A facile preparation of highly interconnected macroporous PLGA scaffolds by liquid–liquid phase separation II

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Abstract

A regular and well-interconnected macroporous (from 50 to 200 \textmu m) poly(l-lactic acid-co-glycolic acid) (PLGA) scaffold was fabricated by means of the thermally induced phase separation (TIPS) method. Poly(l-lactic acid) (PLLA) was blended with PLGA to increase the viscosity of polymer solution; a block copolymer of poly(ethylene glycol) (PEG) with PLGA was added as a surfactant to decrease the interfacial tension between the polymer-rich and polymer-lean phases. The effect of TIPS parameters including the concentration of diblock copolymer and PLGA/PLLA ratio was also studied. The cloud-point curve shifted to higher temperatures with both increasing the PLLA composition in the PLGA/PLLA blend and the PEG contents in the additives (PEG itself and PEG–PLGA diblocks). This shifting to higher temperature increases the quenching depth during phase separation. Addition of a PEG–PLGA diblock copolymer (0.5 wt\% in solution) to the PLGA/PLLA (1/1) blend polymer in a dioxane/water solution stabilized the morphology development during TIPS with respect to interconnection and macropores, and avoided segregation or sedimentation in the late stage.

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1. Introduction

After the loss or failure of bodily tissues or organs, traditional surgical treatment, such as implantation of a healthy organ from a donor, is limited by the problems of immune rejection from the patient and the number of available donors [1]. The use of cell transplantation (‘tissue engineering’) is under investigation as a strategy for tissue repair and organ replacement [2–6]. Transplanted cells, cultured from a patient’s healthy tissues, can be implanted back without antagonizing the immunosolation system. In culturing the cells, the shape of the scaffold, a temporary substrate to allow growth and specialization of the cell culture, plays an important role [7–10]. Biodegradable and biocompatible synthetic polymers, such as poly(lactic acid) (PLA), poly(glycolic acid) (PGA), and poly(l-lactic acid-co-glycolic acid) (PLGA), have been widely utilized as three-dimensional scaffolds [11–13]. Polymeric scaffolds must be porous enough to allow a high density of cells to be seeded, yet also possess sufficient mechanical stability and a well-defined network of interconnected pores to permit ingrowth into the implanted structure [9,14]. The optimum pore size of the scaffold required differs depending on the cells or tissues; for example, pore sizes close to 20 \textmu m are required for the ingrowth of fibroblasts and hepatocytes [15], from 50 to 150 \textmu m for skin regeneration [16], and in the range of 100–150 \textmu m for bone regeneration [17,18].

Numerous techniques have been developed for fabricating polyester scaffolds, including porogen leaching/salt leaching, emulsion freeze-drying, gas expansion, fiber bonding, and phase separation [19–23]. Recently, the method of freeze-drying through thermally induced (liquid–liquid) phase separation (TIPS) was developed for the preparation of biodegradable polyester scaffolds [21,23–28]. TIPS and freeze-drying were used to prepare a three-dimensional macroporous poly(l-lactic acid) (PLLA)…