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PLLA Based Composites with α-Tricalcium Phosphate and a PLLA-PEO Diblock Copolymer

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Summary: Hybrid composites consisting of poly(L-lactide), PLLA, or blends of PLLA with a PLLA-poly(ethylene oxide) diblock copolymer (15–30 wt%), COP, as a biodegradable polymeric matrix and of bioactive α-tricalcium phosphate, α-TCP, microparticles as dispersed phase (25–40 wt-%) were prepared by melt extrusion and their thermal, mechanical and degradation behaviour was investigated. SEM analysis of surfaces broken in liquid N_2 showed a good dispersion of α-TCP in the polymer matrix. A lowering of the glass transition temperature of the polymer matrix and enhanced crystallization rates of PLLA, both from the melt and from the glassy state, were observed in the presence of COP. Ternary PLLA/COP/α-TCP composites containing about 10 wt-% of COP and 25–40 wt-% of α-TCP showed improved compressive strength and deformation at yield as compared to pure PLLA. Degradation experiments revealed that in simulated body fluid the presence of α-TCP particles promoted the formation of inorganic deposits of a poor crystalline apatitic phase on composite surfaces as compact sferoids.

Keywords: compression mechanical properties; diblock copolymers; poly(L-lactic acid); thermal properties; tricalcium phosphate

Introduction

Bioceramics, such as calcium phosphates, and synthetic biodegradable polymers, such as poly(hydroxyacids) (PHA), have been proposed as biomaterials for applications in hard tissue replacement and in bone-tissue engineering. Tricalcium phosphate, α-$Ca_3(PO_4)_2$ (α-TCP), is one of the main components of several bone cements.[1] α-TCP displays a greater solubility than hydroxyapatite, and in aqueous solution it undergoes hydrolytic scission through a mechanism that implies dissolution and successive precipitation of a more stable phase. The products of hydrolysis are dicalcium phosphate dihydrate ($CaHPO_4 \cdot 2H_2O$; DCPD), octacalcium phosphate ($Ca_8H_2(PO_4)_6 \cdot 5H_2O$; OCP), or apatite, depending on the experimental conditions.[2,3] Composites made of bioceramic microparticles dispersed in a polymeric matrix may combine the bioactivity of α-TCP with the mechanical properties and processability of PHAs to meet the physiological and mechanical characteristics of bone.[4] Poly(L-lactide) (PLLA) is a stiff, semi-crystalline, bioresorbable and biocompatible PHA, widely investigated for orthopaedic application, which undergo hydrolytic scission to lactic acid when implanted in the body. Blends of PLLA and more flexible biocompatible polymers have been proposed with the aim to improve the resilience of PLLA.[5–7] Recently, the use of polymer blends in polymer/ceramic composites has been investigated

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with the aim to better control the mechanical properties and the degradation rate of the biomaterial.[8] In this work we report some preliminary results on the preparation and characterization of biodegradable hybrid composites where the polymer matrix consists of PLLA or PLLA/PLLA-poly(oxyethylene) diblock copolymer blends (PLLA/COP) and α-TCP is the inorganic bioactive filler.

Experimental

Materials and Preparation of Composites

α-TCP was obtained by solid state reaction of a mixture of $CaCO_3$ and $CaHPO_4 \cdot 2H_2O$ in the molar ratio of 1:2 at 1300 °C for 5 hours. The solid product was ground and sieved through a 400-mesh sieve (38 μm). The specific surface area, evaluated by BET method using a Carlo Erba Sorpty 1750, was 1 $m^2 \cdot g^{-1}$. PLLA (Biomer) had $M_n =$ 60 kDa. A $PLLA_{21000}$-PEO_{5000} di-block copolymer was prepared by ring opening polymerisation at 130 °C for 24 h of purified and dried L-lactide (Aldrich), 12.8 g, initiated by methoxy-poly(ethylene glycol) ($M_n = 5$ kDa), 3.2 g, and catalysed by Sn(ethylhexanoate)$_2$, 48 mg. The copolymer was purified by dissolution in $CHCl_3$ and precipitation in cold methanol (87% yield). The composition was determined by ^{1}H-NMR spectroscopy comparing the peak area of PEO methylene hydrogens at 3.6–3.7 δ with that of PLLA methine hydrogens at 5.16 δ The polymeric components were dried and stored under dry nitrogen. Polymer blends and polymer/α-TCP composites were prepared by mixing the components (4.5–5.0 g) in a co-rotating twin-screw mini-extruder at 200 °C and 50 rpm for 5 min.

Techniques

Degradation was investigated after soaking at 37 °C 3 mm thick discs obtained by compression moulding at 200 °C for different periods of time in simulated body fluid (SBF) or, alternatively, in physiological solution (0.9% NaCl). X-ray diffraction analysis was carried out by means of a Philips PW 1050/81-powder diffractometer equipped with a graphite monochromator in the diffracted beam. CuKα radiation was used (40 mA, 40 kV). The 2θ range was from 3 to 60° at a scanning speed of 0.75°/minute. Morphological investigation was performed using a Philips XL-20 Scanning Electron Microscope. The samples were sputter-coated with gold prior to examination. ^{1}H-NMR spectra (400 MHz) were recorded at 25 °C on a Brucker DRX 400 spectrometer using $CDCl_3$ as a solvent. Differential scanning calorimetric (DSC) analysis was performed on a Mettler DSC 30 calorimeter under nitrogen at a 20 °C · min^{-1} rate from −100 °C to 200 °C. Second heating runs were performed after a quenching step from the melt to −100 °C. The compression mechanical tests were performed on cylindrical specimens (h = 10 mm, d = 13 mm) obtained by compression moulding at 200 °C using an Instron 4505 dynamometer with a 1 mm · min^{-1} deformation rate. The thermogravimetric analysis, TGA, was carried out on a Mettler TGA-SDTA 851 instrument from 25 °C to 600 °C under a N_2 flow at a 20 °C · min^{-1} rate. The spherulitic growth was observed at 120 °C on melted samples using a Axioscope-Zeiss optical microscope equipped with a THMS 600 hot-stage and a Linkam TMS 91 temperature programmer.

Results and Discussion

X-ray diffraction pattern and SEM micrographs of prepared α-TCP powders showed that they are constituted of α-TCP as sole crystalline phase and that the particles display an average size of 5–7 μm. PLLA/COP/α-TCP composites were obtained by high efficiency melt mixing of PLLA at 200 °C with variable amounts of α-TCP microparticles and of a $PLLA_{21000}$-PEO_{5000} diblock copolymer. PLLA/COP blends and PLLA/α-TCP binary composites were also prepared in the same conditions and investigated in order to shed some light on the effect that COP and α-TCP individually have on the properties of the PLLA matrix.

Table 1.
Composition of blends and composites.

Code	PLLA (wt%)	COP (wt%)	α-TCP (wt%)
C-15	85	15	0
C-30	70	30	0
T-27	73	0	27
T-40	60	0	40
CT-11/26	63	11	26
CT-22/24	54	22	24
CT-9/40	51	9	40
CT-18/39	43	18	39

Thermogravimetric analysis of the extruded specimens under N_2 atmosphere showed that the onset of thermal degradation of the polymeric components was in the range of 300–330°, at least 100 °C higher than the mixing temperature. The degradation temperature T_d of pure PLLA, 330 °C, was unaffected in the presence of the inorganic filler, while T_d values of 300–315 °C were observed in the case of blends and composites containing the COP, reasonably because of the lower thermal stability of oxyethylene units. As the organic components are fully degraded at 600°, the residual mass at this temperature was used to calculate the actual content of TCP in the composite. The code and the composition of the investigated materials are reported in Table 1, where the C and T codes refer to binary PLLA/COP blends and PLLA/α-TCP composites, respectively, and the CT code refers to ternary PLLA/α-TCP/COP composites.

SEM analysis was performed on the surface of samples broken in liquid nitrogen. PLLA and C-15 samples showed a rather brittle fracture behaviour, while C-30 exhibits fracture surfaces characteristic of a more ductile system. α-TCP containing materials generally showed a fine dispersion of the mineral filler embedded in the polymeric matrix as shown for the T-40 and CT-9/40 blends in Figure 1. The thermal behaviour was investigated by DSC. The melting temperature and enthalpy of PLLA were scarcely affected by the presence of COP or α-TCP. Evidence of a crystalline PEO phase was not found in DSC thermograms, as well as in the X-ray diffraction diagrams of both C blends and COP containing CT composites.

The results of DSC and optical microscopy investigations on polymer blends and composites are summarized in Table 2 together with those obtained on extruded PLLA and COP samples. Single glass transition temperatures, T_g, were observed for PLLA/COP blends at 55 °C (C-15) and 50 °C (C-30) suggesting a partial miscibility of the amorphous phases of PLLA ($T_g = 62$ °C) and PEO ($T_g \approx -60$ °C), in agreement with previous findings on multicomponent PLLA/PEO systems.[9] It is worth to note that also the copolymer exhibits a single T_g at 31 °C. This effect was retained in the presence of the mineral component, α-TCP. As a consequence of the increased chain flexibility of amorphous PLLA in the presence of the COP, the cold

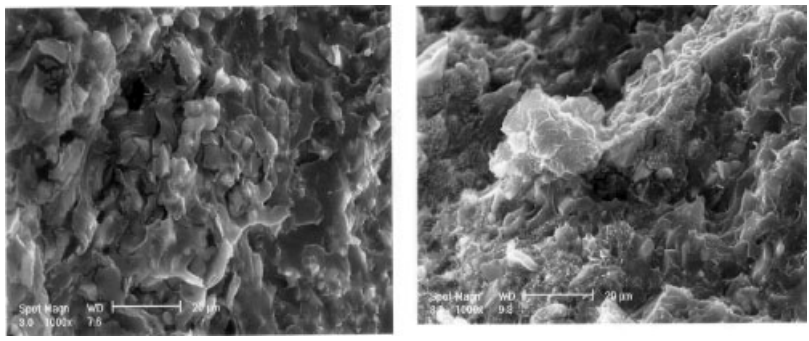

Figure 1.
SEM micrographs of surfaces fractured in liquid N2 of T-40 (left) and CT-9/40 (right) composites.

Table 2.
Thermal properties of PLLA, COP, C blends, T and CT composites and spherulitic growth rate G of PLLA, COP and their blends.

Code	T_g [a] (°C)	T_c [a] (°C)	T_m [a] (°C)	ΔH_m [a] (J · g^{-1})	G (μm · min^{-1})
PLLA	62	116	168	29	2.82
COP	31	71	168	44	24.45
C-15	54	99	166	34	6.99
C-30	50	98	166	28	6.35
T-27	62	121	170	34	–
T-40	62	122	167	37	–
CT-11/26	55	107	168	32	–
CT-22/24	51	93	165	32	–
CT-9/40	55	109	166	32	–
CT-18/39	54	100	169	44	–

[a] Obtained in a second heating scan after melt quenching.

crystallization temperature of PLLA in PPLLA/COP blends and in ternary CT composites was lowered down to 98–99 °C and 93–109 °C, respectively, as compared to pure PLLA (116 °C) and binary T composites (121–122 °C). The crystallization behaviour of CT composites is mainly controlled by the PLLA/COP weight ratio. Optical microscopy investigations on the crystallization of PLLA/COP blends from the melt at 120 °C showed that the radial growth rate of spherulites is enhanced as compared to pure PLLA. The copolymer itself showed a rate one order of magnitude higher than pure PLLA. As separated PEO microphases were not evidenced in the spherulites or in the intra-spherulitic regions of PLLA blends or of COP (see Figure 2), it is likely that PEO chains are mainly located in the interlamellar regions.

The compression mechanical properties of the investigated materials are reported in Table 3. The moduli of both C blends and T or CT composites were slightly lower than that of PLLA, decreasing, as general trend, with increasing the amount of COP and α-TCP. This finding may be ascribed to the higher chain flexibility and lower MW of COP with respect to PLLA, in the case of C blends, and to a high interfacial energy between α-TCP microparticles and PLLA matrix in T and CT composites. The rigidity of materials with lower amounts of α-TCP and COP, such as C-15, T-27 and CT-11/26 is, however, quite close to that of PLLA, within experimental errors. On the other hand, the deformation at yield, ε_y, increased significantly in the presence of α-TCP, indicating a more ductile behaviour of composites with respect to PLLA. The high compression strength of pure PLLA decreased, as expected, upon addition of the COP in the C blends, while it was not only retained, but even increased in the composites as evidenced in Table 3.

As a matter of fact, the strength and deformation at yield in ternary CT composites increased regularly with decreasing the weigh ratio COP/α-TCP, the lowest values being observed for CT-22/24.

The degradation behaviour was investigated at 37 °C both in SBF and in physiological solution on 3 mm thick discs obtained by compression moulding. Significant weight loss (≥2%) were not observed over a 3 month period, in agreement with bulk degradation data reported for PLLA.[10] The X-ray patterns

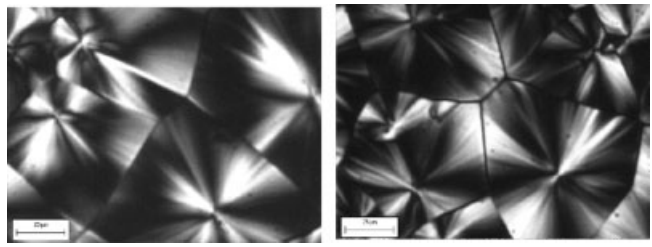

Figure 2.
Optical micrographs of spherulites obtained by crystallization at 120 °C of the C-30 blend (left) and of the PLLA-PEO copolymer (right).

Table 3.
Compressive modulus (E_c), strength at yield (S_y) and deformation at yield (ε_y) of PLLA, C blends and T or TC composites.

Code	E_c (GPa) ± 0.2	S_y (MPa) ± 5	ε_y (%) ± 0.2
PLLA	2.9	61	2.6
C-15	2.7	50	2.4
C-30	2.4	44	2.5
T-27	2.8	87	4.4
T-40	2.3	88	5.9
CT-11/26	2.8	80	3.8
CT-22/24	2.5	61	3.3
CT-9/40	2.6	90	6.0
CT-18/39	2.1	81	5.4

recorded from the samples before degradation showed the diffraction peaks characteristic of the crystalline α-phase of PLLA at 16.8° and 19.2° of 2θ together with those characteristic of α-TCP (in the samples containing the inorganic phase). After different periods of soaking in SBF, the appearance of a broad diffraction maximum around 30° of 2θ, superimposed to those recorded from the same samples before immersion in solution, was observed in the X-ray patterns. At 14 weeks, the patterns showed just the broad maximum and a further peak at about 25.9° of 2θ, in agreement with the presence of a poor crystalline apatitic phase deposited from the SBF solution. The SEM images allowed to appreciate the presence of inorganic deposits on the surface of the samples after just 6 weeks of interaction with SBF. The deposits are laid down as compact spheroids, with the typical morphology of the material deposited from SBF. Their relative amount is quite small in the samples that do not contain α-TCP, and it increases with increasing α-TCP content.

At variance, no inorganic deposition can be appreciated in the SEM micrographs of the samples submitted to immersion in physiological solution (0.9% NaCl) for increasing periods of time. In particular, the images of the samples not containing α-TCP are quite similar to those recorded before immersion in NaCl solution. The fracture surface of the samples containing α-TCP show inorganic crystals immersed into the polymeric matrix, as before immersion, but a few of the crystals display a porous structure suggesting some modification of the α-TCP phase. Examples of such structures are displayed in Figure 4.

As a matter of fact, the X-ray diffraction patterns of these samples indicate a partial conversion of α-TCP into hydroxyapatite as it can be appreciated in Figure 5 where the full triangles indicate the most intense peaks of α-TCP and the void triangles the most intense peaks of hydroxyapatite.

The relative intensities of the diffraction peaks indicate that the relative amount of conversion of α-TCP into HA increases with the increase of α-TCP content of the blends.

Conclusions

Hybrid composites obtained by melt extrusion of a blend of PLLA and a PLLA-PEO copolymer with α-TCP exhibit a homogeneous matrix-dispersed phase morphology. The presence of the COP influences

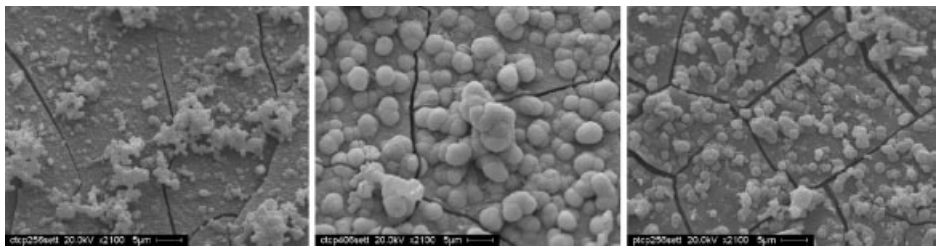

Figure 3.
SEM micrographs of surfaces of CT-11/26 (left), CT-9/40 (middle) and T-27 (right) samples after 6 weeks of soaking in SBF at 37 °C.

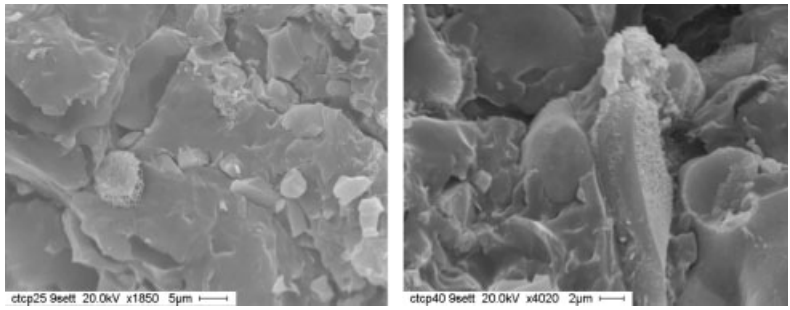

Figure 4.
SEM micrographs of fracture surfaces of CT-11/26 (left) and CT-9/40 (right) composites after 9 weeks immersion in a 0.9% NaCl solution.

the thermal properties of the polymeric matrix inducing a lowering of the T_g and enhancing the crystallization rates of PLLA both from the glassy state and from the melt. High contents of COP in C blends or of α-TCP in binary CT composites adversely affect the compression modulus of such materials while increasing the strength and deformation at yield in the case of CT composites. Ternary PLLA/COP/α-TCP composites containing as much as 10% of COP represent the best compromise between the need of a good yield properties and the maintenance of a sufficient rigidity of the material. Short term degradation behaviour of PLLA

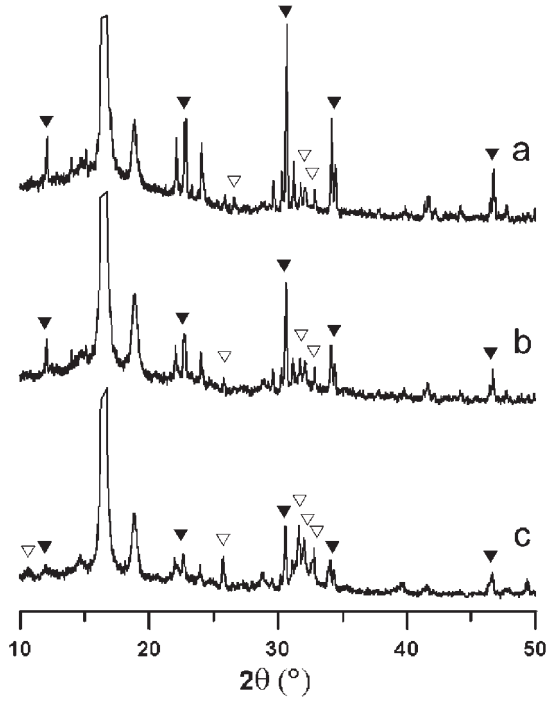

Figure 5.
X-ray diffraction patterns of surfaces of T-27 (a), CT-11/26 (b) and CT-9/40 composites after 9 weeks immersion in 0.9% NaCl solution.

matrix is scarcely affected by the presence of the hydrophilic PEO segments in the COP, while embedding of α-TCP into the composites delays its hydrolysis into apatite. The presence of α-TCP promotes the formation of bone-like apatitic deposits from SBF solution.

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