Materials Research, Vol. 4, No. 2, 117-125, 2001.

Preparation and Characterization of Poly (L-Lactic Acid) and Poly (Ethylene Oxide) Blends

R.A. Zoppi[a*], *E.A.R. Duek*[b], *D.C. Coraça*[c], *P.P. Barros*[a]

[a]*Instituto de Ciências Biológicas e Química, PUC - Campinas, C.P. 1111, 13020-904 Campinas - SP, Brazil*
[b]*Faculdade de Engenharia Mecânica, Unicamp, 13083-970 Campinas - SP, Brazil*
[c]*Instituto de Biologia, Unicamp, 13083-970 Campinas - SP, Brazil*

Received: November 11, 2000; Revised April 20, 2001

Poly(L-lactic acid) (PLLA) and poly(ethylene oxide) (PEO) blends were prepared by mechanical mixture and fusion of homopolymers. Samples were submitted to *in vitro* degradation tests (immersion in a phosphate buffer solution with pH = 7.4 at 37 °C). Independently of the blend composition, PEO was dissolved after 14 days of immersion. As expected, after immersion, scanning electron microscopy showed that the blends were porous, contrary to the samples, which were not immersed in the buffer solution. Phase separation was not evident. Using differential scanning calorimetry, the melting points (T_m) of both PLLA and PEO crystalline fractions were observed and remained practically constant, indicating no miscibility. Thermogravimetry showed that the temperature where the main mass loss stage starts (T_{onset}), depended on the blend composition and period of immersion in the buffer. The blends and the PLLA homopolymer were implanted in defects produced in the tibias of rats. The blends were as biocompatible as the PLLA.

Keywords: *poly(L-lactic acid), poly(ethylene oxide), blends, biomaterials*

1. Introduction

Biodegradable polyesters based on poly(L-lactic acid), PLLA, have been used as biomaterials for temporary therapeutic applications mainly in orthopedic devices, controlled drug release and support for cell culture[1-4]. The main advantage of PLLA is its degradation by simple hydrolysis of the ester backbone in aqueous environments such as body fluids. This makes it very convenient for devices with a temporary function. The degradation products are finally metabolized to carbon dioxide and water or excreted *via* the kidneys, so is not necessary to remove the device from the implantation site after tissue healing[1,5]. Pure PLLA devices in general have a long degradation time[6-9].

Mainil-Varlet and co-workers have been using poly(L-lactic acid) and poly(DL-lactic acid) in implants in the tibia of sheep and verified that the absorption of these materials were not complete even after one year of implantation; the molecular weight, however, decreased from 40000-50000 to 500-3000 g/mol[8].

PLLA degradation and biocompatibility have been investigated in rats. The histological reaction in PLLA implants is slow but, the decrease in the polymer molecular weight is fast. The complete absorption of PLLA has not been observed in rats and it has been estimated that this phenomenon should occur after 3.5 years of implantation[6].

Based on the positive results observed for animals, PLLA has been used in the fixation of bone fractures in humans. After 3.5 years of implantation, the slow polymer degradation caused a swelling of the implanted region, without however the necessity of extracting the implant[10].

An alternative procedure to change degradation time, is the blending of PLLA with other polymers, which can be degradable or non-degradable polymers. In general, this kind of blends exhibits advantageous physical and mechanical properties[5,11]. The degradation time of the device can be varied from months to years, depending on its amorphous/crystalline and hydrophilic/hydrophobic properties[5,12].

*e-mail: rita@iqm.unicamp.br
Trabalho apresentado no 14° CBECIMAT, Águas de São Pedro, Dezembro 2000.

Most of the investigated systems represent mixtures of two amorphous polymers, such as poly(phenylene oxide)/polystyrene, or mixtures in which one of the components is semi-crystalline, such as poly(vinyl chloride)/caprolactone[12]. Semi-crystalline/semi-crystalline polymer blends, which have been reported in literature, include poly(vinylidene fluoride)/(acrylates)[13], poly(ethylene oxide)/poly(hidroxybutyrate)[14], poly(vinylidene fluoride)/poly(hidroxybutyrate)[15], poly(caprolactone)/poly(carbonate)[16-18], poly(vinylidene fluoride)/poly(1,4-butylene adipate)[19,20]. In these systems, the phase behavior and morphological properties have been investigated.

Meikle and co-workers implanted poly(DL-lactic acid)/poly(glycolic acid) blends into the head of rabbits, using as a control spontaneous bone regeneration. By histomorphometry analysis they verified that the differences in bone regeneration were not statistically significant, after 1, 2 or 3 months of implantation[21], when compared to the control.

Poly(ethylene oxide), PEO, is a hydrophilic non-degradable polymer, while PLLA is hydrolytically degradable and hydrophobic. Both of these polymers are semi-crystalline. PEO is also of particular interest in biomedical applications mainly due to its good biocompatibility and low toxicity. The glass transition temperatures of PEO and PLLA are -54 °C and 57 °C, and the melting temperatures are 74 °C and 180 °C, respectively[11]. Blends of PLLA and poly(ethylene oxide)[11,22-24] or poly(ethylene glycol)[25-27] have been described in literature, where their miscibility, compatibility and mechanical properties are focused on. In these cases, the blend preparation was carried out from the mixture of the homopolymers which were dissolved in a common solvent.

It has been verified that PLLA/PEO blends, which were submitted to the degradation process by immersion into a buffer solution, became porous due to the PEO fraction dissolution, while pure PLLA films remained dense. This porous morphology depended on the method employed for the blend preparation. In a previous research, blends were prepared from the casting of a solution containing both PLLA and PEO dissolved homopolymers. In these cases, the pores had a circular shape and their dimension depended on the composition of the blend[28].

A porous morphology can promote film hydration, which plays an important role in the PLLA degradation rate *via* hydrolysis of the ester backbone. The PEO fraction dissolution could also be interesting in cases where soluble drugs in the PEO fraction could be controlled delivered. A porous morphology can also be very desirable in most of biomedical applications. In some cases, the polymeric matrix must present a uniform and interconnected porous structure to allow cell growth to be easily distributed throughout the device. This way, an organized network of the tissue constituents can be formed.

Here, the poly(L-lactic acid)/poly(ethylene oxide) blends, which were prepared by mechanical mixture and fusion of the homopolymers, were investigated. PLLA homopolymer and PLLA/PEO blends were implanted into defects produced in the tibia of rats, in order to investigate blend biocompatibility and its potential application in the manufacturing of devices used for bone repair. The first *in vivo* results obtained for 50/50 (w/w) PLLA/PEO blends after 2 and 4 weeks of implantation, are presented here. The results for longer periods of implantation and for 80/20 and 20/80 PLLA/PEO blends are in progress.

2. Experimental

Blends were prepared by mixing PLLA (Medisorb; MW = 300000 g/mol) and PEO (Aldrich; MW = 200000 g/mol) in a mini injector LMM-2017 Mini Max Molder. Sticks of PLLA and PLLA/PEO of different compositions (80/20, 50/50 and 20/80 w/w) were prepared by the melting of homopolymers at 190 °C, using a 2.0 mm diameter and 9.3 cm high (internal dimensions) mold, which remained at 120 °C during the processing. The heating of the homopolymer mixture was carried out for 1 min followed by 2 min of shearing and mold injection. The mold was cooled at room temperature for 20 min.

In vitro degradation tests were carried out using 80/20, 50/50 and 20/80 PLLA/PEO blends. Samples were immersed in a buffer solution (KH_2PO_4 – NaOH; pH = 7.4) at 37 °C, which was changed all week. Tests were performed during a 2-week period. These conditions have often been referred to in literature as degradation tests[27, 29].

Blends were immersed for different periods (7 or 14 days). After each period, samples were dried at 50 °C until they reached a constant mass, and characterized as described below. The mass loss percentage was calculated comparing the mass values of the samples before and after submitting them to degradation tests. Samples are denoted here as a function of the degradation time. PLLA/PEO t = 0 was used for blends that were not immersed in the buffer solution, and PLLA/PEO t = 7 or t = 14 days was used for blends after the degradation process.

Samples were fractured by immersion into liquid nitrogen. Surface fracture was covered with gold by sputtering and observed in a JEOL JXA 840 scanning electron microscope.

Thermogravimetric analysis was carried out in a TG209 Netzsch thermal analyzer from 25 to 800 °C at 10 °C.min^{-1} under nitrogen.

Differential scanning calorimetry was performed in a DSC200 Netzsch thermal analyzer using the following temperature program: rapid cooling from 25 to -100 °C; heating from -100 to 200 °C at 10 °C.min^{-1}; isotherm at 200 °C for 5 min; cooling from 200 to -100 °C at

10 °C.min^{-1}; isotherm at -100 °C for 5 min; heating from -100 to 200 °C at 10 °C.min^{-1}. Samples were analyzed under nitrogen.

Dynamic-mechanical analysis was performed in a 409 DMA Netzsch thermomechanical analyzer from -100 to 230 °C, under air, using the following conditions: duo cantilever mode, force = 1N, amplitude = 15 μm and frequency = 1 Hz.

In vivo tests were carried out following a standard method described in reference 30. Fifty-two male Wistar rats (200 - 250 g) were used in the study. Prior to surgery, the animals were anaesthetized with a solution of Ketamine plus Xylazine administered by an intramuscular injection using a dose of 1.5 mL per kg of body weight. After the asepsis of the site, a longitudinal incision in the skin, approximately 1 cm long, parallel to the tibia, was carried out. The muscular tissue was parted and moved away until the periosteum appeared. With a low rotation mini motor and a 3.0 mm diameter drill, sockets were produced in the tibia in order to allow the introduction of the test bodies in the shape of a 2 mm diameter and 2 mm long toggle. This procedure was carried out in the legs of all animals, which were divided into the following groups: the PLLA/PVC group: 20 animals received PLLA in the tibia of their left leg, and poly(vinyl chloride) PVC in the tibia of their right leg as a control. The BLEND/PVC group: 20 animals received the 50/50 PLLA/PEO blend in the tibia of their left leg and poly(vinyl chloride) PVC in the tibia of their right leg as a control. The CONTROL group: 12 animals were submitted to surgery for the insertion of a socket in the tibia of the left leg, in which test bodies were not implanted.

Immediately after the insertion of the sockets and/or rank of the test bodies, the muscular tissue was sutured.

During all this process, the area was continuously irrigated with a physiological solution, so the heating of the tissue did not occur. After the skin suture, the surface was washed with an anti-septic solution. During the post-surgical periods the animals received doses of an analgesic diluted in water in a dose 2.5 mL/L, supplied for 2 days after the surgery. The animals remained lodged in river steamers in groups of 3 animals for each streamer, with burst light and ventilation, with solid ration and water supply without restriction.

After 2, 4, 8 and 16 post-surgical weeks, the animals were killed by an intraabdominal injection with an overdose of 10% Chloral Hydrate solution, after which specimens of the tissue were removed. Immediately, the bone specimens were fixed in a 10% formal solution at room temperature, for 48 h. Decalcified sections were made and stained with hematoxylin and eosin (HE) for histological observations under a light microscope.

Test bodies of PVC (Aldrich) were prepared from the casting of a 5wt% polymer/THF solution. Thick films (2 mm of thickness) were cut in a 2 mm diameter disk shape.

3. Results and Discussion

Table 1 shows the mass loss percentage for PLLA/PEO blends occurred during the period of 14 days of *in vitro* degradation. The highest mass loss percentage occurred during the first week of the *in vitro* degradation. This process is related to the water diffusion in the blend followed by the dissolution of the PEO fraction. Since the PLLA fraction presents a low degradation rate, mass loss practically did not change during the period from 7 to 14 days of degradation.

Figure 1 shows the surface fracture of PLLA/PEO blends of different compositions observed by scanning electron microscopy as a function of the degradation time. For samples which were not immersed into the buffer solution (t = 0), the occurrence of phase separation was not clear. Contrary to 80/20 PLLA/PEO which presented a dense morphology, pores with a circular shape and different dimensions (near 1 to 10 μm), could be observed for blends containing higher PEO contents.

After a period in a buffer, all the channels could be observed. The morphology of the blends (t = 7days) was similar to that shown for blends (t = 14 days). For 80/20 PLLA/PEO blends channels with holes in them are distributed in a dense structure, while for 20/80 PLLA/PEO blends, the channels are distributed into a more porous structure. For 50/50 PLLA/PEO blends, an intermediate situation was verified, where the dense structure became cracked and surrounded by channels with holes in them.

Figure 2a shows the thermal analysis measurements for pure PLLA, pure PEO and PLLA/PEO blends (t = 0). For blends two main thermal degradation processes were observed. The first one was due to the PLLA, and the second one to the PEO thermal degradation processes, respectively. After the immersion in the buffer, one main mass loss stage was observed for 80/20 and 50/50 PLLA/PEO blends, Fig. 2b. Considering that the PEO fraction is extracted during the *in vitro* degradation tests, this mass loss stage was due to the thermal degradation process of the

Table 1. Mass loss percentage obtained from the *in vitro* degradation tests for PLLA/PEO blends of different compositions as a function of the period of immersion in the buffer.

PLLA/PEO	Mass loss percentage (%)	
	t = 7 days	t = 14 days
80/20	18.7	19.9
50/50	47.0	46.0
20/80	71.0	80.2

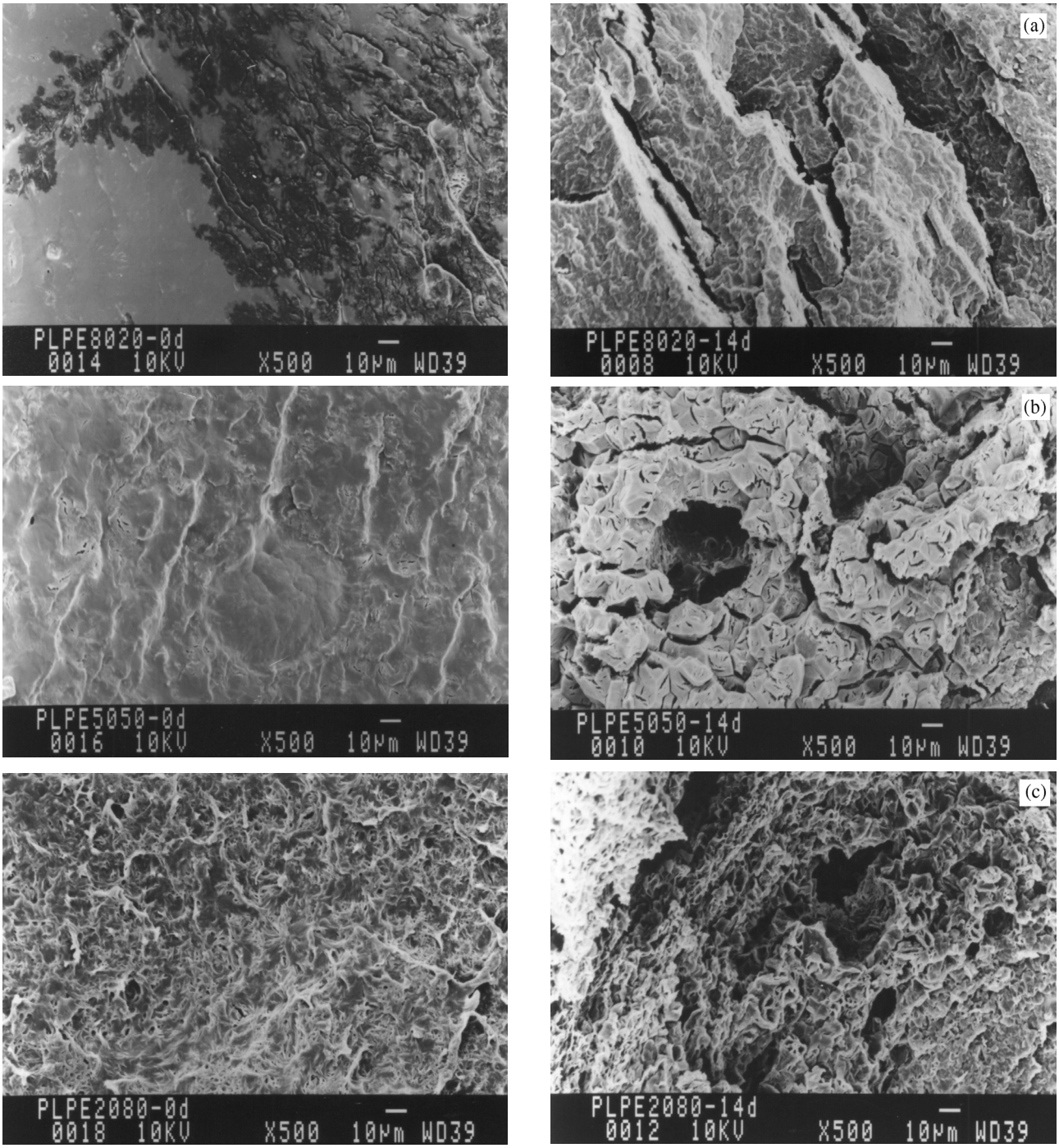

Figure 1. Scanning electron microscopy of (a) 80/20, (b) 50/50 and (c) 20/80 PLLA/PEO blends t = 0 (left hand side) and t = 14 days (right hand side).

PLLA fraction. For 20/80 PLLA/PEO blends (t = 7 or t =14 days) a second mass loss stage near 400 °C was also observed. Although the *in vitro* degradation tests and differential scanning calorimetry had indicated that PEO is absent after 14 days of immersion in a buffer, this second mass loss process could be assigned to one PEO fraction, which had not yet dissolved.

Table 2 shows T_{onsed} values as a function of the blend composition and the immersion time. T_{onset} represents the temperature where the main thermal degradation stage starts. For blends, T_{onset}, after the immersion in the buffer, was lower than that observed for blends t = 0, except for the 80/20 PLLA/PEO composition, indicating that the incorporation of PEO in the PLLA and its posterior extraction, may favor the thermal degradation of PLLA. In all

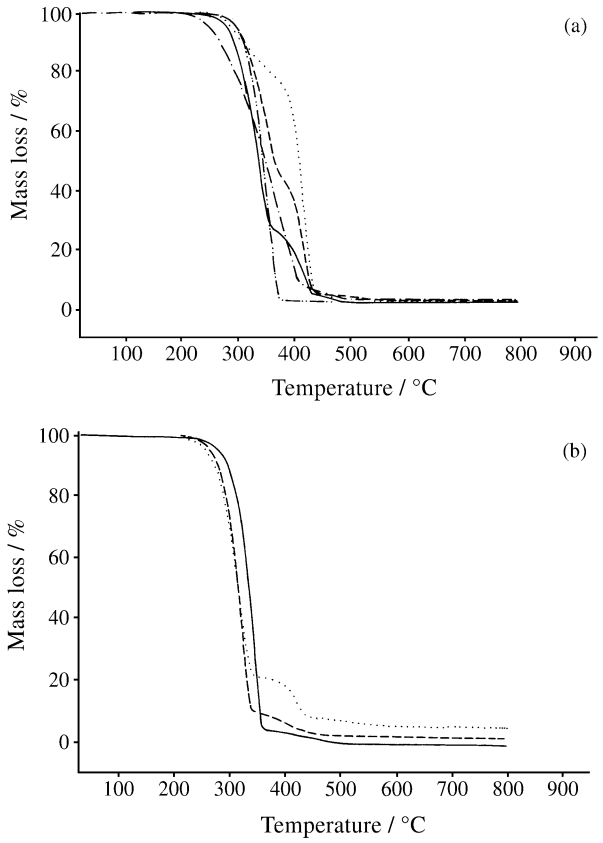

Figure 2. (a) Thermogravimetric curves of (-..-..-) pure PLLA, (-.-.-) pure PEO, (–) 80/20, (- - -) 50/50 and (. . . .) 20/80 PLLA/PEO blends (t = 0). (b) Thermogravimetric curves of (–) 80/20, (- - -) 50/50 and (. . . .) 20/80 PLLA/PEO blends (t = 14 days).

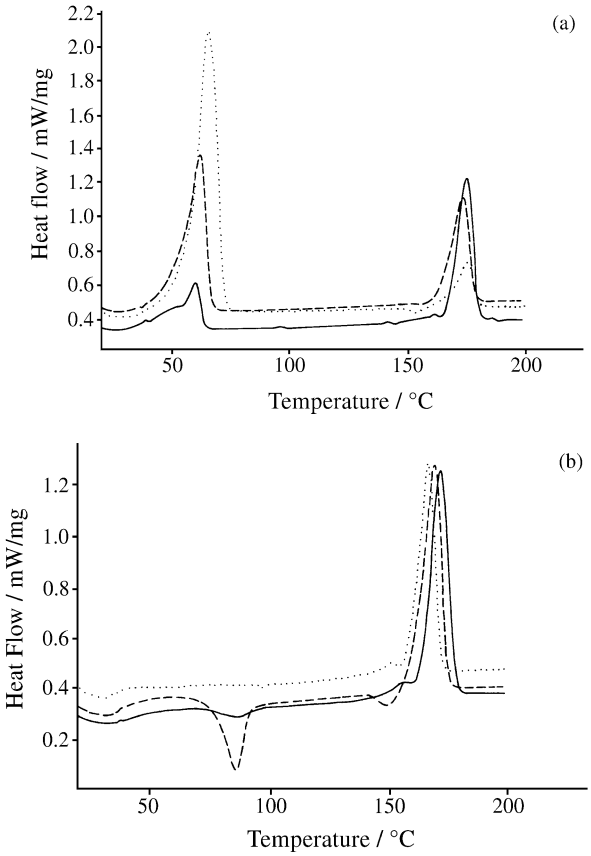

Figure 3. (a) Differential scanning calorimetry curves of (–) 80/20, (- - -) 50/50 and (. . . .) 20/80 PLLA/PEO blends (t = 0). Second heating. (b) Differential scanning calorimetry curves of (–) 80/20, (- - -) 50/50 and (. . . .) 20/80 PLLA/PEO blends (t = 7 days). Second heating.

cases, the residue percentage at 800 °C was lower than 5%.

For differential scanning calorimetry, the results obtained from the second heating, have been shown. Figure 3 shows the curves for PLLA/PEO blends t = 0 and t = 7. For pure PLLA a transition near 50 °C was observed, which was assigned to the glass transition temperature, T_g, and the polymer melting which occurred at 174 °C. For pure PEO an endothermic peak at 67 °C was observed and assigned to the polymer melting. The PEO glass transition, which occurred near -55 °C, could not be visualized.

For PLLA/PEO blends, PEO glass transition was also not evident, probably due to the high crystallinity of the sample. Due to the overlapping of the melting endothermic of PEO and the glass transition of PLLA, T_g of PLLA was not determined. So, the T_g method to evaluate miscibility could not be applied to the PLLA/PEO blends. In these cases, the melting temperature (T_m) depression method can be used.

Table 2. T_{onset} values for PLLA/PEO blends of different compositions as a function of the period of immersion in the buffer. In parenthesis, the mass loss percentage associated to the process, is given.

PLLA/PEO	T_{onset} (°C) t = 0		T_{onset} (°C) t = 7 days		T_{onset} (°C) t = 14 days	
	1st Stage	2nd Stage	1st Stage	2nd Stage	1st Stage	2nd Stage
100/0	306	----	----	----	----	----
80/20	302 (85)	400	314	----	294	----
50/50	318 (60)	400	286	----	278	----
20/80	275 (25)	371	274	388 (10)	274	400 (12)
0/100	257	----	----	----	----	----

A composition-dependent melting endotherm usually indicates a miscible blend, whereas a fully phase separated immiscible system will display a constant T_m. Under complete immiscibility conditions, each of the crystallizable components of the mixture will exhibit the T_m of the corresponding pure homopolymer.

Table 3 shows the values of T_m for run 1 (T_{m1}) and run 2 (T_{m2}) of pure PLLA, pure PEO and for the binary mixture with different weight fractions. The melting temperature of PLLA is almost constant for both run 1 and run 2, independently of the blend composition, suggesting that there were no interactions between PLLA and PEO molecules in the mixture as grown from fusion and melt-crystallized samples. For PEO, both T_{m1} and T_{m2} decreased slightly with the increasing PLLA in the mixture, but this change may be due to the morphological effects. PEO seems to be more sensitive to the presence of PLLA chains, while a much smaller influence is exerted by PEO on the crystalline phase of PLLA. This behavior can be related to the different degrees of crystallinity of both polymers, with PEO being more crystalline. Therefore, relatively small PLLA contents will interfere with the PEO crystalline array, causing shifting of the melting temperature. For PLLA, considerable amounts of PEO can blend with the amorphous phase of PLLA, without significantly affecting the crystalline domains.

Table 4 shows the variation of the fusion enthalpy (ΔH_f) of PLLA and PEO, which was correlated with the blend composition, for run 1 and run 2. Independent of the blend composition, ΔH_f values of PEO for run 2 decreased compared with run 1. Crystallization of PLLA is complete before crystallization of PEO commenced, showing that the two polymers crystallize in different and well-separated temperature regime. The crystallization of PEO seems to be severely hampered by PLLA, which may be explained by the fact that the PLLA component has already completely solidified at the temperatures where PEO crystallizes, thus restricting free crystal growth for this polymer.

For PLLA/PEO blends, which were immersed in a buffer, independent of the immersion time or the blend composition, only one endothermic process could be observed. Table 5 shows T_m and ΔH_f values for samples which were immersed in the buffer solution. Comparing with non-immersed samples, T_m values for blends t = 7 or t =14 days were slightly lower than t = 0. In relation to ΔH_f, the values were lower after immersion in a buffer, except for the 80/20 PLLA/PEO blends, where ΔH_f actually increased slightly. It is interesting to note that the variation of ΔH_f was more drastic for the 20/80 PLLA/PEO blends. In this case, immersed samples seemed to be much more amorphous than non-immersed ones. ΔH_f is directly related to the degree of crystallinity. During the immersion of a semi-crystalline polymer in a buffer, if degradation occurs, it is expected that the amorphous fraction degrades before the crystalline one does. So, one would also expect that the crystallinity of the remaining porous matrix, to increase with degradation time, since the amorphous phase was being removed. After this process, the degradation of the crystalline fraction started and consequently a decrease in the degree of crystallinity was expected. The results shown in Table 5 can indicate that, depending on the blend composition, it would be possible to control the degradation rate of the material. Using higher contents of PEO the material seems to be more susceptible to the degradation process.

Figure 4 shows the dynamic-mechanical curves obtained for the homopolymers and PLLA/PEO blends t = 0. For pure PEO one can observe two transitions, which occurred near -10 °C and the other near 100 °C. For pure PLLA two main transitions were observed near 100 °C and 200 °C. In both PEO and PLLA homopolymers, the first

Table 3. Melting temperatures T_{m1} and T_{m2} for run 1 and run 2 of pure PLLA, pure PEO and PLLA in the mixture with PEO. These values correspond to t = 0.

PLLA/PEO	T_{m1} (°C)	T_{m2} (°C)	T_{m1} (°C)*	T_{m2} (°C)*
100/0	173	163	----	----
80/20	179	175	65	59
50/50	179	173	68	61
20/80	178	175	73	64
0/100	----	----	69	66

* Melting temperatures of PEO in the mixture with PLLA.

Table 4. Fusion enthalpy variation values of PLLA and PEO corrected as a function of the blend composition, for run 1 and run 2. These values correspond to t = 0.

PLLA/PEO	ΔH_f of PLLA (J/g)	ΔH_f of PLLA (J/g)*	ΔH_f of PEO (J/g)	ΔH_f of PEO (J/g)*
100/0	65	66	----	----
80/20	54	47	130	103
50/50	71	66	152	125
20/80	76	80	168	142
0/100	----	----	166	160

* ΔH_f values for run 2.

Table 5. Melting temperature and fusion enthalpy variation values (for run 2) for PLLA/PEO blends which were immersed in the buffer for 7 or 14 days.

	t = 7		t = 14	
PLLA/PEO	T_m (°C)	ΔH_f (J/g)	T_m (°C)	ΔH_f (J/g)
80/20	172	50	171	51
50/50	170	52	147	46
20/80	167	39	166	29

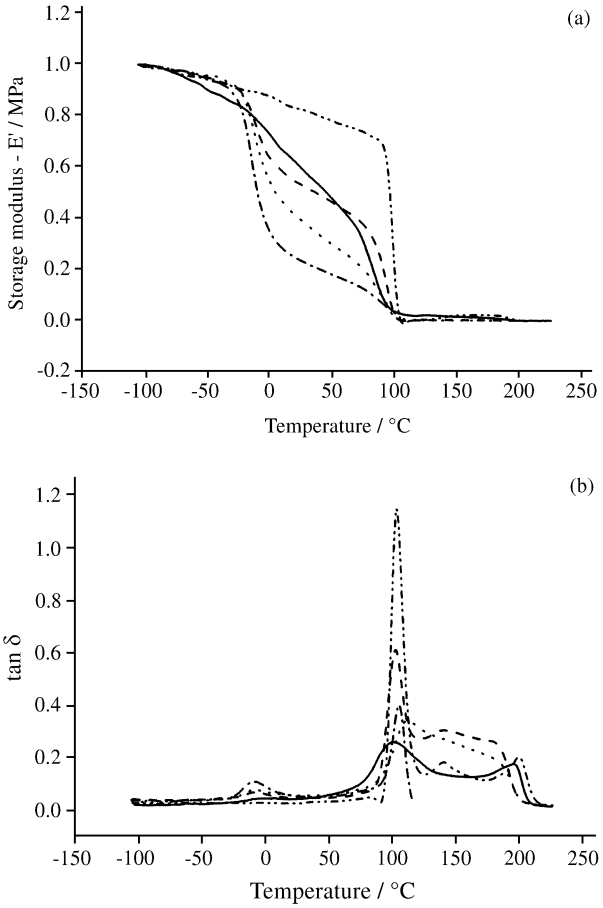

Figure 4. Dynamic-mechanical analysis for (-..-..-) pure PLLA, (-.-.-) pure PEO, (–) 80/20, (- - -) 50/50 and (. . . .) 20/80 PLLA/PEO blends (t = 0). (a) Storage modulus and (b) damping as a function of temperature.

transition could be due to the glass transition and the second one to the melting of the polymer. For blends, the mechanical properties are determined primarily by the mutual solubility of the two homopolymers. If two polymers are completely soluble in one another the properties of the mixture are nearly the same as those of a random copolymer of the same composition. In these cases, the damping peak for the mixture occurred at an intermediate temperature between the glass transition temperatures observed for the homopolymers. If the two polymers in a mixture are insoluble, they exist as two separated phases, and two glass transitions are observed instead of one, as can be seen for PLLA/PEO blends. Two damping peaks were observed, which were very close to those in pure PLLA and pure PEO. These results are in accordance with those obtained from differential scanning calorimetry, which showed that PLLA/PEO is an immiscible system. After immersion in a buffer, samples were far too fragile to allow dynamic-mechanical tests.

From the *in vivo* tests, different bone tissue responses in the presence of the PLLA, PLLA/PEO blend and PVC implants were observed. Figures 5 and 6 show the histological analysis for 2 and 4 week post-implantation periods. The PLLA implants, as well as the PVC, did not allow the proliferation of cells. On the other hand, cell proliferation was observed in animals, which received the PLLA/PEO blend implants. In the PVC implants, as expected, evidence of degradation were not visualized.

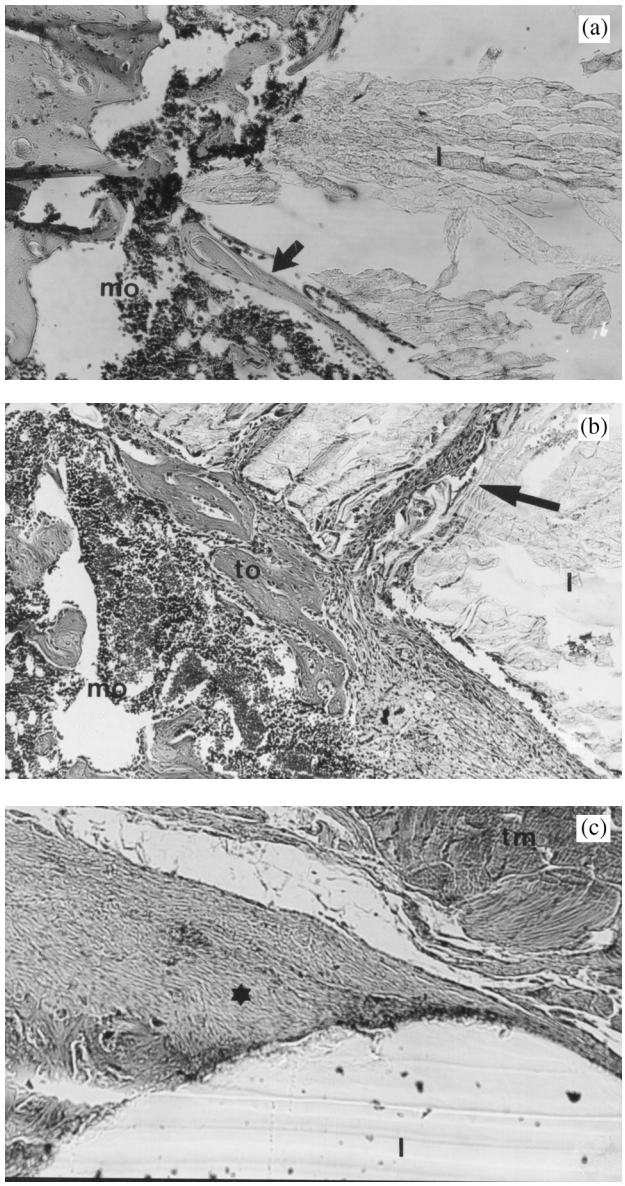

Figure 5. Transversal cut of the tibia with implantation of (a) PLLA, (b) PLLA/PEO blend and (c) PVC after 2 weeks post-surgery. In (a) it is possible to note the presence of bone growth around the implantation (arrow). In (b) cell infiltration into the implant (arrow) can be noted. In (c) it is possible to observe a fibrous tissue (star) in contact with the implant. Implantation (I), bone tissue (to), muscular tissue (tm) and bone marrow (mo). 3.2x10 HE.

For all implants, after 2 and 4 weeks of post-implantation, a bone tissue growth surrounding the implanted material was observed. The neoformed bone presented non-organized fibers. After 4 weeks of implantation, the

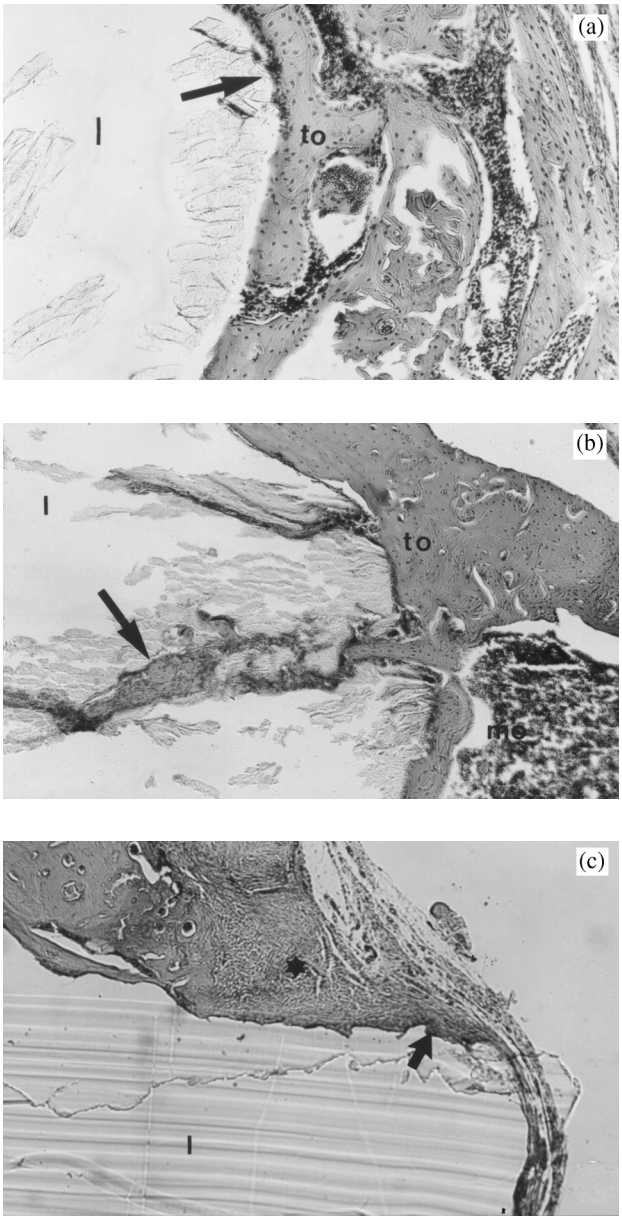

Figure 6. Transversal cut of the tibia with implantation of (a) PLLA, (b) PLLA/PEO blend and (c) PVC after 4 weeks post-surgery. In (a) it is possible to note the cellular proliferation between the bone and the implantation (arrow). In (b), the bone formation on the inside of the implant (arrow) can be noted. In (c), it is possible to observe a fibrous tissue (star) and inflammatory infiltration (arrow). Implantation (I), bone tissue (to) and bone marrow (mo). 3.2x10 HE.

formation of a secondary or mature bone could be visualized.

In the PVC group, it was possible to note the presence of a tissue with a fibrous aspect on the bone defect and also the presence of inflammatory infiltrated components. These components were in contact with the implant and in disperse regions in the collagen fibers for the two experimental periods.

For the PLLA and PLLA/PEO blend implants, the components of the inflammatory infiltration demonstrated low intensity for the first 2 post-surgery weeks, gradually decreasing after 4 weeks post-implantation. In these cases, the fibrous tissue, visualized for PVC, was not observed.

The surgical procedures are under way and a histomorphometric analysis will allow results with statistical significance, to be obtained. However, these preliminary results show that the PLLA/PEO blends were as biocompatible as PLLA, with the advantage of the possible control of the implant degradation rate.

4. Conclusion

PLLA/PEO blends were prepared by the mechanical mixture and fusion of the homopolymers. Differential scanning calorimetry and dynamic-mechanical analysis showed that PLLA/PEO blends are an immiscible system. PLLA/PEO blends after immersion in a buffer had an open morphology. For blends containing higher PLLA contents, channels with holes in them, surrounding dense regions were visualized. By increasing the PEO content, a porous morphology was verified. This porous morphology can allow a cell growth distributed throughout the biomedical devices with the formation of an organized network of the tissue constituents.

In vivo tests are under way, but the preliminary results showed that PLLA/PEO blends were as biocompatible as the PLLA homopolymer, with the advantage of the possibility of a control of the implant degradation rate. These materials presented a set of particular properties allowing their utilization in the manufacture of devices for bone repair.

Acknowledgements

The authors wish to thank FAPESP for the financial support (Proc. 95/9506-4 and 99/11520-6).

References

1. Pistner, H.; Bendix, D.R.; Mühling, J.; Reuther, J.F. *Biomaterials*, v. 14, p. 291, 1993.
2. Engelberg, I.; Kohn, J. *Biomaterials*, v. 12, p. 292, 1991.
3. Amecke, B.; Bendix, D.; Entenmann, G. *Clin. Mater.*, v. 10, p. 47, 1992.
4. Davis, M.W.; Vacanti, J.P. *Biomaterials*, v. 17, p. 365, 1996.
5. Park, T.G.; Cohen, S.; Langer, R. *Macromolecules*, v. 25, p. 116, 1992.
6. Bergsma, J.E.; de Bruijn, W.C; Rozema, F.R.; Bos, R.R.M.; Boering, G. *Biomaterials*, v. 16, p. 25, 1995.
7. Pistner, H.; Stallforth, H.; Gutwald, R.; Mühling, J.; Reuther, J.; Michel, C.. *Biomaterials*, v. 15, p. 439, 1994.

8. Mainil-Varlet, P.; Rahn, B.; Gogolewski, S. *Biomaterials*, v. 18, p. 257, 1997.
9. Mainil-Varlet, P.; Gogolewski, S.; Nieuwenhuis, P. *J. of Mater. Sci.: Mater. in Med.*, v. 7, p. 713, 1996.
10. Bos, R.R.M.; Rozema, F.R.; Boering, G. *J. Oral Maxillofac. Surg.*, v. 45, p. 751, 1987.
11. Nijenhuis, A.J.; Colstee, E.; Grijpma, D.W.; Pennings, A.J. *Polymer*, v. 37, p. 5849, 1996.
12. Penning, J.P.; Manley, R.St.J. *Macromolecules*, v. 29, p. 77, 1996.
13. Eshuis, A.; Roerdink, E.; Challa, G. *Polymer*, v. 23, p. 735, 1982.
14. Avella, M.; Martucelli, H. *Polymer*, v. 29, p.1731, 1988.
15. Edie, S.L.; Marand, H. *Polym. Prep.(Am. Chem. Soc., Div. Polym. Chem.)*, v. 32, p. 329, 1991.
16. Jonza, J.M.; Porter, R.S. *Macromolecules*, v. 19, p. 1946, 1986.
17. Cheung, Y.W.; Stein, R.S. *Macromolecules*, v. 27, p. 2512, 1994.
18. Cheung, Y.W.; Stein, R.S.; Lin, J.S.; Wignall, G.D. *Macromolecules*, v. 27, p. 2520, 1994.
19. Penning, J.P.; Manley, R.St.J. *Macromolecules*, v. 29, p. 84, 1996.
20. Fujita, K.; Kyu, T. *Macromolecules*, v. 29, p. 91, 1996.
21. Meikle, M.C.; Papaioannou, S.; Ratledge, T.J. *Biomaterials*, v. 15, p. 513, 1994.
22. Nakafuku, C. *Polymer Journal*, v. 26, p. 680, 1994.
23. Nakafuku, C. *Polymer Journal*, v. 28, p. 568, 1996.
24. Nakafuku, C.; Sakoda, M. *Polymer Journal*, v. 25, p. 909, 1993.
25. Younes, H.; Cohn, D. *Eur. Polym. J.*, v. 24, p. 765, 1988.
26. Yang, J.-M.; Chen, H.-L.; Hwang, J.C. *Polymer Journal*, v. 29, p. 657, 1997.
27. Sheth, M.; Kumar, R.A.; Davé, V.; Gross, R.A.; McCarthy, S.P. *Journal of Applied Polymer Science*, v. 66, p. 1495, 1997.
28. Zoppi, R.A.; Contant, S.; Duek, E.A.R.; Nunes, S.P., submitted.
29. Lam, K.L.; Nieuwenhuis, P.; Molenaar, I.; Esselbrugge, H.; Feijen, J.; Dijkstra, P.J.; Schakenraad, J.M. *J. Mater. Sci.: Mater. in Med.*, v. 5, p. 181, 1994.
30. *Standard practice for assessment of compatibility of biomaterials for surgical implants with respect to effect of materials on muscle and bone*, Annual Book of ASTM Standards, F 981-93, ASTM, 1973.

FAPESP helped in meeting the publication costs of this article