Polymer Bulletin 58, 703–709 (2007)
DOI 10.1007/s00289-006-0699-8

Polymer Bulletin

Controlled degradation of porous poly(lactide) stereocomplex films prepared by the selective extraction of co-assembled poly(vinyl alcohol)

Yuuya Arikawa[1], Takeshi Serizawa[2], Takashi Mukose[3], Yoshiharu Kimura[3], and Mitsuru Akashi[1] (✉)

[1]Department of Molecular Chemistry, Graduate School of Engineering, Osaka University,
2-1 Yamada-oka, Suita 565-0871, Japan
[2]Research Center for Advanced Science and Technology (RCAST), The University of Tokyo,
4-6-1 Komaba, Meguro-ku, Tokyo 153-8904, Japan
[3]Department of Polymer Science and Engineering, Faculty of Textile Science, Kyoto Institute of Technology, Goshokaido-cho, Matsugasaki, Sakyo-ku, Kyoto 606-8585, Japan
E-mail: akashi@chem.eng.osaka-u.ac.jp; Fax: +81-6-6879-7359

Received: 9 August 2006 / Revised version: 12 October 2006 / Accepted: 21 October 2006
Published online: 28 October 2006 – © Springer-Verlag 2006

Summary

Poly(vinyl alcohol) (PVA) layers of different thicknesses were intercalated into stereocomplex films composed of poly(L-lactide) and poly(D-lactide). The immersion of composite films into boiling water selectively extracted the water-soluble PVA components, resulting in porous stereocomplex films. The hydrolytic properties of the porous films under alkaline conditions were then quantitatively analyzed. It was observed that the hydrolytic rates decreased with increasing pore sizes.

Introduction

Poly(lactide)s (PLAs) are well-known as biodegradable polyesters, and are frequently used for biomedical applications [1,2]. A significant requirement for PLA materials in the biomedical fields is to control their biodegradability, because crystalline α-form PLAs are barely hydrolyzed under physiological conditions. A decrease in the crystallinity of the PLA materials is a simple method to accelerate the degradation rates. However, PLA crystals gradually grow in materials at ambient temperature, resulting in changes in their hydrolytic properties. Hydrophilic monomers were copolymerized with lactic acid to accelerate their water penetration and to decrease their crystallinity. However, the original mechanical properties of the PLA materials would be changed.

In our previous studies, stereocomplex films composed of poly(L-lactide) (PLLA) and poly(D-lactide) (PDLA) [3-11] were prepared by layer-by-layer (LbL) assembly, which is commonly used for the preparation of polyelectrolyte multilayers based on the alternate soaking of solid substrates into polymer solutions [13]. These films showed considerably higher crystallinity, with more than 90 % β-form content [14]. Although it was believed that the degradation rates of the PLA stereocomplexes were almost the same as those of PLA crystals, we first demonstrated that stereocomplex films are rapidly hydrolyzed under alkaline conditions, the same as amorphous PLAs films [15]. Therefore, the next target would be the control of hydrolytic rates using LbL assembled PLA stereocomplex films.

LbL assembly can essentially deposit polymers when the polymers are stably bonded on the surfaces due to adequate interactions after rinsing with the same solvent. To generally extend this concept, we previously demonstrated that poly(vinyl alcohol) (PVA) [16] and poly(vinylamine) [17] were homogeneously deposited by repetitive adsorption and drying cycles for solid substrates. These polymers in the dried state formed strong intra- and intermolecular hydrogen bonds, and the generated surface could function as substrates.

It has been demonstrated that a single component in LbL assembled films can be selectively extracted by good solvents, resulting in porous films [18]. In cases of stereocomplex films composed of isotactic poly(methyl methacrylate) and syndiotactic poly(methacrylic acid), the resulting porous films were utilized as stereoregular polymerization templates [19,20]. When hydrophilic polymers intercalated into PLA stereocomplex films are selectively extracted, the hydrolytic properties of the porous stereocomplex films might be modulated.

In this study, PVA-intercalated PLA stereocomplex films were prepared by LbL assembly, and the PLA components were selectively extracted in boiling water to prepare porous stereocomplex films. Then, alkaline hydrolyses of the PLA stereocomplex films with various porous ratios were analyzed with regard to the PVA layer numbers previously deposited. This study is schematically shown in Figure 1. The assembly and hydrolysis of the films were quantified by quartz crystal microbalance (QCM) substrates, which can detect the mass of the substrate from a frequency shift [21].

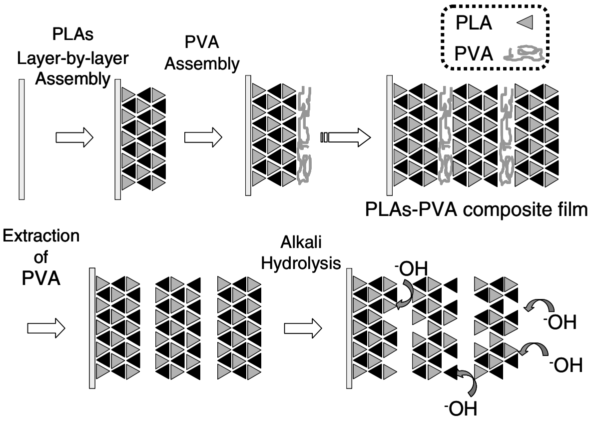

Figure 1. Schematic representation of this study.

Experimental

PVA (degree of polymerization 2000) and acetonitrile were purchased from Nacalai Tesque (Japan). PLLA and PDLA with average number molecular weights (M_n) of 27700 and 30800, and the distributions (M_w/M_n) (M_w: average weight molecular weights) of 1.51 and 1.55, respectively, were prepared following methods reported in previous studies [22]. Ultra distilled water (17.8 ΩM cm^{-1}) was provided by the MILLI-Q labo system.

An AT-cut quartz crystal with a parent frequency of 9 MHz was obtained from USI Systems (Japan). The crystal (9 mm in diameter) was coated on both sides with gold electrodes 4.5 mm in diameter. After rinsing with their solvents and drying with N_2 gas at each deposition step, a frequency counter (Iwatsu Model SC7201) analyzed the frequency decrease of the QCM (ΔF) to estimate the amount of polymer deposited (Δm) from Sauerbrey's equation:

$$-\Delta F = \frac{2F_0{}^2}{A\sqrt{\rho_q \mu_q}} \times \Delta m$$

where F_o is the parent frequency of the QCM ($9\text{x}10^6$ Hz), A is the electrode area (0.159 cm^2), ρ_q is the density of the quartz (2.65 g cm^{-3}), and μ_q is the shear modulus ($2.95\text{x}10^{11}$ dyne cm^{-2}). Before the assembly measurements, the QCM electrodes were treated twice with a piranha solution (H_2SO_4:H_2O_2=3:1) for 1 min each time, followed by rinsing with pure water and drying with N_2 gas, to clean the surface.

Enantiomeric PLAs were assembled from their acetonitrile solutions at concentrations of 10 mg ml^{-1} at 50 °C by the alternate immersion of QCM substrates for 15 min in each solution, following our previous studies [12]. For PVA assembly, the substrate was immersed into aqueous PVA solutions at concentrations of 0.02 unitM containing 2 M NaCl for 15 min at 25 °C, rinsed with solvent, and dried by a N_2 blast, following our previous study [16]. The frequency decreases were then measured. For every 3 cycles of the stereocomplexes ($(\text{PLLA-PDLA})_3$), 1-3 PVA layers were deposited. The total assembly amounts were constant at 3500 ng/QCM, which corresponded to 11 μg cm^{-2}, by changing the total assembly number. Assuming the films to be smooth and the densities to be 1 g cm^{-3}, the apparent film thickness was estimated to be approximately 90 nm. For PLA extraction, the composite films were immersed into boiling water.

For alkaline hydrolyses, QCM substrates coated with composite films was immersed into an aqueous 0.01-N NaOH solution at 37 °C, rinsed with solvent, and dried by N_2 blasts. The frequency decreases were then measured.

Attenuated total reflection (ATR) spectra were obtained with a Parkin-Elmer Spectrum. QCM electrodes with a refractive surface were used directly to observe the ATR spectra. The interferograms were co-added 16 times and Fourier transformed at a resolution of 4 cm^{-1}.

Results and Discussion

Figure 2 shows the frequency decreases of the QCM, corresponding to the amount of assembled polymer, against the assembly step. In all cases, the frequencies decreased in a stepwise fashion without frequency increases, indicating that polymers were assembled at each step. It is reasonable to assume that the interactions between PLLA and PDLA are stereocomplex formation, and that those between the PVAs are hydrogen bonds, as shown in previous studies [16]. Although there is no specific interaction between PLAs and PVA, hydrogen bonds between the ester groups of PLAs and the hydroxy groups of PVA might be formed, followed by stepwise polymer assembly.

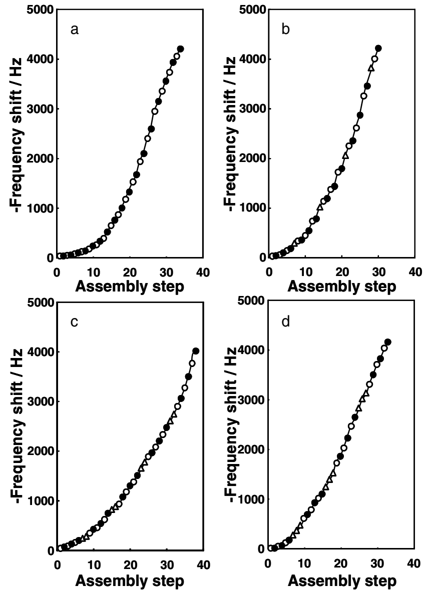

Figure 2. Frequency shift of the QCM against the assembly step for: (a) $(PLLA/PDLA)_n$, (b) $((PLLA/PDLA)_3/PVA_1)_n$, (c) $((PLLA/PDLA)_3/PVA_2)_n$, and (d) $((PLLA/PDLA)_3/PVA_3)_n$ films. The open and closed circles indicate PLLA and PDLA steps, respectively. The triangular symbols indicate PVA steps.

The ATR spectra for the composite films in Figure 3 showed OH vibration bands at around 3100-3600 cm^{-1} as well as carbonyl vibration bands for the ester groups of PLAs at around 1750 cm^{-1}, indicating that the PVA was really assembled with PLA stereocomplexes. Increases in the number of PVA assembly steps slightly increased the area for the OH vibration bands, suggesting that greater amounts of PVA were

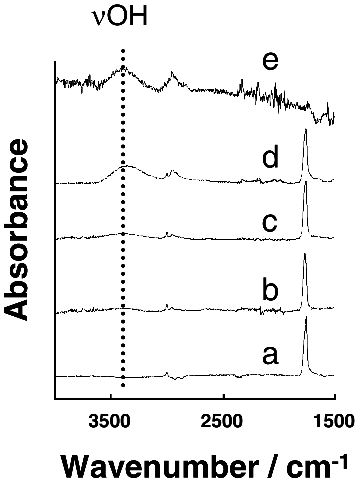

Figure 3. ATR spectra of: (a) $(PLLA/PDLA)_n$, (b) $((PLLA/PDLA)_3/PVA_1)_n$, (c) $((PLLA/PDLA)_3/PVA_2)_n$, (d) $((PLLA/PDLA)_3/PVA_3)_n$, and (e) PVA films.

assembled with increasing step number. It is noted that the aforementioned wavenumber of the carbonyl vibration bands is the same as that for the stereocomplexes [23], suggesting that stereocomplexes were formed between the PVA layers. Accordingly, different amounts of PVA were successfully assembled between (PLLA-PDLA)$_3$ stereocomplex films.

Figure 4 shows the remaining weights of polymers analyzed by the QCM, when PLA stereocomplex films co-assembled with a single step PVA were immersed in boiling water. After 5 minutes of immersion, approximately 15 % of the total polymers desorbed, and almost reached equilibrium. The desorbed amount was significantly consistent with the amount of assembled PVA. The ATR spectra after 5 min of immersion in the inset of Figure 4 showed the absence of OH vibration bands. These observations indicate that the assembled PVA was quantitatively extracted from the PLA stereocomplex films, thus forming porous stereocomplex films. Other composite films were also immersed into boiling water for 5 min to extract the PLA. The films may collapse after PVA extraction. However, since the PVA layers prepared by 3 assembly steps should not fully cover the stereocomplex surface, a stereocomplex layer would contact the next complex layer. This is one possible reason why pores are stably formed. As a consequence, PVA was successfully extracted from the composite films.

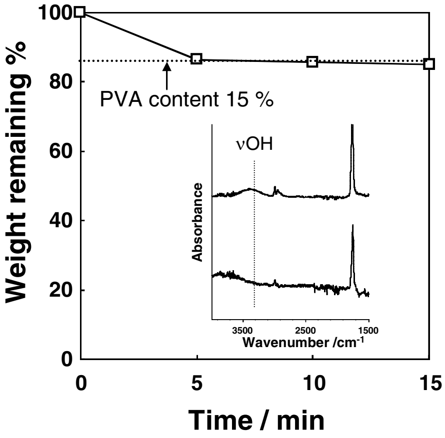

Figure 4. QCM analysis of the selective extraction of PVA from ((PLLA/PDLA)$_3$/PVA$_1$)$_n$ films. The inset shows the ATR spectra before (upper) and after (lower) PVA extraction.

Alkaline hydrolyses of the resulting stereocomplex films were analyzed quantitatively, as shown in Figure 5. PLAs desorbed with time, indicating that the PLAs were hydrolyzed and desorbed from the substrate. The rates were dependent on the PVA amounts previously assembled, and increased remarkably with increasing PVA amounts. It is reasonable to consider that the PVA extraction formed pores in the stereocomplex films. Pore sizes should increase upon increasing the number of PVA assembly steps. Therefore, these observations suggest that the formation of pores with greater sizes within PLA stereocomplex films resulted in lower hydrolytic rates. Accordingly, it was observed that porous stereocomplex films prepared by LbL assembly were more slowly hydrolyzed than non-porous films, and that the hydrolytic rates of these stereocomplex films were controlled by the amount of previously assembled PVA.

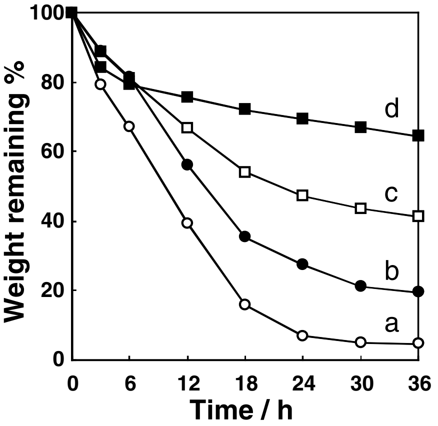

Figure 5. Alkaline hydrolysis of: (a) $(PLLA/PDLA)_n$, (b) $((PLLA/PDLA)_3/PVA_1)_n$, (c) $((PLLA/PDLA)_3/PVA_2)_n$, and (d) $((PLLA/PDLA)_3/PVA_3)_n$ films.

It is well-known that porous PLA materials are slowly hydrolyzed as compared to non-porous materials [24]. Lactic acid and lactic acid oligomers generated by these hydrolyses can be readily desorbed from porous materials. On the other hand, they are very slowly desorbed from non-porous materials. The carboxyl groups of the lactic acid and lactic acid oligomers remaining in the non-porous materials behave as hydrolytic catalysts against other PLAs, resulting in an acceleration of the hydrolytic rates. In our system, the pores prepared by selective PVA extraction from thin PLA stereocomplex films also decreased the hydrolytic rates. Greater numbers of pores seemed to be prepared in stereocomplex films by increasing the number of PVA steps.

Conclusions

Composite films composed of PLA stereocomplexes and PVA were prepared by LbL assembly for the first time. The PVA amounts were changed upon changing the number of assembly steps. Water-soluble PVA components were successfully extracted in boiling water, resulting in porous stereocomplex films. The porous films were more slowly hydrolyzed under alkaline conditions as compared to non-porous films. The hydrolytic rates decreased with increasing PVA amounts, possibly due to the greater number of pores in the stereocomplex films. It is significant that the stereocomplex films were prepared on variously shaped substrates using LbL assembly. Molecularly porous films have the potential for loading and releasing functional molecules. We are further characterizing these porous PLA stereocomplex films.

References

1. Ikada Y, Shikinami Y, Hara Y, Tagawa M, Fukada E (1996) J Biomed Mater Res 30:553
2. Asahi T, Fukase H, Ichiki M, Kobayashi J, Fukada E (1990) Ferroelectrics 109 : 339
3. Ikada Y, Jamshidi K, Tsuji H, Hyon S –H (1987) Macromolecules 20:906
4. Tsuji H, Horii F, Hyon S –H, Ikada Y (1991) Macromolecules 24:2719
5. Tsuji H, Hyon S –H, Ikada Y (1991) Macromolecules 24:5651
6. Tsuji H, Hyon S –H, Ikada Y (1991) Macromolecules 24:5657

7. Tsuji H, Hyon S –H, Ikada Y (1992) Macromolecules 25:2940
8. Tsuji H, Ikada Y (1992) Macromolecules 25:5719
9. Tsuji H, Horii, Nakagawa M, Ikada Y, Odani H, Kitamaru R (1992) Macromolecules 25:4114
10. Tsuji H, Ikada Y Macromolecules (1993) 26:6918
11. Brizzolara D, Cantow H –J, Diederichs K, Keller E, Domb A J (1996) Macromolecules 29:191
12. Serizawa T, Yamashita H, Fujiwara T, Kimura Y, Akashi M (2001) Macromolecules 34:1996
13. Decher G (1997) Science 277:1232
14. Arikawa Y, Serizawa T, Mukose T, Kimura Y, Akashi M J Nanosci Nanotechnol in press
15. Serizawa T, Arikawa Y, Hamada K, Yamashita H, Fujiwara T, Kimura Y, Akashi M (2001) Macromolecules 36:1762
16. Serizawa T, Hashiguchi S, Akashi M (1999) Langmuir 23:5363
17. Serizawa T, Yamamoto K, Akashi M (1999) Langmuir 15:4682
18. Serizawa T, Ken-ichi H, Tatsuki K, Akashi M (2003) *Angew Chem* 115:1150 (2003) Angew Chem Int Ed 42:1118
19. Serizawa T, Ken-ichi H, Akashi M *Nature* (2004) 429:52
20. Ken-ichi H, Serizawa T, Akashi M (2005) *Macromolecules*, 38:6759
21. Sauerbrey G Z (1959) Phys 155:206
22. Amass W, Amass A, Tighe B (1998) Polym Int 47:89
23. Zhang J, Sato H, Tsuji H, Noda I, Ozaki Y (2005) Macromolecules 38:1822
24. Lu J, Peter J S, Lyman D M, Lai H –L, Leite M S, Tamada A J, Vacanti P J, Langer R, Mikos G A (2000) 21:1595