Fabrication of Porous Polylactic Acid Films Assisted by Dip-Coating and Template Leaching Techniques

Ta-I Yang,[1] Tai-Lun Su,[1] Po-Liang Lin,[1] I-Hsiang Tseng,[2] Chih-Hung Chang,[3,4] Hsu-Wei Fang[1,5]

[1]Department of Chemical Engineering and Biotechnology, National Taipei University of Technology, Taipei, Taiwan
[2]Department of Chemical and Materials Engineering, National Chin-Yi University of Technology, Taichung, Taiwan
[3]Division of Orthopedics, Department of Surgery, Far Eastern Memorial Hospital, Banciao,
New Taipei City, Taipei, Taiwan
[4]Graduate School of Biotechnology and Bioengineering, Yuan Ze University, Chungli, Taoyuan, Taiwan
[5]Division of Medical Engineering Research, National Health Research Institutes, Miaoli, Taiwan

ABSTRACT: A new simple method was developed to fabricate porous polylactic acid (PLA) films coated directly on substrates. The PLA films with a controllable thickness were realized using a dip-coating technique. The pore structure of the resulting porous PLA films was tailored by utilizing phase inversion process and template leaching techniques. The experimental results show that the resulting PLA films became thicker when using the coating solution with a higher viscosity or applying a faster withdrawal speed. The porous structures (pore size and void density) of the resulting PLA films are significantly influenced by the polymer concentration, the nonsolvents, and the addition of poly(ethylene glycol) templates. The analyses of solubility parameters was utilized to explain the porous structures of the resulting PLA films in details. © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 124: 2333–2339, 2012

Key words: polylactic acid; porous thin film; dip coating; template leaching; biomaterial

INTRODUCTION

There has been a recent research focusing on the development of porous polylactic acid (PLA) based materials. Synthetic polylactic acid has been used for advanced applications in tissue engineering, food packaging, and drug delivery systems due to its great biodegradability, biocompatibility, and good mechanical strength.[1] In tissue engineering applications, porous PLA could be used as scaffolds mimicking natural tissue structures to promote tissue regeneration and guide tissue growth.[2–4] Studies in literature have successfully prepared PLA films with porous structures using various techniques including aerosol-assisted method,[5] template (additives/porogens) leaching method,[6] thermally induced phase separation method (TIPS),[7] and liquid-induced phase separation method (LIPS).[8] However, most techniques did not provide a simple and easy way to coat a porous PLA film on substrates with a controllable film thickness.

In this study, we demonstrate the feasibility of coating porous PLA films with a controllable film thickness directly on substrates using dip-coating process assisted by phase inversion method. Dip-coating technique was chosen because of its ease-of-processing, low cost, and high resulting coating quality.[9] The pore structure of the resulting porous PLA films was tailored by utilizing phase inversion process and template leaching technique. The effect of nonsolvent (water and ethanol) and the evaporation step of phase inversion process on the resulting structure of porous PLA films were investigated. The poly(ethylene glycol) (PEG) with various molecular weights was also used as the porogens to create desired porous structures.

EXPERIMENTAL

Materials

PEG templates with molecular weight of 190–210 (PEG-200), 950–1050 (PEG-1000), and 8500–11500 (PEG-10000) were purchased from Sigma-Aldrich. Medical grade poly (DL-lactic) acid (PLA) was supplied by Bio-Invigor (Taipei, Taiwan). PLA solutions were prepared using acetone as a solvent. The
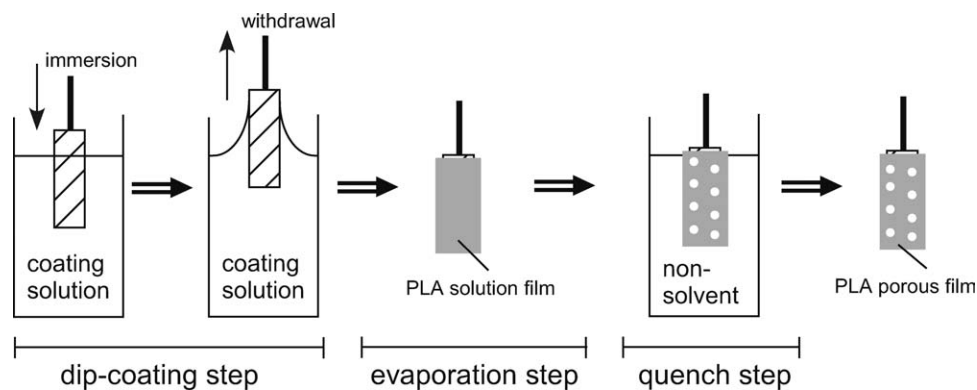
Figure 1 Scheme depicting the preparation process for PLA films. Note: the side views of the disks are used in the scheme to represent the substrate of the stainless steel disks.

medical grade 316 stainless steel disks (3 mm in thickness, 15 mm in diameter) were prepared as the substrates for porous PLA films. The surface of the 316 stainless steel disk was polished to a mirror surface with the roughness (R_a) of 0.11 μm.

Preparation of porous PLA thin films via phase inversion process

The schematic for the porous PLA film fabrication is shown in Figure 1. A self-developed controller, which allowing the clamp to move vertically at a constant speed, was used for the dip-coating process. The stainless steel disks were first immersed into the PLA coating solution with required concentrations and then withdrawn from the bath at a constant withdrawal speed (υ). The wetted disks were subsequently exposed to ambient environment (air) for 5 or 60 s (evaporation step). Exposing the as-cast films in air with different durations was to investigate the effect of evaporation time in evaporation step on the resulting porous structures. After the evaporation step, the films were immersed into the nonsolvents (quench step) for 1 min to form the porous PLA films. The drying process of the coated disk was done by leaving the disk in its natural vertical position in the hood at room temperature.

Preparation of porous PLA thin films using phase inversion process and template leaching technique

The procedure was the same as with the preparation of porous PLA thin films via phase inversion process except the addition of PEG templates in the PLA coating solution. The withdrawal speed for dip-coating process was 32 mm/s and the PLA coating solution was 30 wt %. The as-cast PLA films were exposed to air for 60 s (evaporation step) prior to immersing into water overnight (quench step) to form the porous PLA films and also to leach out the PEG templates.

Characterization

The roughness of the steel disks was measured by a profilometer (Perthometer S2, Mahr, Germany). The images of porous PLA structures (cross-section and top-layer) were obtained using scanning electron microscope (SEM, Hitachi S-3000H). Their equivalent circular diameter (ECD) representing pore size and void density (VD) of the resulting porous PLA films were analyzed by Scion Image software.

RESULTS AND DISCUSSION

Dip coating process

Dip-coating process starts at immersing a substrate into a coating solution. A coherent liquid film is entrained on withdrawal of the substrate from the coating solution, which then consolidating after solvent evaporation, leading to a uniform solid film deposited upon the surface of the substrate. The film thickness (h) is determined by the balance of the forces involving in the process, including viscous drag force, gravitational force, capillary force, and inertia force.[10] Theoretical prediction of resulting film thickness (h) from Newtonian solution, based on the assumption that there is no solvent evaporation during the dip-coating process, has been reported in literature as follows:

$$h \propto \frac{(\upsilon\eta)^{2/3}}{\sigma^{1/6}(\rho g)^{1/2}}$$

where υ is the withdrawal speed, η is the solution viscosity, ρ is the solution density, and σ is the solution surface tension.

The thickness of the films deposited from a given coating solution could be easily controlled by changing the drag force, which is proportional to $(\upsilon\eta)^{2/3}$. In this study, the PLA acetone solutions used for dip coating were Newtonian fluid, i.e., their viscosities
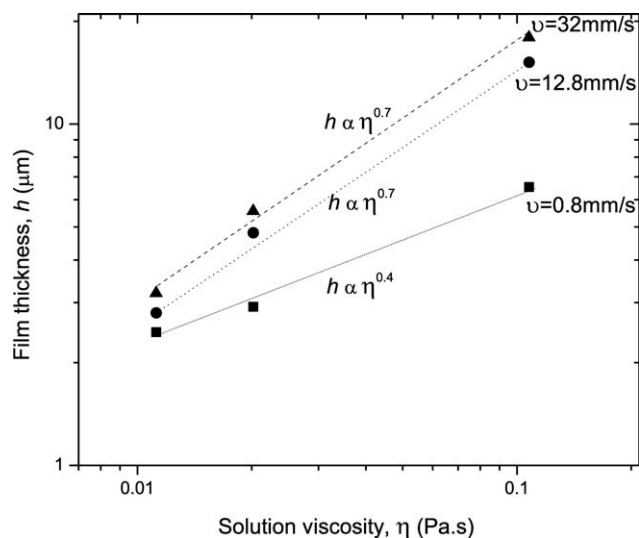
Figure 2 Effect of solution viscosity (η) on PLA film thickness at various withdrawal velocities (υ).

were independent of shear rates. The resulting PLA films became thicker when using the coating solution with a higher viscosity (η) or applying a faster withdrawal speed (υ), as shown in Figure 2. This is because high η or υ leads to larger drag force so that the amount of the liquid moving upwards with the substrate is larger, resulting in thicker films. The film thickness (h) is proportional to η^x, where the x is close to 0.67 from prediction eq. (1), at a given withdrawal speed and coating solution. The results for withdrawal speed (υ) of 12.8 and 32 mm/s are in a good agreement with the model prediction where x is close to 0.7. However, lower value of x (0.4) was found for $\upsilon = 0.8$ mm/s. This result contributed to the solvent evaporation at low withdrawal speed (0.8 mm/s).[10] The prediction that film thickness (h) is proportional to $\eta^{0.67}$ is based on the assumption that there is no solvent evaporation during the dip coating process. However, the effect of solvent evaporation became significant at low withdrawal speed (υ) compared to high υ, leading to solution viscosity change during dip coating process. Therefore, the film thickness is not simply proportional to $\eta^{0.67}$ at low υ as reported in literature.[10] In summary, we have demonstrated the feasibility of using solution viscosities and withdrawal speeds to control the thickness of the resulting PLA films. The required thickness was able to be tailored by simply changing the solution viscosity or the withdrawal speed.

Preparation of porous PLA films

The porous PLA films were fabricated by phase inversion process after dip-coating step. The phase inversion process was done, specifically in this study, through immersion precipitation technique, which immersing the as-cast thin film into a nonsol-

vent (quench step). Subsequently, the exchange of solvent and nonsolvent across the interface leads to the phase separation into a polymer-rich phase and a polymer-lean phase, resulting in a continuous polymer film and a porous substructure within the film, respectively. The porous structures of the resulting films are significantly influenced by the concentration of the polymer solution, the type of nonsolvents, and the evaporation time prior to immersing into a nonsolvent.[11]

Effect of polymer concentration

The pore size of the top surface of the porous PLA film was 4.4 ± 1.77 μm with 16% VD when using 20 wt % of PLA solution and water as the nonsolvent [Fig. 3(a)]. However, the pore size became smaller (1.5 ± 0.25 μm) with less VD (5%) when using 30 wt % of PLA solution [Fig. 3(b)]. It was also shown in the cross-sectional images that the resulting porous film has a smaller pore size with less VD as the concentration of PLA solution increased from 20 to 30 wt % [Fig. 3 (d,e)]. These results contribute to different diffusion rates of solvent (acetone) and nonsolvent (water) in quench step. When the as-cast film was prepared using a higher PLA concentration, the rate of water diffusing into the as-cast films was lower than the rate of acetone diffusing out of the film. Therefore, the surface part of the PLA film solidified easily and further prevented water from diffusing into the film, leading to a porous structure with smaller pores and less VD.

Effect of solvent/nonsolvent

The porous PLA film with a dense surface layer was able to be fabricated using ethanol as the nonsolvent, as shown in Figure 3(c,f). The resulting porous PLA films also have smaller pores and less VD compared to the PLA films prepared using water as the nonsolvent [Fig. 3(b,e)]. These results could be explained by the total solubility parameter (δ_t) which was utilized as a tool to predict the solubility of polymers. The polymers are more soluble in solvents whose solubility parameters are closer to their own.[12] Both water and ethanol were used as the nonsolvents for precipitating PLA polymer in quench step. However, compared to their δ_t difference ($\Delta\delta_t$) with PLA polymer, ethanol has a smaller $\Delta\delta_t$ (Table I), meaning that PLA is more soluble in ethanol than in water. Therefore, the PLA polymer showed delayed demixing from acetone when immersing in ethanol instead of instantaneous demixing as immersing in water, resulting in porous films with a smaller pore size and less VD.[11]

Effect of evaporation time

The porous films with an asymmetric structure were able to be fabricated using a dry/wet phase
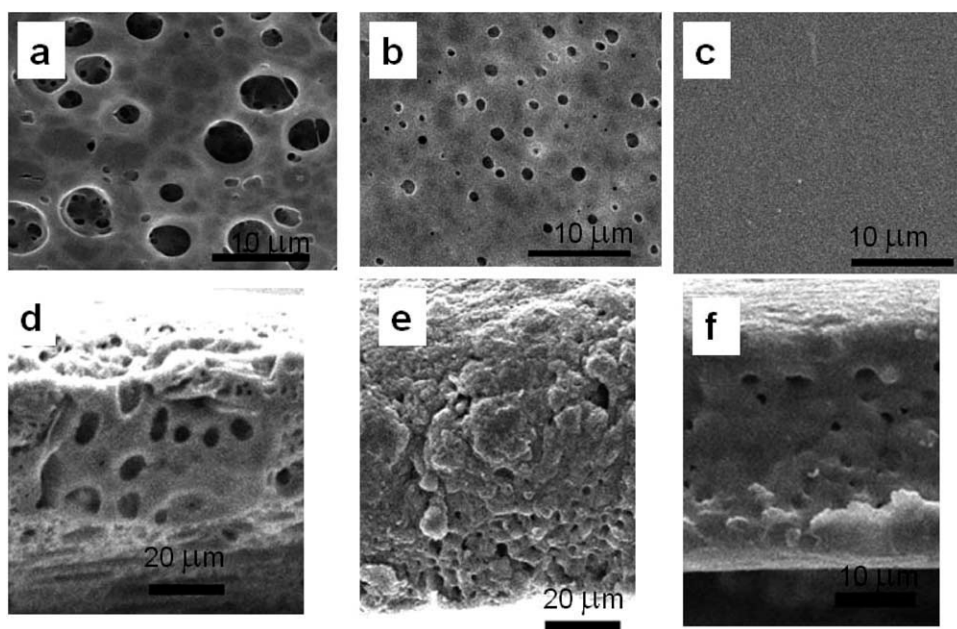
Figure 3 SEM images of porous PLA films prepared with different conditions: (a and d) PLA: 20 wt %, nonsolvent: water; (b and e) PLA: 30 wt %, nonsolvent: water; (c and f) PLA: 30 wt %, nonsolvent: ethanol. Note: (a–c) are surface morphologies, (d–f) are cross-sectional structures. Withdrawal speed: 32 mm/s. Evaporation time: 5 s.

inversion process, which inducing the phase separation for the surface and the bulk of the as-cast film through different ways.[14] Figure 4 shows the porous PLA films with a asymmetric structure prepared by exposing the dip-coated substrate to air for 60 s (evaporation step) prior to immersing into ethanol (quench step). The surface of the dip-coated PLA film underwent phase separation induced by solvent (acetone) evaporation when exposing in air, leading to a dense layer on the top surface of the film. After immersing into nonsolvent, the bulk of the film subsequently became porous due to the phase separation induced by the solvent/nonsolvent exchange.

Effect of template (PEG) addition on the structure of porous PLA films

Traditionally, the template leaching technique involves casting thin films from a polymer solution with water soluble templates such as sugar and chitosan, consolidating the films, and leaching out the templates to generate porous thin films.[4,6] In our study, three water-soluble PEGs with different molecular weights (PEG-200, PEG-1000, and PEG-10000) were used to further control the porous structure of the films.

Effect of molecular weight

The pore size of the top surface of the porous PLA film was 2.6 ± 0.48 μm with 30% VD when adding 33 wt % of low molecular weight PEG-200 as the template (Fig. 5). However, the pore size distribution

became nonuniform (2.7 ± 2.07 μm) with less VD (14%) as using PEG-1000 templates. Furthermore, there are no obvious pores present on the surface of the porous film as using higher molecular weight PEG-10000 templates, meaning that a dense layer formed on the top surface of the film. These results indicated that there is fewer PEG left on the surface prior to quench step when the templated PEG molecular weight increased, leading to less voids on the surface after leaching out the PEG. It was also shown in the cross-sectional images that the pores become smaller from bottom (substrate side) to top surface (air side), suggesting that more PEG were present near the substrate side and more PLA were present on the air side after acetone evaporating step. In the analyses of the total solubility parameters (δ_t), the δ_t of PEG decreases with its molecular weight increase (Fig. 6), leading to poorer compatibility with acetone solvent since their total solubility parameter difference becomes larger. Therefore, acetone carried more PLA to the film surface and left more PEG closer to the bottom side during evaporation, resulting in the asymmetric porous structure.

TABLE I
Total Solubility Parameter (δ_t) for PLA Polymer and Solvents[12,13]

	PLA	Acetone	Ethanol	Water
δ_t	19.8	20.0	26.5	47.9
$\Delta\delta_t$	–	0.2	6.7	28.1

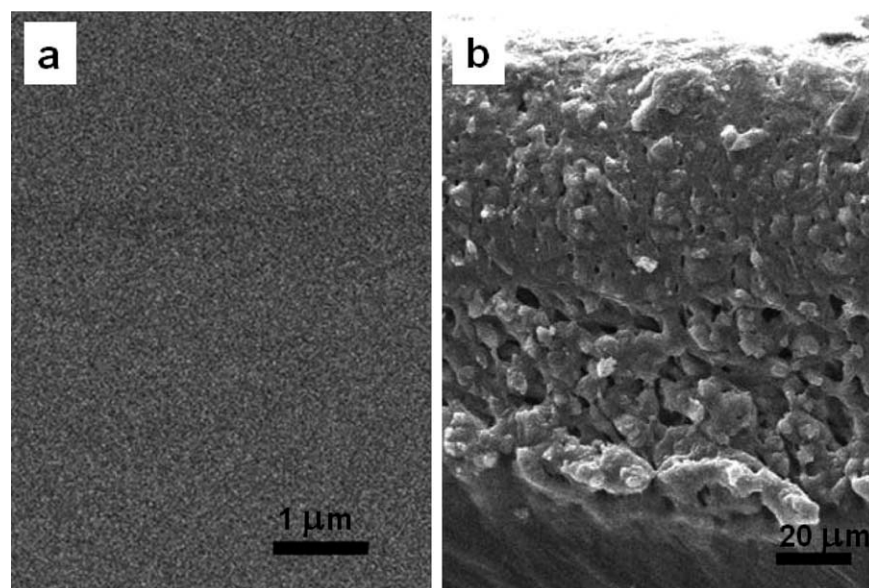$\Delta\delta_t$ represents the δ_t difference between PLA polymer and the solvent.

Figure 4 SEM images of porous PLA films prepared using dry/wet phase inversion process: (a) surface morphology; (b) cross-sectional structure. Note: PLA: 30 wt %. Withdrawal speed 32 mm/s.

Effect of different amounts of PEG doping

Figure 7 shows that the resulting pore size on the surface of PLA films with different amounts of PEG-200 templates doping are close to 2.8 μm with uniform size distribution (standard deviations less than 0.5). Their calculated VD increased with increasing amounts of PEG-200 doping. The cross-sectional structures also show the same results: similar pore sizes for all three porous films and an increased VD with increasing amounts of PEG-200 doping (Fig. 8). These results contribute to the good compatibility between PLA and PEG-200 so that the PEG-200 templates dispersed well within the PLA matrix, leading to a uniform size distribution with controlled VD for the resulting films. For using PEG-1000 as the templates, the pore size on the surface of the resulting porous films became larger with a poorer pore size
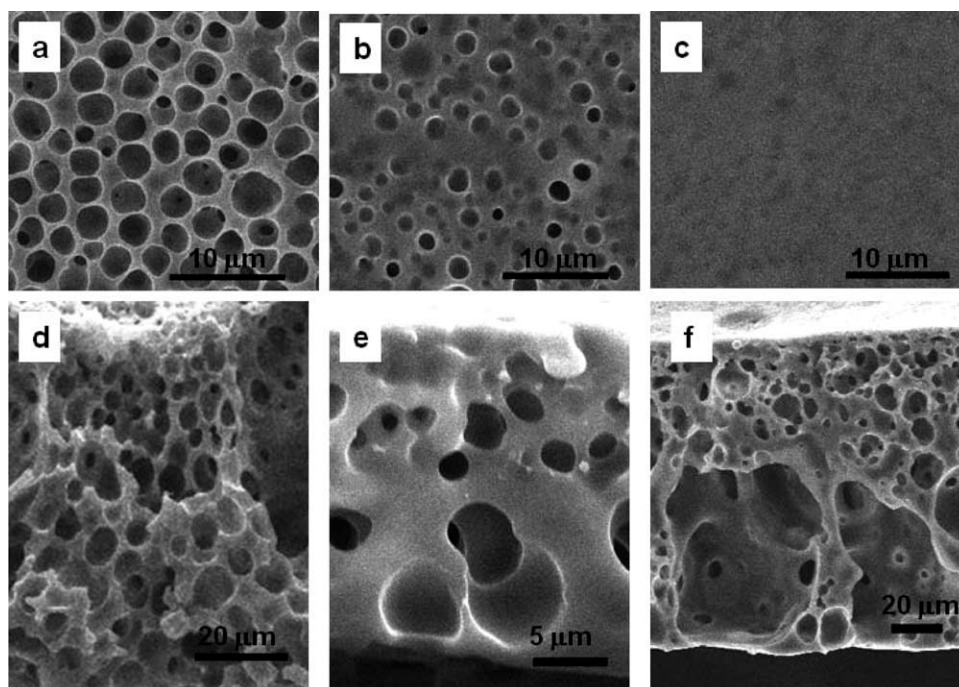

Figure 5 Effect of molecular weight of PEG on porous structures of PLA films: (a and d) PEG-200; (b and e) PEG-1000; (c and f) PEG-10000. Note: (a–c) are surface morphology. (d–f) are cross-sectional structures.
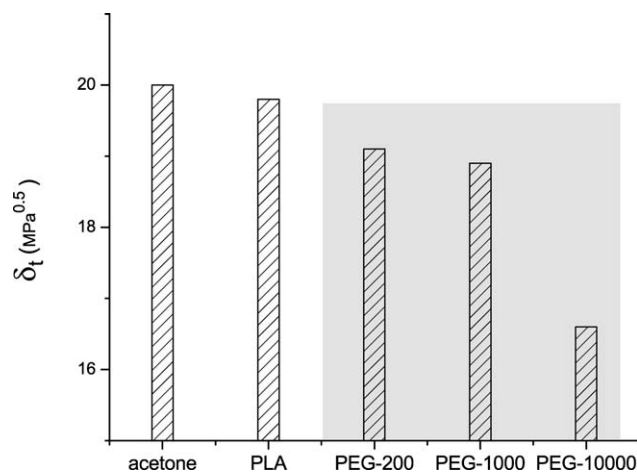
Figure 6 The total solubility parameters (δt) of acetone, PLA, and PEG with various molecular weight.[12,13]

Figure 8 Effect of PEG addition on cross-sectional structures (pore size (closed symbol) and void density (open symbol)) of porous PLA films at various PEG amounts. ($\triangle$: 16 wt %; $\square$: 23%; $\bigcirc$: 33%).

distribution when the amounts of templates increased (Fig. 7). This is because larger amounts of PEG-1000 within the casting solution resulted in higher solution viscosities and faster solvent evaporation rate so that templates were "freezed" more randomly near the surface during evaporation step. Therefore, the surface of porous films showed a large VD and poor size distribution when increasing amounts of PEG-1000. Furthermore, the adverse effect of increased amounts of PEG-1000 also affected the cross-sectional structures. The bulk porous films (cross-sectional structure) showed a poorer pore size distribution and a higher VD with larger amounts of PEG-1000 doping (Fig. 8). For using PEG-10000 as the templates, the surface of the resulting porous film showed a dense layer on the surface as low as 16 wt % of PEG-10000 doping (Fig. 7) due to the poor compatibility with the acetone solvent and PLA matrix. The bulk structure (Fig. 8)
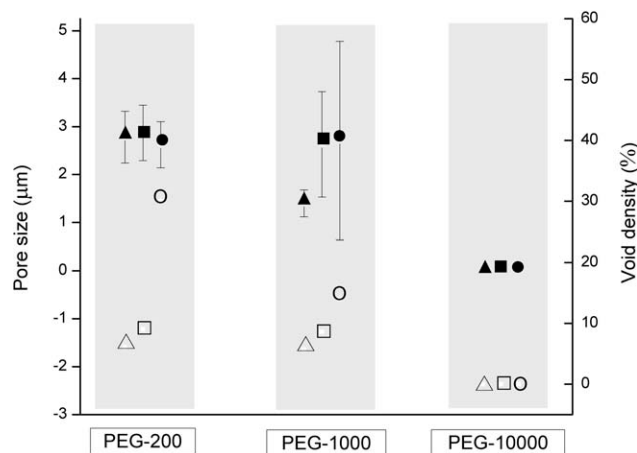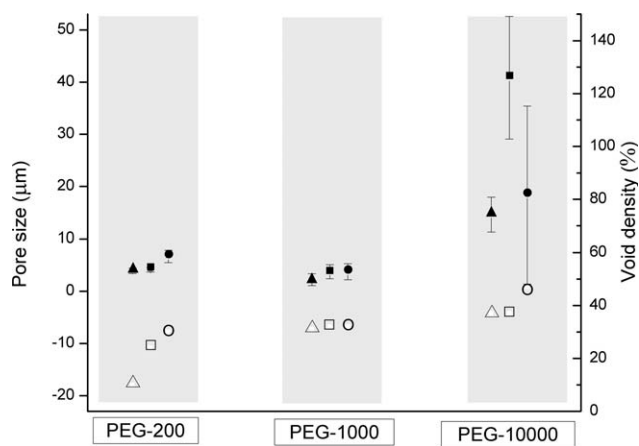
revealed that the pore size was more difficult to control and a higher VD was present as the doping amount increased.

CONCLUSIONS

We have demonstrated the feasibility of coating porous PLA films with a controllable thickness directly on substrates using dip-coating process assisted by phase inversion method. The thickness of the resulting films was able to be easily controlled by changing the drag force, which is related to the withdrawal speed and the solution viscosity in dip-coating step. Porous PLA films with various pore structures could be prepared by phase inversion process and template (PEG) leaching technique. The porous PLA films have smaller pores and less VD by changing nonsolvent from water to ethanol. The addition amounts and the molecular weight of the PEG templates also significantly affected the pore structures of the resulting PLA films. PEGs with higher molecular weight led to PLA films with larger pore and greater VD due to their incompatibility with acetone solvent. Furthermore, the pore size and VD of the porous PLA films were more difficult to control as the doping amounts of PEGs increased because of their incompatibility with the solvent and PLA matrices.

Figure 7 Effect of PEG addition on the surface morphology (pore size (closed symbol) and void density (open symbol)) of porous PLA films at various PEG amounts. ($\triangle$: 16 wt %; $\square$: 23%; $\bigcirc$: 33%).

References

1. Gupta, B.; Revagade, N., Hilborn, J Prog Polym Sci 2007, 32, 455.
2. Miao, X.; Sun, D. Materials 2010, 3, 26.
3. Ghosh, S.; Viana, J. C.; Reis, R. L.; Mano, J. F. Acta Biomater 2008, 4, 887.
4. Wei, G.; Ma, P. X. Biomaterials 2009, 30, 6426.
5. Hou, X.; Choy, K. L.; Yan, J. Surf Coat Technol 2008, 202, 5175.

6. Wu, H.; Wan, Y.; Cao, X.; Wu, Q. Acta Biomater 2008, 4, 76.

7. Barroca, N.; Daniel-da-Silva, A. L.; Vilarinho, P. M.; Fernandes, M. H. V. Acta Biomater 2010, 6, 3611.

8. Papenburg, B. J.; Bolhuis-Versteeg, L. A. M.; Grijpma, D. W.; Feijen, J.; Wessling, M.; Stamatialis, D. Acta Biomater 2010, 6, 2477.

9. Aegerter, M. A.; Mennig, M. Sol-Gel Technologies for Glass Producers and Users; Springer: Norwell, MA, 2004.

10. Yimsiri, P.; Mackley, M. R. Chem Eng Sci 2006, 61, 3496.

11. Kim, Y. D.; Kim, J. Y.; Lee, H. K.; Kim, S. C. J Membr Sci 2001, 190, 69.

12. Rissanen, M.; Puolakka, A.; Nousiainen, P.; Kellomaki, M.; Ella, V. J Appl Polym Sci 2008, 110, 2399.

13. Ozdemir, C.; Guner, A. Eur Polym Mater 2007, 43, 3068.

14. Pinnau, I.; Koros, W. J. J Appl Polym Sci 1991, 43, 1491.