Tougher biodegradable polylactide system for bone fracture fixations: Miscibility study, phase morphology and mechanical properties

J.M. Ugartemendia\textsuperscript{a,b,⁎}, A. Larrañaga\textsuperscript{a,b}, H. Amestoy\textsuperscript{a,b}, A. Etxeberria\textsuperscript{c}, J.R. Sarasua\textsuperscript{a,b}

\textsuperscript{a} University of the Basque Country (UPV-EHU) Department of Mining-Metallurgy Engineering and Materials Science, School of Engineering, Alameda Urquijo s/n, 48013 Bilbao, Spain
\textsuperscript{b} Basque Excellence Research Center in Macromolecular Design & Engineering, POLYMAT, P. Manuel de Lardizabal 3, 20009 Donostia-San Sebastián, Spain
\textsuperscript{c} Department of Polymer Science and Technology, Institute of Polymer Materials, University of Basque Country (UPV/EHU), M. de Lardizabal, 3, 20018 Donostia, Spain

ARTICLE INFO

Keywords:
Poly-L-Lactide
Poly(L-lactide-co-ɛ-caprolactone)
Polymer blends
Miscibility
Toughening
Fracture fixation implants

ABSTRACT

Choosing materials for orthopedic implants often imposes strict requirements for the mechanical properties. Poly-L-lactide (PLLA) is widely employed for this purpose, however toughening schemes are necessary for its suitable application. Blending of PLLA and biodegradable poly(L-lactide-co-ɛ-caprolactone) copolymer (PLCL) showing a thermoplastic-elastomeric behavior has been performed in an effort to toughen the PLLA without compromising its biodegradability and biocompatibility. The miscibility state of PLLA/PLCL blend system is studied by means of Differential Scanning Calorimetry (DSC) and Dynamic Mechanical Analysis (DMA). The mechanical properties will be also discussed, as well as, phase morphology observed by Scanning Electron Microscopy (SEM).

Blends of PLLA/PLCL show different miscibility degrees depending on the blending process and the copolymer content. Blends prepared by melt-quenching show a miscibility window for compositions \(\leq 30\) wt\% of PLCL, while a phase separation occurred in the rest of compositions. The toughness of PLLA was considerably improved by the addition of PLCL. The elongation at break was significantly increased.

1. Introduction

In the past decade new researches have further expanded the feasibility of bioresorbable polymeric fixation, eventually leading to clinical application as devices. Choosing materials for orthopedic implants usually focuses on the material and structural properties of the bone or skeletal defect to be replaced which often imposes strict requirements for the mechanical properties. Usually high mechanical strength and stiffness are extremely important in designing biodegradable devices, such as, screws, plates or pins, for bone fracture fixation (osteosynthesis procedures).

In this sense, poly(L-lactide) (PLLA) and its composites have been reported to be suitable for designing bone fracture fixations [1–10]. PLLA is a semicrystalline biodegradable thermoplastic polymer with a glass transition temperature (\(T_{g}\)) ~ 60 °C and melting temperature (\(T_{m}\)) ~ 180 °C that it is obtained by ring opening polymerization (ROP) of \(L\)-lactide. Despite the fact that PLLA shows suitable elastic modulus and mechanical strength comparable to poly(ethylene terephthalate) (PET) [11], its inherent brittleness when processed using standard processing conditions [12], limits its use in the above mentioned applications. The impact strength of PLLA has been reported to be on par with poly-styrene (26 J m\(^{-1}\)) [13], another relatively brittle polymer.

From a clinical point of view, a ductile mode of deformation is desirable, since a brittle breakage of an implant before union of a fracture results in bone redisplacement and loose of material fragments, which might cause irritation or some adverse reaction [14–16]. Therefore, in order for PLLA to be suitable for applications where mechanical toughness is required, toughening schemes and improved composites or blends are needed. This strategy will improve the functionality and reliability of PLLA based implants, and in turn leading to more stable surgical processes.

Many strategies have been developed to alter the properties of a polymer. The chemical synthesis of copolymers is an interesting method in order to design new polymers with special properties. However, this method is generally more expensive, as well as, less-industrial-practiced method than the blending operation. A proper selection and combination of polymeric components in a certain ratio might result in a blend material with optimal properties for a specific application. Numerous attempts have been made to toughen polylactides trough blending with different commercial thermoplastics and rubbers [17–21]. Nonetheless,
for biomedical applications biocompatible and/or biodegradable polymers have to be used. Although several works has been published regarding the use of various biodegradable polyurethanes as the dispersed phase [12,22–23], one of the most studied polymer blends of polylactide (PLA) are those containing polycaprolactone (PCL). In spite of the rubbery characteristics shown by PCL (with an elongation at break of approximately 600%) make it an ideal counterpart for toughening polylactide, it is known that this immiscible binary blend generally leads to insignificant improvements in mechanical properties [12,24–28]. As an alternative, this work focuses on improving the toughness of PLLA by blending it with a biodegradable and bioreusable poly(L-lactide-co-ε-caprolactone) copolymer (PLCL). In this work a PLCL copolymer with a molar composition of approximately 70% L-lactide and 30% of ε-caprolactone has been employed. It is an amorphous polymer with a Tg of ∼24 °C and presents a thermoplastic-elasticomer character, i.e., elastomeric behavior, high elongation at break and high elastic recovery capacity. Moreover, in general, PLCLs offer better thermal stability during processing as well as a suitable toughness for being used as raw material in the design of implants and medical devices [29–31]. These characteristics can provide an improvement in the mechanical properties of PLLA.

In this work, a novel polymer blend system composed of PLLA and PLCL copolymer, PLLA/PLCL, is presented as an alternative biodegradable and bioreasurable material to tune the properties of PLLA. The aim of this work is to study the miscibility state, phase morphology and mechanical properties of this polymeric system.

2. Materials and methods

2.1. Materials

Poly(L-lactide) (PLLA) was supplied by Biomer (Germany). The weight average molecular weight (Mw) and polydispersity index (D) were 1,600,000 g mol⁻¹ and 1.70, respectively. Poly(L-lactide-co-ε-caprolactone) (PLCL) of approx. 70:30 L-lactide/ε-caprolactone in molar ratio was supplied by Purac Biochem (The Netherlands). The weight average molecular weight (Mw) and polydispersity index (D) measured were 1,76,400 g mol⁻¹ and 1.68, respectively.

The composition of this statistical copolymer and its chain-microstructural features were well resolved with the determination of several parameters such as the randomness character (R = 0 block character to R = 1 random) and the number average sequence lengths of its constituent L-Lactide (LA) and ε-caprolactone (CL) blocks (I_LA and I_CL) by ¹H and ¹³C Nuclear Magnetic Resonance spectroscopy (Spectra shown in Fig. 1 of the supporting information). The results of the molecular characterization indicate that PLCL composition consists of 67.1% LA and 32.9% of CL, in molar ratio, and that presents a slight multiblock character as revealed by a randomness value of R = 0.69. The average sequence lengths of LA and CL sequence blocks, I_LA and I_CL, were calculated to be 4.35 and 2.13.

In both cases, the molecular weight distribution was analyzed by gel permeation chromatography using a Waters 1515 chromatograph apparatus equipped with a Waters 2414 refractive index (RI) detector. Chloroform at 35 °C was used as the eluent and the Styrigel columns were calibrated with polystyrene standards.

2.2. Blend preparation

Blends of PLLA/PLCL systems were prepared in three different ways.

- Solution/precipitation method: Chloroform solutions of polymers and their blends were prepared at concentration of 5 wt%. Large excess of methanol was used for precipitation of polymer solutions. The precipitants were then air dried for 1 day in air and 2 days at vacuum.

- Solvent Casting method: Films of neat polymers, PLLA and PLCL, and their blends were prepared using solvent evaporation method from 5 wt% solutions in chloroform. The resulting polymer films were first air dried for 48 h and then dried for 7 days at vacuum at room temperature in order to assure the complete solvent evaporation.

- Melt mixing method: Sheets of neat polymers and their blends were prepared by melt-mixing by DSM Xplore micro-compounder (Netherlands) at 200 °C and speed of 100 rpm for 4 min and then conformed by compression moulding in a Collin P200E hydraulic press (Germany) at 200 °C followed by water quenching. The resulting sheets had a thickness of 1 mm.

2.3. Determination of polymer blend miscibility

The miscibility state of the PLLA/PLCL blend system was evaluated according to the unique glass transition temperature (Tg) criterion. The most common use of Tg in determination of polymer/polymer miscibility is based on the premise that a single Tg indicates the domain size is comparable to the macromolecular radius of gyration, i.e., 2 ≤ d ≤ 15 nm, which is necessary requisite for fulfilling the condition of the thermodynamic miscibility, viz. ΔG_m ≈ ΔH_m ≤ 0, and d²ΔG_m/δφ² > 0. Therefore, following this criterion it is accepted, that blends displaying a single Tg are miscible [32]. The Tg behavior was analyzed by means of Differential Scanning Calorimetry (DSC) and Dynamic Mechanical Analysis (DMA).

Thermal behavior was analyzed by a Q200-Differential Scanning Calorimeter (TA Instruments), calibrated with pure indium and sapphires. Two subsequent scans were performed from −60 °C to 200 °C at 20 °C min⁻¹. Thermal properties were measured in the second scan. The glass transition temperature (Tg) was determined from the inflection point of the heat flow curve, the cold crystallization temperature (Tc) and the melting temperature (Tm) from the exothermic and endothermic peak position, respectively, and the cold crystallization enthalpy (ΔHc) and melt enthalpy (ΔHm) were obtained calculating the area under the corresponding crystallization and melting peaks. The sample weight was between 5 and 10 mg in all cases. Dynamic mechanical measurements were carried out using a DMA/SDTA861e (Mettler Toledo) in tensile mode. The PLLA/PLCL samples were heated from −20 °C to 90 °C at a heating rate of 3 °C min⁻¹ and a frequency of 1 Hz. The displacement and force amplitude were maintained at 30 µm and 3 N for compositions with ≥50 wt% of PLCL, and 25 µm and 0.5 N for compositions < 50 wt% of PLCL.

2.4. Mechanical properties

Tensile tests were performed at 22 °C and 50% of relative humidity (RH) with an Instron 5565 testing machine at a crosshead speed of 5 mm min⁻¹. Dumbbell-shaped samples were punched out from sheets following ISO 527-2 (ISO 527-2/5A/5).

2.5. Phase morphology

A JSM-6400 (JEOL) Scanning Electronic Microscope was used to observe the fracture surfaces of the broken specimens after tensile tests and analyze phase morphology of the blends. Previous to observation the polymeric specimens were coated with a thin layer of gold using a BAL-TEC SCD 004 sputter coater.

3. Results and discussion

3.1. Miscibility study

The miscibility of any blend system mainly depends on the behavior of the blend components. Three different miscibility behaviors can be expected in any polymeric blend system: The components demix at all