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Electrospun polycaprolactone/polyglyconate blends: Miscibility, mechanical behavior, and degradation

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ABSTRACT

Electrospun blends of polycaprolactone and polyglyconate were prepared for the first time to evaluate the synergistic properties. The morphology and thermal properties of the blends were used to determine the degree of miscibility. Dynamic mechanical analysis was used to evaluate the mechanical performance and viscoelastic properties of the blends. *In vitro* degradation studies in phosphate buffered saline (pH of 7.3) were carried out to investigate the hydrolytic degradation of the polymer system. FT-IR and SEM analysis, DSC, and mechanical testing were performed to evaluate the degradation profiles of the blends. A 3:1 ratio of polyglyconate to polycaprolactone was concluded to be a partially miscible blend with enhancements in tensile strength, flexibility, and percent elongation to failure over neat polyglyconate. In addition, the 3:1 ratio of polyglyconate to polycaprolactone scaffold exhibited a stable morphology, modulus of elasticity, and mass up to 6 weeks *in vitro*.

1. Introduction

Biodegradable polymer blends are an exciting class of tissue engineering biomaterials that can be tailored for individual tissue systems to match the morphological, mechanical, and degradation properties [1–4]. The goal of these polymer systems is to create a biocompatible and structurally biomimetic scaffold to support cell growth without inducing severe inflammatory responses [3]. In attempts to fulfill these requirements, researchers have focused on the use of novel synthetic and nature-derived polymers. Biocompatible synthetic polymers such as poly(lactic acid) (PLA), poly(glycolic acid) (PGA), and poly(caprolactone) (PCL) have been studied in part because they inert; this allows these materials to be used *in-vivo* without causing an immune response [5]. Various compositions of copolymers such as poly(lactic-*co*-glycolic acid) (PLGA) have been studied to combine the properties of PGA and PLA for tunable mechanical and degradation properties by altering the molecular weight or ratio of PGA to PLA [6]. PLGA is FDA approved for drug delivery and clinical applications including tissue engineering [7]. The unique morphologies of copolymers and blends have been utilized to achieve specific degradation profiles and vehicles for drug delivery systems [8–13].

Several fabrication methods have been employed to utilize the attractive properties of bioresorbable polymer blends to structurally mimic specific tissue systems [1,14]. Electrospinning is a common technique for achieving a nanoscale fibrous network that mimics various native tissue structures [15]. This set-up utilizes a high power source, typically in the kilovolt range, attached to a syringe with polymer solution pumped out at a low rate, in the range of 1–5 mL/h. During the extrusion process, the high voltage applied to the tip of the syringe evaporates the solvent and fibers are drawn towards a grounded collector due to the electric field overcoming the surface tension of the polymer solution [16,17]. Fibers collected on the grounded collector plate can be tuned to the nanometer range as controlled by the parameters of voltage, syringe pump rate, and distance of the syringe tip to the collector [15]. This technique can be used to produce nanofiber scaffolds in various configurations to not only control the morphology but also mechanical properties by spatially aligning the fibers [18].

PCL is a commonly used absorbable polymer for biomaterials mainly because of the favorable degradation time of 24 months *in vitro* as an electrospun scaffold for long-term tissue regeneration [1,19]. Current applications of PCL include the major components in sutures under the trade name Monocryl® and dental root canal fillings under the trade name Resilon®. These applications rely on the long degradation time of PCL to maintain structural integrity. The structure of PCL and overall hydrophobicity hinders water uptake which delays hydrolytic degradation of the ester bonds [19].

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Mechanical properties of PCL as a randomly oriented electrospun scaffold include a relatively low modulus and tensile strength which limits structural applications requiring high tensile strength [3]. However, PCL scaffolds exhibit high porosity of up to 70%, which aids in cell migration into the scaffold [20].

Polyglyconate is a copolymer of glycolic acid (PGA) and trimethylene carbonate (TMC) currently used for absorbable sutures under the trade name Maxon®. The monofilament suture form of Maxon is an A–B–A triblock copolymer consisting of a random copolymer of glycolic acid and trimethylene carbonate as the middle block (B) and glycolic acid as the ends (A) of the random copolymer [21]. The beneficial properties such as high elasticity, high tensile strength, a reported 67% porosity as an electrospun scaffold, and ability to complex with other biomolecules are attractive for many applications including tissue scaffolds [18]. However, the degradation for Maxon is 4–6 weeks as a monofilament suture, which poses challenges for long term reconstructive use such as tissue engineering applications [22]. The high percentage of glycolic acid in Maxon contributes to a hydrophilic nature with subsequent fast degradation due to water uptake and the breakdown of ester linkages [23,24]. Maxon is currently used in temporary structures such as surgical sutures and bioabsorbable screws [25].

Neat PCL and Maxon offer both opportunities and challenges in terms of mechanical performance and degradation stability as a biomaterial for long term applications for tissue regeneration. For these reasons, PCL is of interest to blend with Maxon to achieve improved degradation times and dimensional stability of Maxon. In addition, the chemical homogeneity of PCL and Maxon, which both contain PCL components, may favor high miscibility in the blends and permit the formation of an ordered structure without phase separation. This article evaluates the miscibility of two compositions of blends with Maxon and PCL to determine the effect on mechanical behavior and degradation.

2. Experimental section

2.1. Materials

Poly(caprolactone) with an inherent viscosity of 1.15 dL/g in chloroform ($CHCl_3$) was purchased from LACTEL Absorbable Polymers, Birmingham, AL. Poly(glycolide-*co*-trimethylene carbonate) was purchased in the form of surgical suture packets under the trade name Maxon® from Advanced Inventory Management, Mokena, IL. The solvent used for electrospinning was 1,1,1,3,3,3-hexafluoro-2-propanol (HFP), purchased from Oakwood Products Inc., West Columbia, SC.

2.2. Fabrication of scaffolds

Four electrospinning solutions were prepared which included a 3:1 PCL/Maxon blend and a 3:1 Maxon/PCL blend, respectively, in comparison to neat Maxon and neat PCL as controls. The blend solutions consisted of a 3:1 mixture of 20% wt/vol PCL to 15% wt/vol Maxon in HFP for a total concentration of 18.75% wt/vol and the 3:1 mixture of 15% wt/vol Maxon to 20% wt/vol PCL in HFP for a total concentration of 16.25% wt/vol. The neat PCL solution was a 20% wt/vol in HFP. The neat Maxon solution was prepared as a 15% wt/vol in HFP by pelletizing the surgical sutures. An electrospinning setup to obtain a randomly aligned nanofiber scaffold was used to pump 2 mL of polymer solution with a 5 mL syringe at a rate of 0.2 mL/h through a 25G needle. The average distance from the needle tip to the grounded collector plate was 20 cm. A high voltage source (M826, Gamma High-Voltage Research, Ormond Beach, FL) of 12–15 kV was chosen to produce an average fiber diameter of 500 nm for each of the polymer solutions. The scaffolds were collected onto a solid sheet of aluminum until a thickness of 0.1–0.3 mm was achieved. This thickness was achieved by 1.5–3 mL of polymer solution electrospun onto a 10 mm × 10 mm collector. Following electrospinning, the samples were placed in a desiccant environment for seven days to allow for the residual HFP to evaporate from the samples. Scanning electron microscopy (SEM) was used to determine a fiber distribution and verify an average diameter of 500 nm using ImageJ software analysis. The scaffolds were sputter coated with Au–Pd and imaged with an accelerating voltage of 10 kV by a field emission SEM (Quanta FEG 650 from FEI, Hillsboro, OR).

2.3. Miscibility studies

The blended samples (~5 mg) were sealed in an aluminum pan and loaded into a differential scanning calorimeter (DSC) (Q100 TA Instruments, New Castle, DE) to analyze the shifts in glass transition temperature, melt behavior, and enthalpy of fusion from the physical mixing of the two polymers. The neat PCL and Maxon samples were tested as controls. Each of the samples were subjected to a single temperature ramp heating from −80 °C to 250 °C at a rate of 10 °C/min.

Etching was also used to investigate the miscibility of the two polymers. Samples with similar thickness and dimensions of 1 cm by 1 cm of the 3:1 Maxon/PCL and 3:1 PCL/Maxon blends were agitated in 5 mL of dichloromethane (DCM) to etch away the PCL component. Samples of neat Maxon and PCL were also used as controls; Maxon does not readily dissolve in DCM. Soaking times of 1 h, 3 h, and 5 h were used to determine the proper amount of soaking to thoroughly dissolve the PCL component. Samples were removed from the DCM followed by rinsing with DCM to remove any dissolved polymer from the surface of the scaffold and dried overnight in a desiccant environment. The resultant scaffolds were imaged by SEM to determine morphological changes. The 3:1 Maxon/PCL etched samples were also analyzed by DSC to examine shifts in melting temperatures and enthalpies as a function of etching time. A single temperature ramp heating from −80 °C to 250 °C at a rate of 10 °C/min was employed to verify the removal of the PCL component in the 3:1 Maxon/PCL blends after etching in DCM.

Phase separation processes of the blends were investigated by DSC with an annealing procedure of first heating the samples to 250 °C at a rate of 10 °C/min and cooling to −80 °C to erase thermal history, followed by cyclic annealing–quenching steps holding at 80 °C–150 °C for 10 min and quenching at 20 °C/min to −80 °C. The heating thermograms from −80 °C to 250 °C at a rate of 10 °C/min after each annealing–quenching cycle were recorded to observe phase separation.

2.4. Mechanical properties evaluation

The scaffolds were sectioned into rectangular strips measuring 5 mm in width, 25 mm in length, and 0.1–0.2 mm in thickness, in accordance with ASTM standard D882 for tensile testing of thin film plastics. Uniaxial tensile testing ($n = 5$) was performed with dry samples at ambient conditions with a minimat tensile tester (Rheometric Scientific Inc.) to determine the modulus of elasticity, percent elongation to failure, and yield strength from the generated stress–strain curves. The scaffolds were tested using a 20 N load cell and a strain rate of 5 mm/min until failure.

Dynamic mechanical analysis (DMA) was used to investigate the viscoelastic properties of the neat and blended samples under cyclic loading over a temperature range from −100 °C to 70 °C with 5° increments. Samples were sectioned to 5 mm × 15 mm rectangular strips for testing in a 2980 DMA (TA Instruments) over a frequency range from 0.1 to 1 Hz with load cell of 18 N. A time temperature superposition master curve was constructed for each sample to