Morphological Observation of Polylactide-b-Poly (Ethylene Glycol)-b-Polylactide Triblock Copolymers Stereocomplex Films

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Abstract:

The objectives of this work were to prepare PLLA-PEG-PLLA/PDLA-PEG-PDLA blend films with and without tetracycline by solvent casting method and to observe their morphology drug under the scanning electron microscope (SEM). The results found that film prepared from pure PLLA-PEG-PLLA had smooth surfaces but composed of some small pores with tetracycline. The PLLA-PEG-PLLA/PDLA-PEG-PDLA blend films showed varied in surfaces and textures depending on the PDLA-PEG-PDLA ratios used. All blend films had small pores on their surfaces but still had homogeneous texture. The number of pores smooth and dense texture of the blend films were gradually increased when the ratio of PDLA-PEG-PDLA increased. This confirmed that stereocomplexation formation between both copolymers. The obtained results indicated the potential of blend films for drug delivery system development.

Keywords: Biodegradable polymer, film, morphology, PLA, stereocomplex

Introduction

Controlled drug release systems are well established as an efficient approach for the treatment of several diseases [1]. This was due to their offer of several advantages, such as appropriate control of release kinetics, reduction of drug concentration variability in the blood which may cause adverse effects [2], decrease of dosage times and improvement of patient compliance [3]. Various types of controlled-release drug delivery systems have been prepared including particles, fibers, powders, gels and films [4]. The drug delivery systems prepared from biodegradable polymers have the advantage over nonbiodegradable polymers in that the removal of these devices at the completion of therapy is not required [5].

Polylactic acid (PLA) is a biodegradable polymer synthesized by ring-opening polymerization of lactic acids. These substances are derived by lactic fermentation of carbohydrates such as beetroot, sweet potato, corn, potato and cassava [6]. Generally, lactic acid (LA), a PLA monomer, exists into 2 stereoisomers, D- and L-lactic acids which further synthesized into poly (D-lactic acid) (PDLA) and poly (L-lactic acid) (PLLA), respectively [7]. The PLA has been used in various applications, especially in biomedical applications such as artificial bones, sutures, scaffold-based tissue engineering and drug delivery system [8]. Many reports have been proved that the PLA is safety in use, sustainability, high biocompatibility, bio-absorbability, good mechanical properties (especially in strength and modulus) and easy processability [9]. However, PLA has some draw back properties which restricted for applications such as inherent brittleness, low toughness and low crystallization ability [10].

Stereocomplexation of PLA is one of an approach to improve its physical properties. The method could be performed by combining poly (L-lactide) (PLLA) and poly (D- lactide) (PDLA). With stereocomplex crystallites, the melting temperature of PLA is enhanced more than 50°C as well as enhancement of barrier, mechanical and thermal properties [11]. The stereocomplex films of PLLA-PEG-PLLA/PDLA-PEG-PDLA have been prepared by compression method [12]. Therefore, in this work polylactide-b poly (ethylene glycol) -b-polylactide triblock copolymers stereocomplex films by solvent casting method were prepared and the effects of PDLA-PEG-PDLA ratios and tetracycline on the morphology of the prepared films were also observed.

Material and methods

Materials

PLLA-PEG-PLLA and PDLA-PEG-PDLA copolymers were synthesized by ring-opening polymerization in bulk at 165 °C under a nitrogen atmosphere for 6 h using 0.075 mol% stannous octoate ($Sn(Oct)_2$) as a catalyst. Polyethylene glycol (PEG) was used as an initiator [12]. Number-average molecular weight (M_n) of the PLLA-PEGPLLA and PDLA-PEG-PDLA obtained from Gel Permeation Chromatography (GPC) were 90,000 and 85,400 g/mol, respectively, as well as dispersity indices were 2.8 and 2.1, respectively. As measure by Differential Scanning (DSC), glass transition temperatures (T_g) of the PLLA-PEG-PLLA and PDLA-PEG-PDLA were 31 and 29 °C, respectively. Their melting temperatures (T_m) were 171 and 170 °C, respectively. The obtained copolymers were granulated before vacuum drying at 110 °C for 3 h to remove any unreacted lactide. Tetracycline ($C_{22}H_{24}N_2O_8$) was used as a water-insoluble model drug. Dichloromethane (CH_2Cl_2) was used as a dissolving solvent.

Preparation of blend film

PLLA-PEG-PLLA and PDLA-PEG-PDLA copolymers were firstly mixed at the ratio of 100/0, 90/10, 80/20, 70/30, 60/40 and 50/50 in a total weight of 0.2 g and then dissolved in 10 mL dichloromethane. The mixture of PLLA-PEG-PLLA and PDLA-PEG-PDLA copolymer solutions were vigorously stirred for 3 h, and then casted onto a 4.5 cm diameter petri dish followed by solvent evaporation at room temperature for 24 h. The films were peeled off and dried in a vacuum oven at 50 °C for 72 h to evaporate any residue solvent.

For drug-loaded blend films, the tetracycline model drug was added into the polylactide-b-poly (ethylene glycol)-b-polylactide triblock copolymer films at 2% wt of each blend film before dissolving the mixture using 100 mL dichloromethane. The drug-loaded blend films were prepared by film casting as described above. The obtained films were kept in a desiccator until investigation.

Morphological observation

All of the films were dehydrated and cut into ~1cm length before observing their morphology using a scanning electron microscope (SEM) (JEOL, JSM-6460LV, Tokyo, Japan). The film fractures were coated with gold (Au) to enhance conductivity before scanning.

Results and discussion

The morphology of all films was observed under scanning electron microscope. Figure 1 shows PLLA-PEG-PLLA/ PDLA-PEG-PDLA blend films at six different ratios without tetracycline at 1000X magnification. The pure PLLA-PEG-PLLA film had smooth both in surfaces and cross-section without phase separation (Fig. 1a). The PLLA-PEG-PLLA/ PDLA-PEG-PDLA blend films (Fig. 1b-f) had irregular patterns of pores in their surfaces with inconsistent shapes and sizes. At 20% (Fig. 1c) and 40% (Fig. 1e) of PDLA-PEG-PDLA ratios, the surfaces of films had the highest number of small pores in range of 1-10 μm. However, the smoothness of the blend films gradually increased when PDLA-PEG-PDLA increased as shown by cross-sections. The details of pores and textures were clearly by increasing higher magnification as shown in Figure 2. The results indicated that the small pores appeared only on the surfaces of films. This was due to the evaporation of the dissolving solvent in the dried process. In addition, the dense and smooth textures of the PLLA-PEG-PLLA/ PDLA-PEG-PDLA blend films were caused by stereocomplexation.

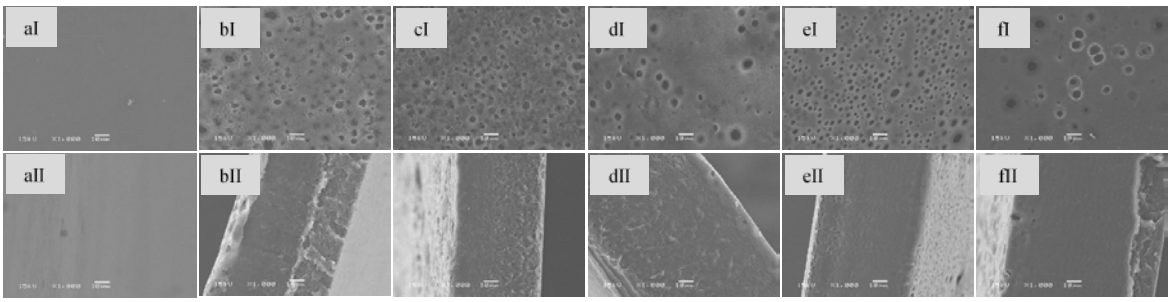

Figure 1 SEM micrographs of the PLLA-PEG-PLLA/PDLA-PEG-PDLA blend films at different ratios; (a) 100/0, (b) 90/10, (c) 80/20, (d) 70/30, (e) 60/40 and (f) 50/50 without tetracycline under 1000X magnifications. I and II present the surface and cross section of films, respectively. (All scale bars = 10 µm).

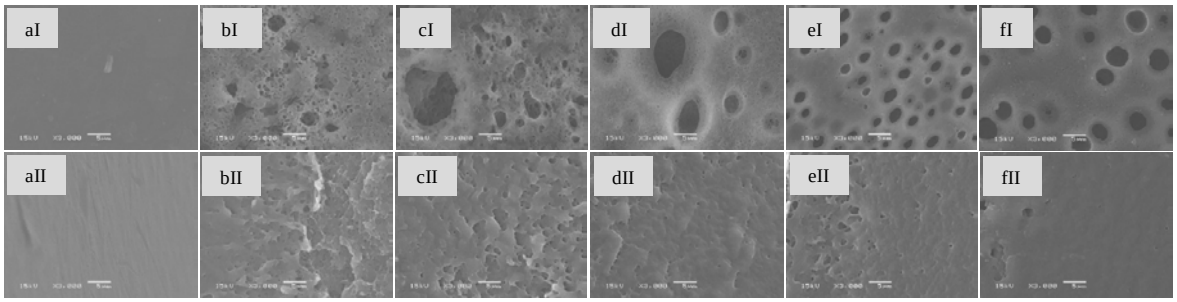

Figure 2 SEM micrographs of the PLLA-PEG-PLLA/PDLA-PEG-PDLA blend films at different ratios; (a) 100/0, (b) 90/10, (c) 80/20, (d) 70/30, (e) 60/40 and (f) 50/50 without tetracycline under 3000X magnifications. I and II present the surface and cross section of films, respectively. (All scale bars = 5 µm).

Figure 3 shows the SEM micrographs of films containing tetracycline prepared from different ratios of PLLA-PEG-PLLA and PDLA-PEG-PDLA both surface and cross-section. The PLLA-PEG-PLLA film (Fig.3a) showed a smooth surface without phase separation as like as a cross-section. The texture of films found some particles (lower 2 µm in size) distributed covered the surfaces which suspected that were tetracycline model drug. Considering the obtained PLLA-PEG-PLLA/ PDLA-PEG-PDLA blend films as shown in Fig. 3b-f, all films had pores with about 2-3 µm on their surfaces. The pores in the surfaces gradually increased in sizes and the number. The results indicated that increasing of PDLA-PEG-PDLA ratio resulted to obtain a high number of pores and consistency of pore sizes. However, cross-sections of all blend films still homogeneous texture and gradually increased when the PDLA-PEG-PDLA increased. At high magnification (Fig.4), the pure PLLA-PEG-PLLA film showed some small pores in its surfaces but still homogeneous texture as shown in cross-section (Fig.4a). In the PLLA-PEG-PLLA/ PDLA-PEG-PDLA blend films (Fig. 4b-f), the surfaces had smoother than pure PLLA-PEG-PLLA film and gradually increased of smooth surfaces by increasing of the PDLA-PEG-PDLA ratios. This might be caused by stereocomplexation between the copolymers. Moreover, pores at the surfaces of films were also increased by increasing PDLA-PEG-PDLA contents but not found as shown in cross-section textures. This was confirmed the stereocomplex formation occurred inside the center of films and resulting in dense and smooth textures.

The results indicated that the tetracycline did not interfere the formation of stereocomplex of PLLA-PEG-PLLA/ PDLA-PEG-PDLA blends. Comparison between non-drug-loaded and drug-loaded blend films, differences in their morphology were observed, especially texture and pore distribution. The drug-loaded blend films slightly had denser in texture than the non-drug-loaded blend films and also had consistent pore on the surfaces. This might be caused by the model drug supported the stereocomlexation of the copolymers. The result was in agree with the previous report about the blend films of this copolymer which prepared by compression method [12]. The obtained results advantaged for using the blended films for encapsulation water-insoluble drugs for drug delivery applications.

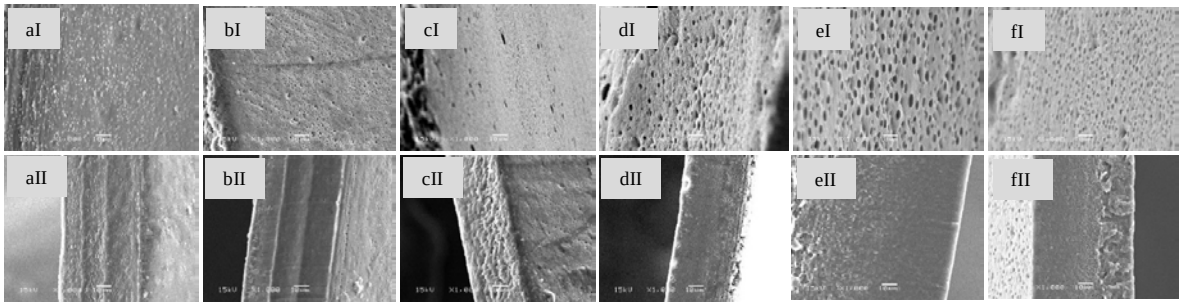

Figure 3 SEM micrographs of the PLLA-PEG-PLLA/PDLA-PEG-PDLA blend films at different ratios; (a) 100/0, (b) 90/10, (c) 80/20, (d) 70/30, (e) 60/40 and (f) 50/50 with tetracycline under 1000X magnifications. I and II present the surface and cross section of films, respectively. (All scale bars = 10 µm).

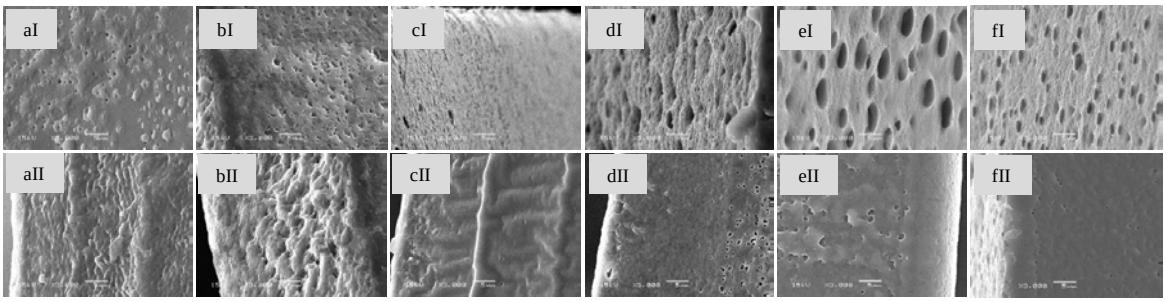

Figure 4 SEM micrographs of the PLLA-PEG-PLLA/PDLA-PEG-PDLA blend films at different ratios; (a) 100/0, (b) 90/10, (c) 80/20, (d) 70/30, (e) 60/40 and (f) 50/50 with tetracycline under 3000X magnifications. I and II present the surface and cross section of films, respectively. (All scale bars = 5 µm).

Conclusions

PLLA-PEG-PLLA/ PDLA-PEG-PDLA blend films were successfully prepared by the solvent casting method. The morphology of the PLLA-PEG-PLLA/PDLA-PEG-PDLA blend films varied by the ratios of PDLA-PEG-PDLA used. The surfaces of the blend films appeared small pores but still had homogeneous texture. The dense and smooth texture of the blend films was caused by stereocomplexation between PLLA-PEG-PLLA and PDLA-PEG-PDLA copolymers which gradually increased by increasing of PDLA-PEG-PDLA ratios. The obtained results could be useful information for the development of controlled-release delivery material, especially water-insoluble drugs.

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