Materials Letters 65 (2011) 2114–2117

Contents lists available at ScienceDirect

Materials Letters

journal homepage: www.elsevier.com/locate/matlet

# Using hydrophilic ionic liquids as a facile route to prepare porous-structured biopolymer scaffolds

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ARTICLE INFO

*Article history:*
Received 7 May 2010
Accepted 3 April 2011
Available online 12 April 2011

*Keywords:*
3D porous structure
Ionic liquids
Biopolymer scaffolds

ABSTRACT

A simple new methodology to preapre 3-dimensional (3D) porous scaffold of biodegradable polymer was exploited by using hydrophilic types of ionic liquids. The mixture of poly(lactic acid) (PLA) and ionic liquid within dichloromethane solvent was phase-separated during the solvent evaporation, after which the ionic liquid phase was selectively extracted to provide interconnected macropores. The pore sizes of the PLA scaffold were highly dependent on the types of ionic liquids (anion variant), ranging from tens to hundreds of micrometers, and the porosity reached to ~85–95%. The ionic liquid-directed technique to prepare porous structure reported for the first time herein will be highly effective in the development of polymer skeletons for tissue engineering biomaterials. In addition, the ionic liquids recovered by a simple extraction with ethanol or water can be reused for subsequent runs without the loss of its physicochemical properties.


## 1. Introduction

The generation of two and three-dimensional (2 and 3D) porous morphology with polymeric materials has attracted considerable interest due to potential applications in diverse fields, including tissue engineering, drug delivery, gas storage and separation, heterogeneous catalysis and polymer gel electrolytes [1–4]. In particular, biopolymers with interconnected macropores have been used as a major scaffolding matereial to host and support tissue cells for tissue engineering purpose. To obtain the micro- and macro-porous polymer skeletons, a phase separation technique afforded by the solubility limit of the mixture solutes has served as a facile strategy [1–5].

Room temperature ionic liquids have many fascinating properties [6–8]. For example, they have the potential as a new medium in organic synthesis, catalyst support and nanostructure construction materials. In particular, the type of anions of ionic liquids greatly affects their wettability, i.e., hydrophilic / hydrophobic nature. Accordingly, the utilization of anion-directed properties has been of special importance in research fields such as surface chemistry and catalysis [9–12]. During our on-going study on ionic liquid chemistry [10–12], we expected that 3-dimensionally micro-structured polymer scaffolds would be easily obtained from ternary polymer solutions including an ionic liquid and an organic solvent. Although specific ionic liquids have previously been used for the preparation of ionic liquid-containing composites such as a thermochromic gel and an electrolyte gel [13, 14], to the best of our knowledge, there have been no reports on controlling the 3D porous structure depending on the anion type. We reported here the preparation method of 3D porous biopolymer scaffolds using varuous anionic forms of ionic liquids and briefly assessed their pore structue and physicochemical properties.

## 2. Experimental

Poly(lactic acid) (PLA, from Boehringer Ingelheim) was used as the biodegradable polymer. 1-butyl-3-methylimidazolium-based ionic liquids bearing different counter-anions ([bmim]X; X = OTf, $BF_4$, and Cl, from C-Tri Co., Ltd, Korea) were chosen as the counter-phase for preparing porous-structured PLA. The preparation method is schematically shown in Fig. 1. Briefly, 0.2 g of PLA, 1.0 g of an ionic liquid and 10 ml of organic solvent (dichloromethane; DCM) were mixed to produce a transparent solution. DCM was then evaporated from the transparent solution under ambient conditions, after which a rubbery white gel remained at the bottom of the dish. To selectively remove the ionic liquid, the rubbery gel was soaked in ethanol (or water) while gentle shaking for 3 h. After three to four times washing with ethanol, the samples were then dried under ambient conditions, which gave white and opaque samples. The ionic liquid could be easily recovered and was reused for the next run.

The morphology of the porous-structured PLA scaffolds was examined with scanning electron microscopy (SEM; Hitachi S-300H, JEOL), after sputter-coating with gold. The pore size of the scaffolds was analyzed from the pictures taken at different sections using

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doi:10.1016/j.matlet.2011.04.007

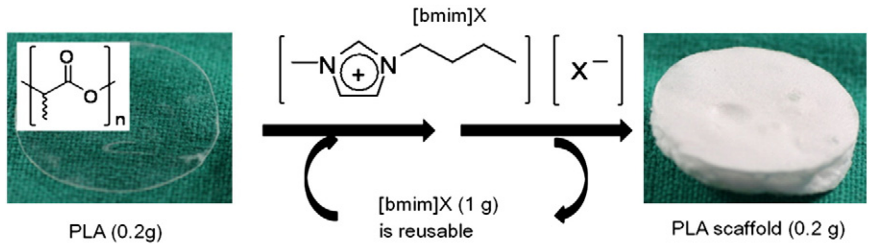


**Fig. 1.** Photographs of biopolymer PLA scaffold before and after ionic liquid-assisted 3D-porous structuring: ionic liquids = [bmim]X = 1-butyl-3-methylimidazolium-based ionic liquids (X = OTf, $BF_4$, and Cl).

an image analyzer. The chemical properties were analyzed with Fourier transform infrared spectrometer (FT-IR; Jasco 470 PLUS). The infrared spectra were recorded in solution condition (DCM) at a range of 400–4000 $cm^{-1}$. Thermogravimetric analysis (TGA; Seiko Exstar 6000 TG/DTA6100, Seico Inst.) was conducted with a heating rate of 10 °C/min at temperatures ranging from 20 to 550 °C under air. Porosity of the scaffolds was determined using an AutoPore IV 9520 type mercury porosimeter (Shimadzu-micromeritics; 60,000 psi).

## 3. Results and discussion

The SEM images of the PLA scaffolds demonstrated that the use of hydrophilic ionic liquids bearing anions such as OTf, $BF_4$ and Cl leads to a highly porous structure, as shown in Fig. 2(a–c). The pore size was variable depending on the type of ionic lqiuids (namely, type of anions). While the use of [bmim]OTf resulted in the pore size of approximetely tens of micrometers (a), when [bmim]$BF_4$ or [bmim]Cl was used, the pore size became greatly increased to even a hundred of micrometers (b,c). The pore structures were quite homogeneous throughout the scaffolds and totally open connected, as seen in the representative images of the PLA scaffolds containing small and large pore sizes, obtained respectively by using [bmim]OTf (d) and [bmim] $BF_4$ (e).

The generation of this open porous structure was facilitated by the phase separation between PLA and ionic liquid. Moreover, the phase separation started to occur in the course of the evaporation of DCM solvent, during which the ionic liquid phase was slowly separated from the polymer phase to form a polymer-ionic liquid interpenetrated gel. Herein, we used a hydorphilic type of ionic liquids by selecting appropriate counter-anions (OTf, $BF_4$ and Cl). As depicted in Fig. 3, the phase of ionic liquid is separated from the hydrophobic polymer which is to solidify during the solvent evaporation, and particularly forms an unwettable interface with the polymer phase featuring a specific curvature. After selective and complete removal of the ionic liquid within ethanol or water, the solvent to selectively dissolve ionic liquid, the 3-dimensionally interconnected channels will come into view as a large skeleton. As the biopolymers are generally hydrophobic, the use of hydrophilic ionic liquids is of special importance to obtain such interconnected pore structure within the polymer network. At this point, it should also be underscored as to the merits of using ionic liquids as the pore generator; along with the simple process described herein, the ionic liquid can be selectively and effectively extracted from the polymer network, and the used ionic liquid can be easily collected and reused for the next runs.

We further analyzed the properties of the PLA porous scaffolds obtained by the assistance of ionic liquids. In particular, the complete removal of ionic liquids was confirmed by thermogravimetric analysis (TGA) and infrared (IR) spectroscopy, as shown in Fig. 4. Results on PLA scaffold using [bmim]$BF_4$ are shown as a representative data. The IR spectra of the PLA porous scaffold showed only the characteristic

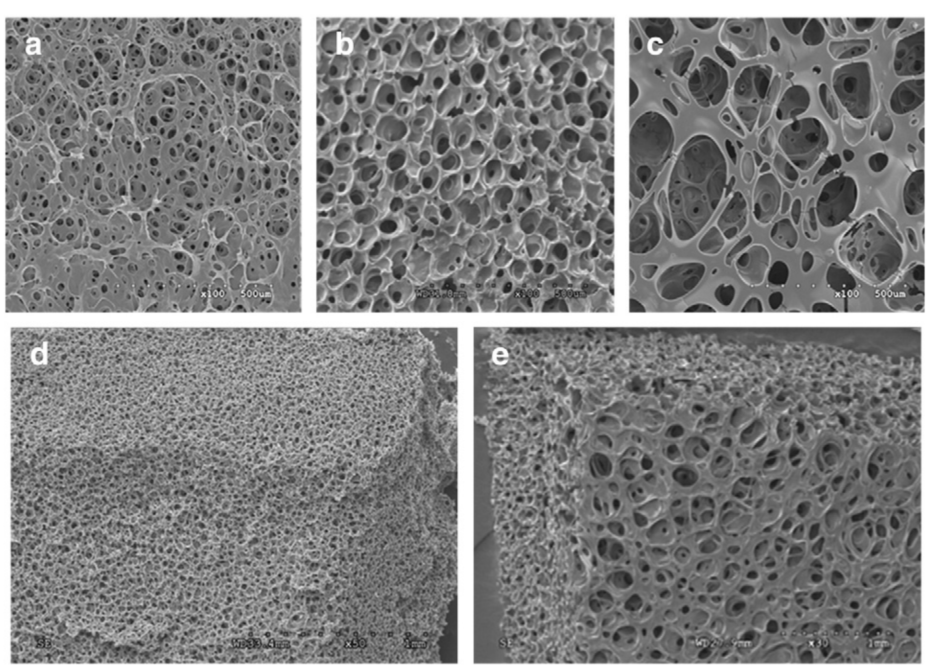


**Fig. 2.** SEM morphologies of the PLA porous scaffolds produced by using three different ionic liquids of [bmim]X, where X = OTf (a), $BF_4$ (b) and Cl (c). Whole scaffold images showing homogeneous pore structure throughout the scaffolds: X = OTf (d) and Cl (e).