

Development of porous lamellar poly(L-lactic acid) scaffolds by conventional injection molding process

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Abstract

A novel fabrication technique is proposed for the preparation of unidirectionally oriented, porous scaffolds by selective polymer leaching from lamellar structures created by conventional injection molding. The proof of the concept is implemented using a 50/50 wt.% poly(L-lactic acid)/poly(ethylene oxide) (PLLA/PEO) blend. With this composition, the PLLA and PEO blend is biphasic, containing a homogeneous PLLA/PEO phase and a PEO-rich phase. The two phases were structured using injection molding into well-defined alternating layers of homogeneous PLLA/PEO phase and PEO-rich phase. Leaching of water-soluble PEO from the PEO-rich phase produces macropores, and leaching of phase-separated PEO from the initially homogeneous PLLA/PEO phase produces micropores in the lamellae. Thus, scaffolds with a macroporous lamellar architecture with microporous walls can be produced. The lamellae are continuous along the flow direction, and a continuous lamellar thickness of less than 1 μm could be achieved. Porosities of 57–74% and pore sizes of around 50–100 μm can be obtained using this process. The tensile elastic moduli of the porous constructs were between 580 and 800 MPa. We propose that this organic-solvent-free method of preparing lamellar scaffolds with good mechanical properties, and the reproducibility associated with the injection molding technique, holds promise for a wide range of guided tissue engineering applications. © 2008 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.

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1. Introduction

Each tissue or organ has its own characteristic architectural organization, which is closely associated with its physiological functions. Some specific tissues, such as bone, tendon, ligaments, spinal cord, peripheral nerve, ureter and intestine, have tubular or lamellar architectures. The repair of such tissues remains an intractable problem due to their poor capacity for natural regeneration. Tissue engineering strategies have great potential in the biological and functional regeneration of such tissues. In general, the growth of nerve cells is highly random and does not extend

through the lesion site to the host tissue. A better strategy is to physically guide the linear growth of axons across a site of injury. This allows retention of the original architecture of regenerating axons across the lesion site and increases the probability of achieving total functional recovery. The essential steps for engineering such strategies are the development of biomimetic and anisotropically oriented scaffolds consistent with the morphology of the natural skeleton of host tissues. In general, the materials of these temporary porous scaffolds are either of natural and synthetic biodegradable polymers [1–5]. Synthetic polymers have design flexibilities in terms of material composition, processability, control over macro- and micro-structures, and mechanical properties [3]. Poly(α -hydroxy acids) including poly(lactic acid), poly(glycolic acid) and their co-polymers are the widely accepted biodegradable synthetic polymers for tissue engineering applications.

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A number of processing techniques based on textile technologies, thermally induced phase separation, solvent casting/particulate leaching, fiber templating, melt extrusion and combinations of the above techniques have been used for the preparation of multi-tubular and simple tubular structures. Hollow conduit-like constructs can be fabricated by melt-based processing techniques such as extrusion of polymer/salt followed by leaching of salt [6]; radial alignment of internal pores across a hollow tube by spinning a polymer suspension followed by freeze drying and sublimation [7]; formation of tubular scaffolds by rolling freeze-dried films into the form of a tube [8]; bonding of non-woven polymer meshes wrapped around a mandrel and spraying a polymer solution onto them [9]; or formation of hollow fabric tubes by knitting of prefabricated yarns followed by dipping in solution, freezing and sublimation [10]. The multitubular porous scaffolds can also be prepared by phase-separation techniques, e.g. (i) freezing of polymer solution and sublimation of solvent [11,12]; (ii) freezing polymer/solvent with a uniaxial temperature gradient followed by sublimation of solvent [13]; (iii) injecting polymer suspension into a prefabricated multiple channel mold followed by sublimation of solvent [14,15]; (iv) freeze-drying with a uniaxial thermal gradient [16–18]; (v) fiber templating technique [19–21]; and (vi) solution coating and gas foaming by porogen decomposition [22]. Scaffolds prepared by the freeze-drying process are limited to thin constructs and the dense outer wall of the scaffolds may not allow interaction between the cells in the lumen and the surrounding tissue. Moreover, the dense outer walls may prevent scar tissue from invading into the scaffolds and suppress tissue regeneration. The permeability of the tubular wall is an important requirement of such scaffolds as it facilitates the supply of oxygen and nutrients and the removal of metabolic waste substances. Moreover, the use of organic solvents in most of these fabrication processes and the potential toxicity of these solvents has already been reviewed [23].

Three-dimensional porous scaffolds can also be produced from selective dissolution of a polymer from blends such as poly(L-lactic acid) (PLLA)/polystyrene, PLLA/poly(ϵ -caprolactone) and poly(ϵ -caprolactone)/poly(ethylene oxide) (PEO) [24–26]. Lee and Kim have demonstrated that a layered structure could also be produced by injection molding a low interfacial tension, partially miscible polymer blend [27]. Injection molding is a versatile, efficient and highly reproducible process, capable of fast production of complex geometric shapes with tight dimensional tolerances. Injection molding has previously been used to prepare scaffolds by compounding polymer with a blowing agent [28]. In that case sphere-shaped pores were obtained. In this work, we intend to fabricate anisotropically oriented PLLA scaffolds by injection molding a blend of PLLA and PEO. PEO is a thermoplastic and water-soluble polymer. Moreover, PEO is biocompatible and is currently used in biomedical applications [29]. PEO has been used in this study as a porogen to obtain porous structures.

Most polymer blends are immiscible because of unfavorable interactions and the small increase in entropy upon blending. In an immiscible blend, the constitutive polymers are immiscible throughout the composition range due to the high interfacial tension and poor adhesion between the phases. In a miscible blend, however, the constitutive polymers are miscible over a wide range of compositions due to specific molecular interactions. In a partially miscible blend, a small part of one blend component is dissolved in the other component. With increased fraction of the minor phase, the system becomes biphasic and both blended phases are homogeneous [30].

A polymer pair tends to be miscible if the difference in solubility parameters is less than $0.5 \text{ (cal cm}^{-3})^{1/2}$ [31]. The solubility parameter is defined as $(CED)^{1/2}$, where CED is the cohesive energy density. The solubility parameters of PLLA and PEO are 10.1 and $9.9 \pm 1 \text{ (cal cm}^{-3})^{1/2}$, respectively [31,32], and the closeness of these values indicates that the miscibility of PLLA and PEO is thermodynamically favorable. The glass transition temperatures (T_g) of pure PLLA and pure PEO are 61 and -54°C , respectively. The miscibility is supported by the detection of a single glass transition temperature in between the T_g s of the pure polymers [33].

In this paper, we describe an original approach to the fabrication of anisotropically oriented porous scaffolds using a conventional melt-based injection molding technique. More specifically, different layered structures were obtained by varying the injection molding processing conditions of a 50/50 wt.% PLLA/PEO blend. The porous constructs were produced by swelling the compact specimens in water followed by aqueous dissolution of water-soluble PEO. The steps describing the fabrication of the unidirectionally oriented porous scaffolds are summarized in Fig. 1. The hypothesis is that this methodology could be a route to fabricate unidirectionally oriented porous scaffolds. We investigated the effect of melt processing temperature and injection flow rate on the morphology of the porous structures observed by scanning electron microscopy. The effects of processing conditions on swelling behavior, porosity and mechanical properties were also studied.

2. Materials and methods

2.1. Materials

A high stereoregular PLLA from Cargill Dow LLC, USA was used in this study. PLLA was estimated to have an L-lactide content of 99.6% based on its specific optical rotation in chloroform using an AA-1000 Polarimeter [34]. The PLLA had $\overline{M}_n = 69,000$ and polydispersity of 1.73 as determined by gel permeation chromatography (Shimadzu LC10A, Japan) in chloroform with the standard of polystyrene. The PEO was Polyox WSR N-10, $\overline{M}_n = 100,000$, from Dow Chemical Company, USA. A 50/50 wt.% blend of PLLA and PEO was used in this study.

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