Poly(L-lactic acid)/Pluronic Blends: Characterization of Phase Separation Behavior, Degradation, and Morphology and Use as Protein-Releasing Matrices

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ABSTRACT: A new series of degradable polymeric matrices were prepared by blending poly(L-lactic acid) (PLA) and nonionic Pluronic surfactants, triblock copolymers of poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO). The water content of the polymer blend films was controlled by mixing different types of block copolymers and by adjusting their amount. Physicochemical and morphological properties such as phase separation behaviors, degradation rates, and surface properties of PLA/Pluronic blend films have been characterized by differential scanning calorimetry (DSC), infrared spectroscopy (IR), gel permeation chromatography (GPC), and scanning electron microscopy (SEM). DSC studies suggested that blends with some degree of Pluronic miscibility in the amorphous region of PLA can be obtained by selecting polymer surfactants with suitable hydrophobicities. This resulted in the formation of films with an overall intact surface morphology (SEM). In aqueous solution, the blends revealed the typical liquid-crystalline phase transition of Pluronic polymers, suggesting the formation of a gellike structure within the PLA skeleton. PLA degradation rates were not affected by the blending procedure although the hydration degree in these matrices was higher, suggesting a complex mechanism of hydrogen bond formation between the carboxylic groups of PLA and the ethers of the surfactant polymers. When used as drug-releasing matrices, these blends extended protein release and minimized the initial protein burst compared to the pure polymer.

Introduction

Recently, a variety of degradable polymers have been used as implantable biomaterials and drug-delivery devices.[1,2] The main advantage of these polymers is that no retrieval of the device is needed after usage. In particular, PLA [poly(L-lactic acid)] has been widely utilized, since its degradation product, lactic acid, is metabolized in the body.[3] The degradation time of a polymeric device and release period of a particular drug can be varied from months to years, depending on the degradation rate of PLA. This is controlled by the molecular weight and chemical composition via copolymerization with its chiral isomeric monomer, D-lactic acid, and/or glycolic acid.[4] Amorphous/crystalline and hydrophilic/hydrophobic properties also determine the degradation time. In an attempt to modify the degradation behavior of PLA, copolymers of lactic acid/ethylene oxide,[5-7] lactic acid/ϵ-caprolactone,[8] and lactic acid/amino acid[9] have been synthesized and characterized.

A different approach is blending two different polymers. Generally, blends exhibit advantageous physical and mechanical properties that each individual polymer does not have.[10] Depending on the thermodynamic compatibility of the two chosen polymers, phase-separated polymers can be obtained, imposing different morphologies and matrix characteristics and different drug release rates. However, only a few attempts to use the blend concept for drug delivery applications have been made. For example, PLA was blended with degradable and nondegradable polymers such as poly(D-lactic acid),[11] poly(glycolic acid),[12] and poly(ethylene–vinyl acetate)[13] in an effort to modify PLA morphology and its degradation behavior, although drug release profiles from these blends have not been examined in detail.

Here we report the preparation and characterization of a new type of PLA blend with a series of nonionic Pluronic surfactants, poly(ethylene oxide) (PEO)/poly(propylene oxide) (PPO)/poly(ethylene oxide) (PEO) triblock (ABA type) copolymers. PEO/PPO/PEO block copolymers exhibit a wide range of hydrophilicity/hydrophobicity as a function of the PEO/PPO ratio, so that one can expect to obtain different phase-separated morphologies with PLA as well as different degrees of hydration of the matrix. In particular, hydration plays an important role in determining polymer degradation via hydrolysis of the ester backbone. These polymeric surfactants exhibited minimal toxicities in vivo, and some of them are in clinical use.[14-16] A series of PLA/PEO–PPO–PEO blend films were prepared by a solvent-casting method. Physical and morphological studies of the resultant films were carried out using differential scanning calorimetry (DSC), infrared spectroscopy (IR), scanning electron microscopy (SEM), and gel permeation chromatography (GPC). A model protein drug, bovine serum albumin, was loaded into the polymer blend films to examine the effect of morphological changes in polymer blends on protein release patterns (i.e., extent of initial protein burst and release period).

Experimental Section

Materials. PLA (MW = 100 000) was obtained from Polysciences. GPC analysis revealed a weight-average and number-average molecular weight of 71 000 and of 60 000, respectively. Pluronic triblock copolymers were kindly donated by BASF Corp. Fluorescein-labeled bovine serum albumin (FITC-BSA) was purchased from Sigma Co. All other reagents were analytical grade.

Methods. Blend Film Preparation. PLA was dissolved in 3 mL of methylene chloride with varying amounts of Pluronic L-101, F-108, and P-104. The total amount of polymer mixture was 0.5 g. Polymer solution was cast onto presilanized glass Petri dishes, and the solvent was evaporated at room temperature overnight under vacuum. For FITC-BSA-loaded blend films, 20 mg of FITC-BSA dissolved in 0.5 mL of 0.1 M phosphate buffer (pH 7.4) was emulsified in the above polymer solution with a

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Table I
Physical Characteristics of Pluronic

	Pluronic		
	F-108	P-104	L-101
physical state at room temp	solid	paste	liquid
water solubility	soluble	moderate	insoluble
molecular wt	14600	5900	3800
ethylene oxide, wt %	80	40	10

vortex mixer and then cast onto the glass plate.

Water Content Determination. Dry blend films without BSA loading were incubated in phosphate-buffered saline (PBS), pH 7.4, at 37 °C. At preset time intervals, hydrated samples were taken and weighed after blotting the surface water with tissue. Thus, the wet weight included the amount of free water in the pore region of the matrix, the amount of bound water associated with the polymer, and the dry weight of the polymer. Dry weights were determined after complete drying of the hydrated samples under vacuum for over 24 h. Water contents were then calculated based on the dry wet weights. Weight change of the blend films was based on the difference of dry weights before and after 1 week of incubation at 37 °C in the buffer.

Infrared (IR) Spectroscopy. IR (Perkin-Elmer Model 1420) spectra were taken by dissolving the blend films in methylene chloride and casting them onto sodium chloride cells.

Differential Scanning Calorimetry (DSC). DSC (Perkin-Elmer Series 7) thermograms were taken using a standard aluminum pan. Nitrogen was used as a sweeping gas, and the heating rate was 10 °C/min. Samples (3–5 mg) were loaded without further heat treatment. For hydrated samples, volatile sample sealer was used to prevent water evaporation during heating. All the samples for DSC were dehydrated or hydrated blend films without BSA loading.

Scanning Electron Microscopy (SEM). Samples were coated with gold particles to a thickness of 200–500 Å. Surface morphology of PLA/Pluronic blend films was examined using an Amary 1000 A scanning electron microscope at 20-kV electron beam radiation.

Gel Permeation Chromatography (GPC). The molecular weight of PLA was determined by a Perkin-Elmer Series 10 liquid chromatograph with an LC-25 RI detector and using a Phenomenex PL gel 5-μm mixed column. Chloroform was used as an eluant. Chromatograms were processed by GPC 5 software to calculate the weight-average molecular weight of the polymer using polystyrene as a standard.

BSA Release Study. FITC-BSA-loaded polymer blend films were punctured in the shape of disks (6.35 mm in diameter and about 0.5 mm in thickness). They were incubated in 5 mL of PBS, pH 7.4, at 37 °C. The amount of released FITC-BSA at various time intervals was assayed by monitoring the absorbance at 495 nm.

Results and Discussion

Water Contents in Polymer Blends. Pluronic surfactants exhibit a wide range of different hydrophilic/hydrophobic properties depending on the molar ratio of the hydrophilic ethylene oxide (EO) unit and the hydrophobic propylene oxide (PO) unit in their triblock copolymers. Table I lists the physicochemical properties of the three Pluronic surfactants used in this study, F-108, P-104, and L-101. L-101, which has a low ratio of EO to PO, is the most hydrophobic (i.e., least water soluble). Since these triblock copolymers have an amphiphilic structure, normally found in surfactants, they exhibit temperature-dependent rheological properties in aqueous solutions, that is, a gelation above a certain temperature.[17] The gel formation is particularly pronounced in water-soluble Pluronic surfactants which have high EO/PO ratios. Water–Pluronic interactions may play an important role in such a thermal phase transition of aqueous polymer solutions.

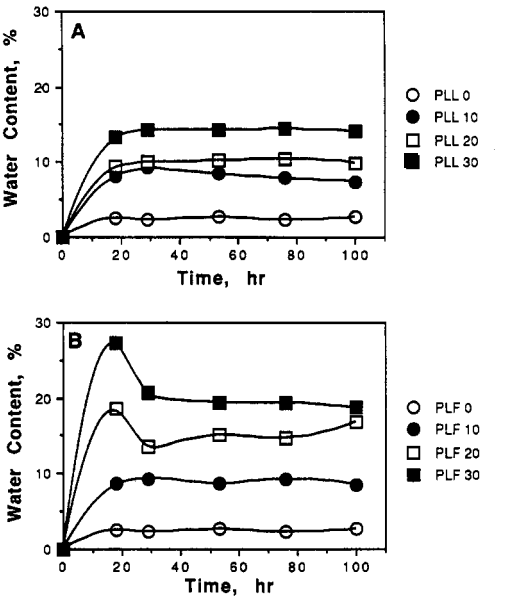

Figure 1. Water contents of PLA/L-101 and PLA/F-108 blend films without BSA loading incubated in PBS, pH 7.4, at 37 °C. PLL(F) X indicates PLA/L-101(F-108) with X% weight fraction of L-101 (F-108) in the blend.

A typical biodegradable PLA is relatively hydrophobic and it has a semicrystalline structure. Degradation proceeds via nonenzymatic, hydrolytic breakage of the ester backbone bond. Water accessibility to these bonds will determine the rate of degradation. It takes months to years for complete degradation of PLA matrices, depending on the molecular weights.[4] Blending PLA with Pluronic is expected to produce different degrees of matrix hydration depending on the choice and amount of Pluronic. Thus, one can expect that degradation will be accelerated by a high water concentration in the vicinity of the hydrolytically labile ester bond. In this study, a variety of blend films, PLA/L-101, PLA/F-108, and PLA/P-104, were prepared. They were denoted as PLL, PLF, and PLP. The PLA/L-101 blend films were mechanically strong enough to handle, while the PLA/F-108 blend films were brittle with increasing F-108 amount.

Figure 1 shows the hydration degree for blends of PLA with L-101 and F-108 without BSA loading as a function of incubation time in PBS, pH 7.4, at 37 °C. All blends showed high water content relative to the homogeneous PLA; the water content increased with increasing amounts of Pluronic in the blends. The more hydrophilic F-108 blends exhibited higher water contents than the L-101 blends. These blends showed an initial overshoot followed by a decrease in the water content. It is believed that this is due to a rapid diffusion of the highly water soluble F-108 out of the blend, as water penetrates and dissolves it. This is supported by the weight change measurements (Figure 2) of the PLA/F-108(70/30) blend that showed a net dry weight loss of more than 20% after 1 week of incubation in PBS. Initially, it was thought that the PLA/F-108 blends might exhibit a small dry weight loss due to a gelation phenomenon at 37 °C, caused by temperature-dependent water–F-108 interactions in the pore of the blend matrix.[17] The weight loss experiment was separately carried out after 1 week of incubation, since leaching of F-108 (MW = 14 600) out of the blend matrix might be a complex mixture of processes such as water diffusion-in, F-108 dissolution, and F-108 diffusion-out. Nevertheless, the finding that F-108 leaches out of the polymer blend film upon hydration, possibly leaving water-filled pores, suggests the possibility of using the blend technology to

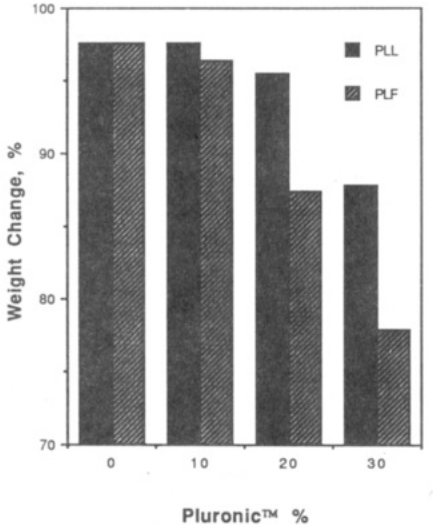

Figure 2. Remaining weight of PLA/L-101 (PLL) and PLA/F-108 (PLF) blends without BSA loading after 1 week of incubation in buffer.

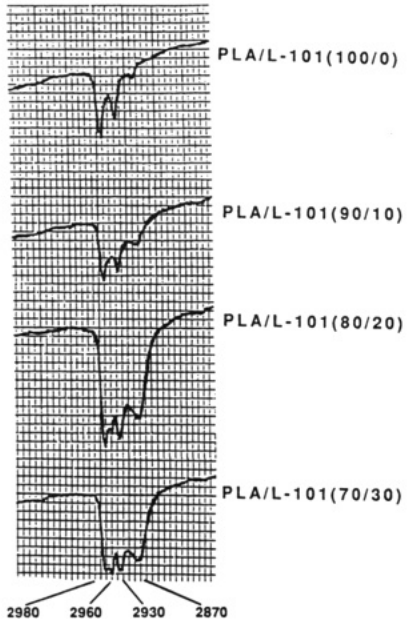

Figure 3. IR spectra of PLA/L-101 blends without BSA loading after a 30-day incubation in buffer.

create highly porous biodegradable matrices to be used as a scaffold for certain applications such as cell delivery.[18] By adjusting the amount of incorporated surfactant, the porosity of the polymer matrix can be controlled.

On the other hand, a relatively high amount of the hydrophobic L-101 was still retained in the blend matrices after this time period (Figure 2). In the case of the PLA/P-104(80/20) blend, the percent weight decrease after 1 week was 7.5%, an intermediate value between L-101 (4.5%) and F-108 (12.6%) blends having the same initial ratios of Pluronic (20%). This result suggests that the water solubility of Pluronic is indeed an important parameter in determining the amount of Pluronic leaching out of the blend matrices. The presence of the L-101 in the blend films was further confirmed by IR spectra acquired after a 30-day incubation (Figure 3). A broad band at 2870 cm^{-1}, corresponding to the CH_2 stretching on the PO unit of L-101, appeared, and its size increased with increasing amount of L-101 in the blend. The peaks at 2980 and 2930 cm^{-1} are assigned to the CH antisymmetric stretching and CH_3 stretching band of PLA.

Table II
Effect of Pluronic Blending on PLA Crystalline Melting Enthalpy[a]

PLA/Pluronic blend	T_m, °C	ΔH, J/g of PLA	T_g, °C
PLA (MW = 71 000)	177.3	46.8	55.9
PLA/F-108	177.3	50.7	47.9
PLA/P-104	177.1	49.4	N/A
PLA/L-101	176.5	46.1	52.9

[a] Weight fraction of Pluronic is 20% in the blend.

Phase Behavior in Polymer Blends. The thermodynamic compatibility between PLA and Pluronic is expected to vary depending on the type of Pluronic. Although the water solubility of Pluronic changes with the PEO/PPO ratio, the solubility parameters of the hydrophobic PPO segment (7.5–9.9)[19] and PLA (9.5–9.8)[5] are close. Thus, some degree of phase mixing can be expected. However, since no significant acid–base interaction and/or hydrogen bonding between PLA and Pluronic can be expected except for those between the hydroxyl and carboxyl end groups in PLA and between the backbone ether and terminal hydroxyl group in Pluronic, PLA/Pluronic blends might have a phase-separated domain structure. Indeed, the PLA/Pluronic blend films are all opaque, indicating the phase-separated structure, while the homo-PLA film is translucent. However, the physical appearance of the blend film is only indirectly indicative of polymer miscibility, and the degree of phase separation cannot be assessed quantitatively. Thus, DSC studies were carried out to examine and quantify the extent of phase separation. A shift in glass transition temperature (T_g) provides direct evidence of polymer miscibility.[19] While PLA has a clear T_g around 55.9 °C (data not shown), the PLA/Pluronic blends exhibited a rather broad endotherm around the glass transition temperature of PLA, making it hard to determine the precise T_g as a function of Pluronic weight fraction. Nevertheless, the estimated T_g's for the blends were lower than that of PLA (Table II), suggesting the disturbed amorphous region of PLA by the Pluronic, which may act as a plasticizer. The crystalline melting temperature (T_m) of PLA is also used to evaluate the extent of phase separation in the blend. When two polymers are compatible in the amorphous state, the T_m is depressed as a result of the disturbed order in the crystalline phase.[19,20] As shown in Table II, a slight shift in T_m of PLA was observed upon blending a more hydrophobic Pluronic surfactant, while T_m is essentially the same when blending with F-108 and P-104. These results indicate a phase separation in the cases of F-108 and P-104 blends and a slight phase mixing in the hydrophobic L-101/PLA blend. The crystalline melting enthalpy (ΔH) data show the higher crystallinity values in blends of F-108 and P-104 than in the L-101 blend or PLA. Since T_m is related to crystalline structure and size and ΔH to crystallinity,[21] this result implies that the hydrophilicity/hydrophobicity of Pluronic appears to affect the nucleation and growth of crystalline spherulites by changing the interfacial free energy between the crystalline and amorphous phase in the PLA. In fact, the hydrophobic L-101/PLA blend had a much smaller crystalline size than the F-108/PLA blend and the homo-PLA. However, one can also not rule out the phase mixing possibility between the amorphous regions of PLA and Pluronic surfactants because these regions have more polymer chain flexibility than the crystalline region for polymer–polymer miscibility. Figure 4 shows the effect of L-101 and F-108 on PLA melting enthalpy. As seen, ΔH decreases with the increase in Pluronic amount due to the smaller weight fraction of PLA in the blends. Although the calculated

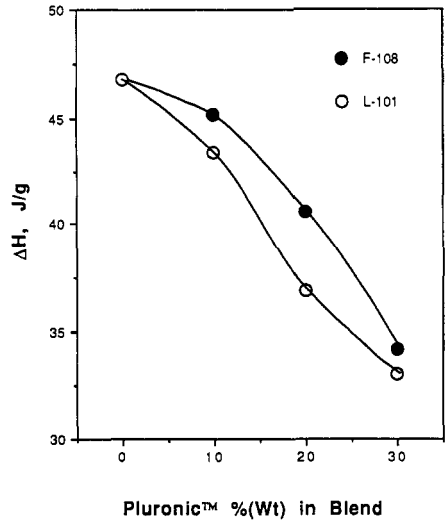

Figure 4. Effect of L-101 and F-108 blending on PLA crystalline melting enthalpy.

crystallinities (normalized to PLA fraction in the blend) are higher for the F-108 than that for the L-101 (Table II), the decrease in ΔH in the blends is more pronounced for the L-101 than the F-108 with increasing amount of Pluronic surfactants. This indicates that the hydrophobic L-101 may be more readily intermixed with the polymer chains of PLA in the amorphous region and is consistent with the finding that a smaller amount of L-101 is leached out during the incubation in buffer (Figure 2). It has been reported that block copolymers act as a phase compatibilizer in the blend to enhance the phase mixing.[20] However, it is unclear at this point to what extent Pluronic surfactants are compatible with the amorphous region in the PLA. Due to the leaching of the hydrophilic F-108 from the blend, only PLA/L-101 blends were further investigated for protein delivery applications.

Since blend films will be incubated in aqueous solutions, phase separation between PLA and L-101 should be considered in the presence of a third component, water. It is expected that water will preferably interact with the hydrophilic ethylene oxide part of a Pluronic surfactant that is entangled in the amorphous region of PLA. PEO/PPO/PEO triblock copolymers exhibit a complicated self-aggregation behavior in aqueous solution due to micelle formation.[17] It has been reported that water–nonionic polymeric surfactant interactions lead to a liquid-crystalline phase at low water concentrations.[22,23] Thus, it is conceivable that in aqueous solution, an L-101–water liquid-crystalline phase will be formed within the porous region of PLA. The term "liquid crystalline" here refers to any self-assembled and ordered molecular structure which includes the "gel" formation, often found in the hydrophilic Pluronic surfactant–water system above a certain temperature range. DSC studies were carried out to prove the existence of such a liquid-crystalline phase. A DSC thermogram of PLA/L-101 blend films, dried after 7 days of incubation, did not show any noticeable peaks except for a very broad T_g around 60 °C and a crystalline melting peak of PLA around 175 °C (data not shown). In contrast, the hydrated films showed an apparent liquid-crystalline phase transition peak which appears to shift to higher temperatures with an increasing amount of L-101 in the blend (Figure 5). It is suggested that a more ordered liquid-crystalline phase may be formed as more L-101 is incorporated. The exact nature of the peaks is not clear at this moment. However, according to previous calorimetric studies of poly(ethylene oxide)[24] and hydrophilic Pluronic surfactants (F-127 and P-104),[17] these may be caused by either the dehydration of ethylene oxide groups[24] or the dehydration (or melting) of propylene oxide groups[17] in the L-101 surfactant, as the temperature was increased. The very broad endotherm for the PLA sample, apparently a typical T_g, may be due to the disturbed glassy structure by the hydration.

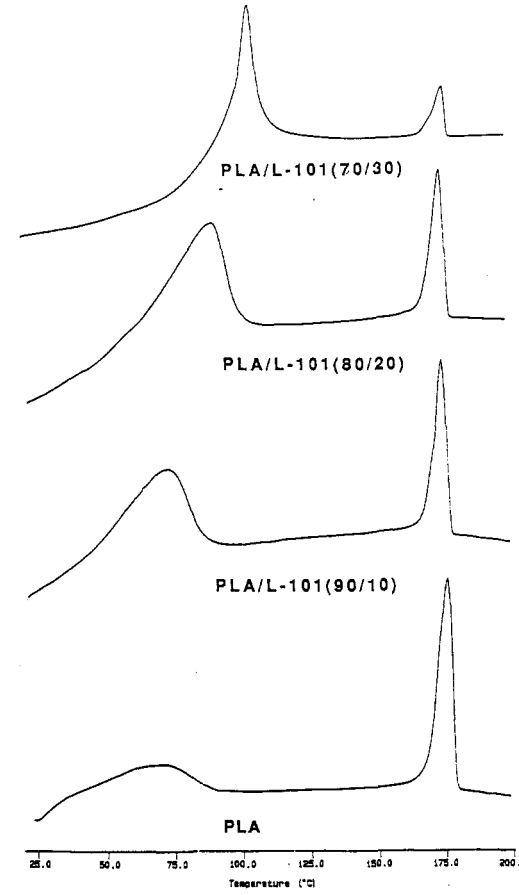

Figure 5. DSC thermogram of hydrated PLA/L-101 blend films without BSA loading.

The surface compactness of the PLA/L-101 blends was examined by SEM. Figure 6 shows that the homo-PLA film surface has spherulites, crystalline domains along with pores, which are probably formed by the rapid evaporation of the organic solvent. On the other hand, the surface of PLA/L-101(80/20) film has a rough morphology without pores. The spherulite sizes are smaller than those observed with the PLA film, supporting the DSC data of a slight T_m shift for the PLA/L-101 blends (Figure 4). A magnified view of the surface revealed that the PLA crystalline domains (spherulites) are covered by L-101 which appears to be also crystallized radially (Figure 6C). Although L-101 is a liquid at room temperature, it is possible that PEO segments are crystallized while PPO segments are anchored on the spherulites. Figure 6 also indicates that a rapid crystallization of PLA upon solvent removal induces spherulite formation, while the polymeric L-101 may be entangled within the amorphous PLA chains, producing an overall nonporous surface. The same surface morphology was observed after 1 week of hydration, again implying that no significant loss of L-101 from the blend has occurred with time.

Degradation Studies. PLA has been known to degrade slowly because of its hydrophobic and semicrystalline structure which does not allow fast water penetration. The degradation rate is proportional to water and ester concentrations and is autocatalyzed by the generated car-

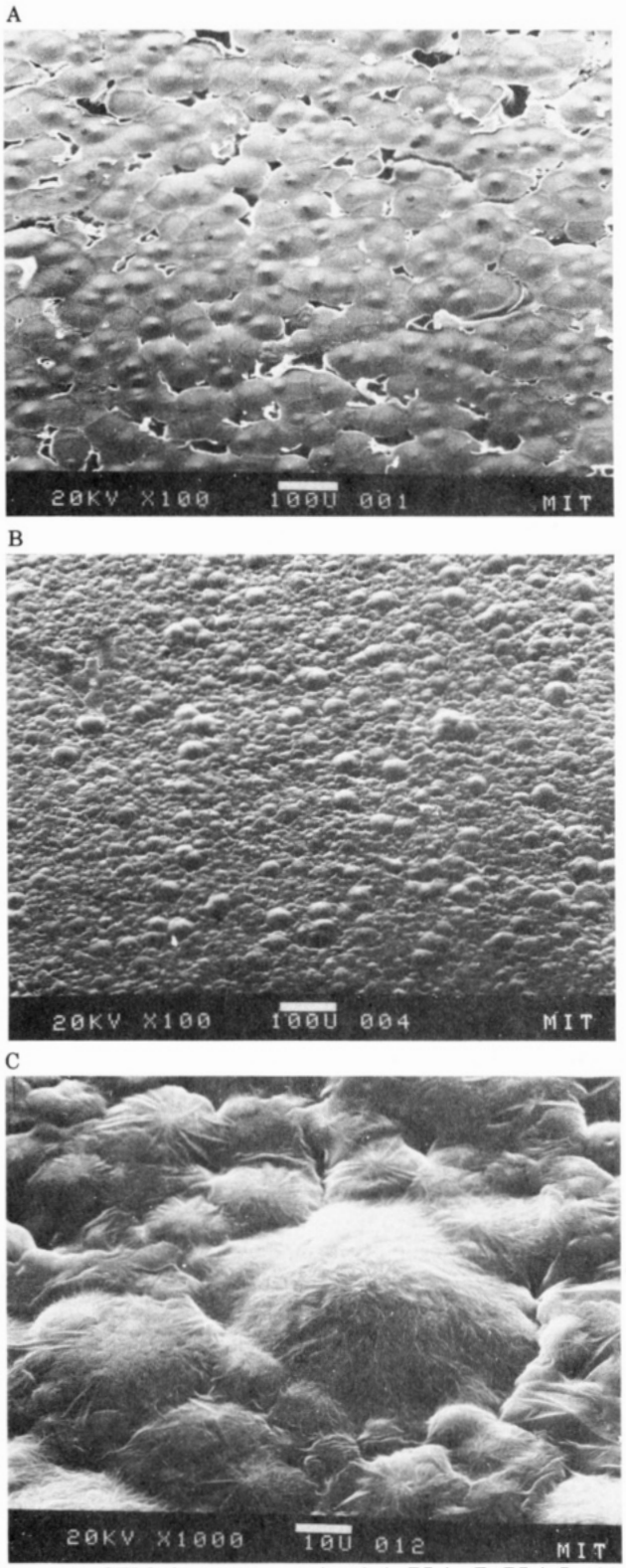

Figure 6. SEM photomicrographs of (A) PLA, (B) PLA/L-101-(80/20), and (C) PLA/L-101(80/20) at increased magnification. Bar in the middle of bottom indicates a scale.

boxylic end groups. It can be expressed as follows:

$$\text{degradation rate} = k[H_2O][COOH][\text{ester}]$$

When Pluronic L-101 is blended with PLA, it is expected that the PLA degradation rate would be modified due to changes in water concentration. A more hydrated sample will be hydrolyzed faster due to water accessibility in the vicinity of the ester bonds. Figure 7 shows the change in the molecular weights of PLA and PLA/L-101(70/30)

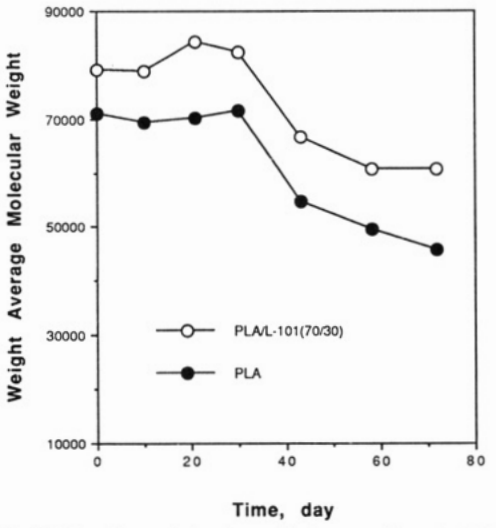

Figure 7. Molecular weight degradation profiles for PLA and PLA/L-101(70/30) blend films without BSA loading.

samples as a function of time. It is of interest to note that PLA molecular weights in a PLA/L-101(70/30) blend are approximately 10 000 higher than those of the homo-PLA at all time points. This might be due to nonspecific chain entanglement and/or complex formation between PLA and L-101 polymer chain (MW = 3800) in chloroform via hydrogen bonding between the terminal carboxylic groups and the ether bonds of L-101. In fact, it is known that the polymers containing carboxylic acid groups are readily miscible with polyethers via hydrogen bonding.[19] After an induction period of 30 days, both the PLA and the PLA/L-101 blend apparently start to degrade at a similar rate. The time lag observed in the degradation may be due to the slow hydration rate in the PLA crystalline region. Weight loss measurements revealed that the films retained their mass during the degradation period (data not shown). This is consistent with the fact that random hydrolytic chain cleavage of the polymer backbone proceeds until a critical molecular weight is reached, from which weight loss begins with the diffusion of cleaved water-soluble fragments out of matrix.[25] The apparent similarity of the degradation rates for both samples, at least during the studied period, suggests that L-101 does not significantly affect the overall degradation of PLA. This might be explained by the two opposite effects that are imposed by L-101 blending on PLA degradation. On the one hand, L-101 increases matrix hydration and thus enhances the degradation rate. On the other hand, formation of hydrogen bonds between the terminal carboxylic groups of PLA and the ether bonds of L-101 reduces the autocatalytic contribution of free carboxylic acid, thus decreasing the rate of degradation. Thus, although the increasing hydration causes cleavage of the ester linkage, the generated terminal carboxylic groups are not available for further catalytic degradation because of immediate hydrogen bonding with ether bonds.

Protein Release from Polymer Blends. Protein release from polymeric matrices has been extensively studied in the past years, where variable release profiles were achieved by selecting suitable polymer matrices, shape, preparation method, protein loading, and particle size as well as many other factors.[26,27] When matrices are prepared by solvent casting, the evaporation rate of the organic solvent plays an important role in the formation of pores in the matrix, eventually leading to protein dumping at an initial stage, i.e., the "burst" effect. Slow removal of the organic solvent at low temperatures is one

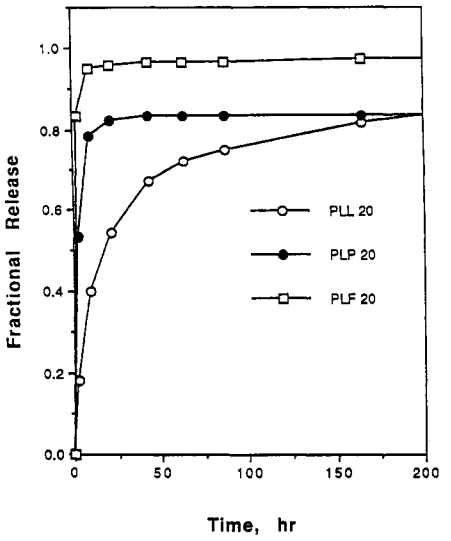

Figure 8. Effect of Pluronic blending on BSA release. Weight fractions of Pluronic are 20%.

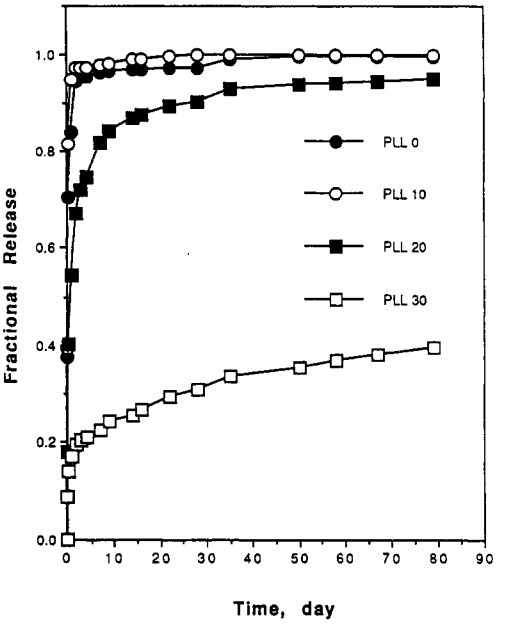

Figure 9. Effect of L-101 blending on BSA release. PLL X indicates X% weight fraction of L-101.

way to decrease the burst effect. Here, the possibility of decreasing the protein burst was examined by blending PLA with Pluronic. This is based on our finding that blends of PLA and L-101 produced films with an intact surface morphology. Figure 8 shows the effect of different Pluronic blends on BSA release. The relatively hydrophobic Pluronic L-101 was more effective than the hydrophilic F-108 in decreasing the initial protein burst as well as prolonging the release period. These results agree with the finding that the relatively hydrophilic Pluronic F-108 is quickly leached out at the initial stage of incubation, leading to a fast BSA release, while the PLA/L-101 blend film, where L-101 is entangled with the amorphous PLA chains, indeed delayed BSA release. The PLA/P-104 blend, which has a moderate hydrophilicity/hydrophobicity, exhibits an intermediate burst. The slow release of BSA may be explained by the morphological changes that occur in the interconnecting porous channels of PLA blended with L-101 upon hydration. When blend films are incubated in aqueous solution, water penetrates into the matrices to first hydrate the amorphous region of the PLA/Pluronic blend. As a result, the PLA/L-101 blend acquires a liquid-crystalline phase which fills the pores. This phase holds the BSA molecules within the pores and prevents their fast release. This is supported by the finding that the release rates of BSA can be controlled by the amount of L-101 that is incorporated into the blends (Figure 9). Thirty percent (w/w) L-101 in the blend resulted in a system that controlled the release of BSA for more than 80 days while with 10% in the blend more than 95% of BSA was released after 3 days of incubation.

There have been a few studies on the liquid-crystalline phase formed by nonionic surfactant–water interactions, yet its physical nature is not well understood. It was reported that a mixture of water and nonionic surfactant, Brij 96 (poly[oxyethylene(10) oleyl ether]) possibly exhibits a variety of liquid-crystalline structures such as lamellar, viscous isotropic, and hexagonal gel, depending on the mixing ratio.[23] The different liquid-crystalline phases demonstrated different diffusion coefficients for a particular drug due to changes in the morphology of the aqueous porosities and tortuosities. Protein release from the above liquid-crystalline phase should occur via arrays of hydrophilic and aqueous pores created by the self-assembled hydrophobic domains. It is, therefore, likely that the macromolecular protein has a low effective diffusion coefficient in such a creamy gel structure, since now the aqueous porous channels have a relatively small volume compared to the hydrophobically organized domains. At this point, it is not certain what type of liquid-crystalline phase is formed in the blend film. It is also puzzling what the role is of the amorphous PLA chains in the formation of the liquid-crystalline phase. If there is a chain entanglement between PLA and L-101 as was implicated earlier, compactness in the liquid-crystalline phase may be disturbed. Possibly, the hydrophilic poly(ethylene oxide) (PEO) segments may preferably be oriented to the aqueous phase, while the hydrophobic poly(propylene oxide) (PPO) segment is anchored onto PLA polymer chains in the amorphous region to minimize interfacial energy. This structure is indirectly supported by other studies that showed that Pluronic surfactants can adsorb to hydrophobic polymer surfaces, lowering their interfacial energy. These types of surfaces do not promote protein adsorption and minimize cell adhesion.[28] Thus, it is probable that the PLA/L-101 blends may be also suitable as biocompatible, implantable materials.

In summary, it has been shown that PLA could be physically blended with nonionic polymeric surfactants, Pluronics, to form a matrix where the surfactants may be entangled in the amorphous region of PLA. Upon hydration, the blends acquire an additional liquid-crystalline phase that is now imbedded between the PLA crystalline phase, producing an overall intact surface morphology. This resulted in drug release profiles with a minimum initial protein burst and a longer time release.

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Registry No. PLA (homopolymer), 26811-96-1; PLA (SRU), 26161-42-2; Pluronic, 106392-12-5.