2 shows the DMA behavior for the PLLA/PHBV blends in different compositions. The storage modulus (E') curves, Figure 2a, presented two steps corresponding to the glass transitions of the two blend components. The values of Tg were obtained from the maximum peaks of the 'E'' x T' (Figure 2b) and 'tan δ x T' curves. The Tg values for PHBV and PLLA were around 42 °C and 96 °C in the 'E'' x T' curve, and 47 °C and 101 °C in the 'tan δ x T' curve, respectively (Table 2). As verified in DSC analysis, the presence of two distinct values for Tg in the blends, compared with the pure polymers, is also an indication of the immiscibility of systems.

In the loss module (E''), Figure 2b, as the composition of one polymer in the blend was increased, its corresponding glass transition peak also increased. However, a significant variation in its temperature value was not observed (Table 2). In the same curves type β and γ secondary transition peaks appeared. This was due to the fact that the blends were injected and, in spite of their being cooled at room temperature, they had a very fast cooling rate, giving no time for the accommodation of the chains. So when they were heated and bent, in DMA, the chain accommodation, which was detected by the loss modulus, began.

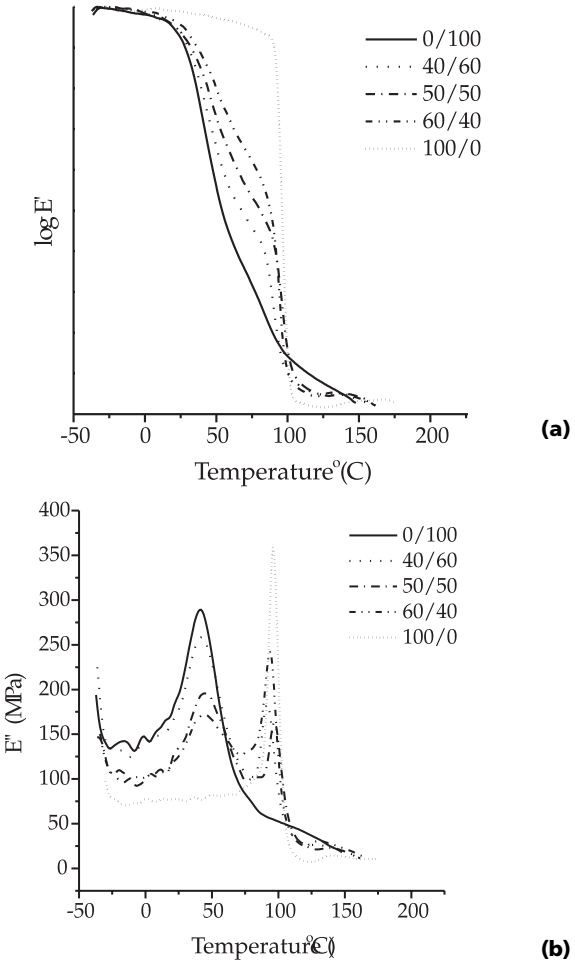

Figure 2: (**a**) Dynamic Storage Modulus (E') and (**b**) Loss Modulus (E") of various PLLA/PHBV blends.

Table 2: Dynamical mechanical analysis of PLLA/PHBV blends in different compositions

PLLA/PHBV	Tg (°C) by E"		Tg (°C) by tan δ	
	PHBV	PLLA	PHBV	PLLA
100/0		96		101
60/40	45	94	51	98
50/50	45	97	49	101
40/60	42	92	47	95
0/100	42		47	

Tg = Glass transition temperature, E" = Loss of Modulus, tan *d* = *damping.*

Scanning Electron Microscopy

Figure 3, shows the micrographs of the PLLA/PHBV blends with different compositions. The cross section of the 100/0 blend, Figure 3a, showed that PLLA had a dense morphology, which was drastically modified when 40% PHBV was added as a dispersed component, (Figure 3b). In the 60/40 and 40/60 blends, Figures 3b and 3c respectively, it is possible to observe a phase separation, where the PLLA phase had a dense surface of fracture and the PHBV phase was non-continuous. The phase separation is in the form of co-continuous phases on a very small scale.

Blends containing 60% PHBV, Figure 3c, showed a non-continuous phase with very small globules. This was more evident in pure PHBV (Figure 3d). The PHBV surface of the fracture showed a non-continuous phase, with very small globules (Figure 3d).

Three-point Mechanical Bending Tests

Three-point mechanical bending tests showed that these polymers behave like a hard and ductile material; when submitted to a constant tension they initially suffered deformation, later elongation, and finally rupturing (Figure 4).

Table 3 shows the value obtained from stress-strain curves of PLLA/PHBV blends in different compositions. It can be verified that although PLLA showed loss of the mechanical properties in the presence of PHBV, the properties of PHBV were improved, not only for the module but also for the elongation.

The Modulus of PLLA/PHBV blend increased from 1.53 GPa (from pure PHBV) to 2.12 GPa in the PLLA/PHBV blend with 40% (w/w) PLLA, and to 2.38 GPa in the blend with 50% (w/w) PLLA, and finally with 60% (w/w) PLLA the Modulus is 2.73 GPa. The same occurs with the Stress at Maximum Load, which increases from 51 MPa, for the pure PHBV, to 87 MPa for the 40/60 blend, and to 97 MPa for the 50/50 blend, and finally to 100 MPa for the 60/40 blend. The mechanism of strain energy dissipation during the deformation of these systems led to tougher materials that show yield behavior or plastic deformation (Iannace *et al.*, 1994).

A bone fracture takes approximately 4 weeks to knit, and this time period can be submitted to a series of alterations such as: patient's age and physical conditions, mechanical stress in the fractured area, among others.

Previous PLLA studies carried out by Duek *et al.* (Duek *et al.*, 1999) and Suming *et al.* (Suming *et al.*, 1990) showed that the PLLA loses its mechanical properties very rapidly during the degradation (around two weeks). According to Holland *et al.* (Holland *et al.*, 1990), pure PHBV maintains its mechanical properties for a long period of time however, it takes longer to degrade.

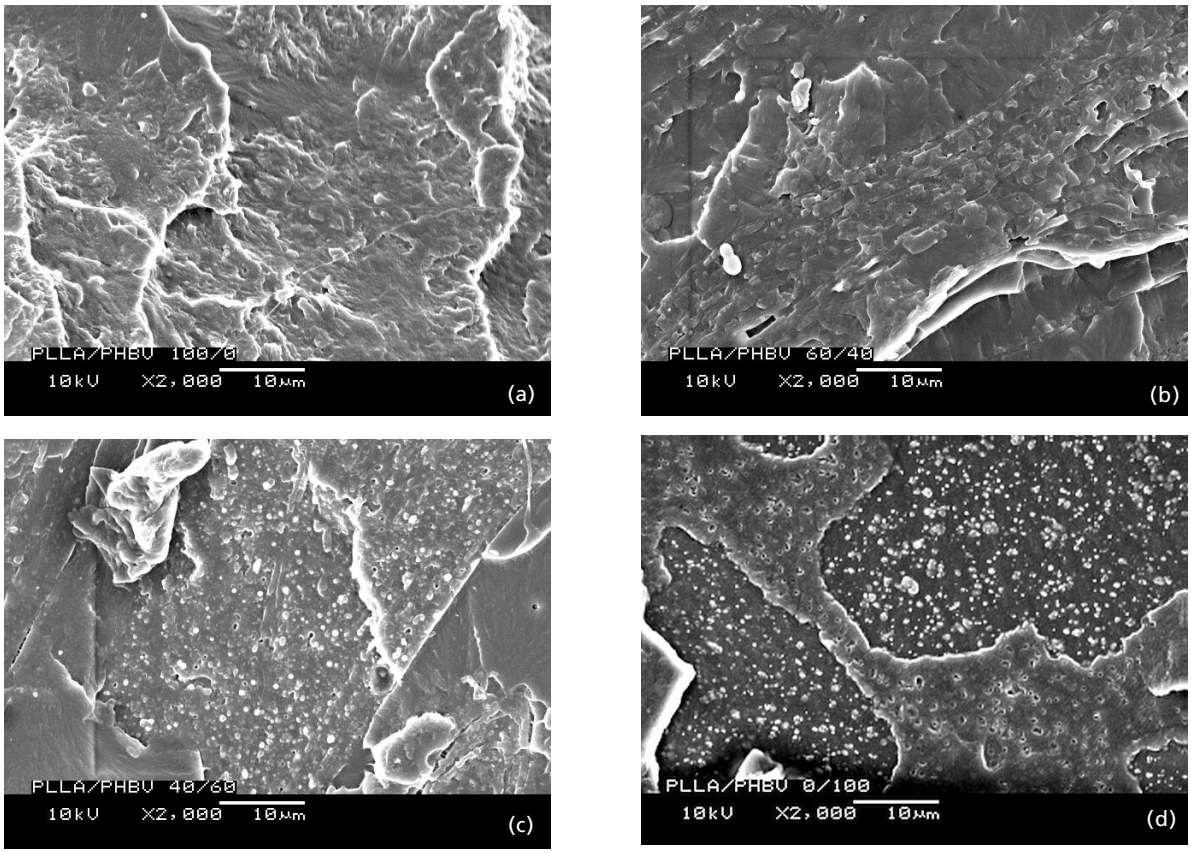

Figure 3: Electron micrographs of the fracture surfaces of PLLA/PHBV blends in different compositions: (**a**) 100/0, (**b**) 60/40, (**c**) 40/60 and (**d**) 0/100.

Table 3: Three-point mechanical bending tests of PLLA/PHBV blends in different compositions

	Modulus E (GPa)		Stress at Maximum Load (MPa)	
PLLA/PHBV		SD		SD
100/0	3.3	0.15	143	4.5
60/40	2.73	0.07	100	6.6
50/50	2.38	0.13	97	5.5
40/60	2.12	0.20	87	8.1
0/100	1.53	0.06	51	3.9

SD = Standard Deviation

The choice of a blend for a specific application will depend on the time which the material can maintain its required properties. For example, blend 60/40 will maintain its mechanical resistance for a longer period than pure PLLA, which on the other hand, will degrade faster than pure PHBV. With the increase of PHBV in the blend, it is possible to maintain the mechanical properties for a longer period of time during the degradation process.

Conclusions

The DSC and DMA data showed that the blends presented two different glass transition temperatures and two different melting temperatures. And besides this, the values of melting temperature did not vary in function of the composition of the blend. All these data are indications of immiscibility of the blends.

The micrographs obtained for SEM showed that the blend presented co-continuous phase separation on a very small scale in all of the compositions.

The flexure testing showed that the Stress at Maximum Load and Modulus values for the blends were between the values of the pure polymers. A great variation in the strain for the samples was noticed. The PLLA enhance the plasticity and stiffness of the PHBV in the blend.

The PLLA/PHBV blend study tried to improve the quality of polymers for use in orthopedics. PLLA is already used for the purpose, however only on small fractures. For large bone fractures, which require a more resistant material, the PLLA loses its use due to the rapid mechanical property loss, thus the need for metal poles. The metal poles, however, present the

disadvantage of deviating all of the mechanical stress towards them, diminishing the resistance of the bone callus formed, and also often require a second surgery for the removal of the implant material. The PHBV presents a lower Stress at Maximum Load and Modulus than PLLA, however degrades slower by hydrolysis, maintaining its characteristics for a longer period of time. Therefore, it is possible to conclude that the PLLA/PHBV blends, due to their good thermal and mechanical compatibility, have proven to be an efficient solution for orthopedic devices.

The study of the degradation *in vitro* of the PLLA/PHBV blends is now in progress.

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