

XPS and Wettability Characterization of Modified Poly(lactic acid) and Poly(lactic/glycolic acid) Films

É. Kiss,^{*,1} I. Bertóti,[†] and E. I. Vargha-Butler[‡]

^{*}L. Eötvös University, Department of Colloid Chemistry, P. O. Box 32, Budapest 112, H-1518, Hungary; [†]Research Laboratory for Materials and Environmental Chemistry, Chem. Res. Center, Hungarian Academy of Sciences, P. O. Box 17, H-1525, Budapest, Hungary; and [‡]Department of Mechanical and Industrial Engineering, University of Toronto, Toronto, Ontario M5S 3G8, Canada

Received June 25, 2001; accepted September 3, 2001

Poly(lactic acid) (PLA) and poly(lactic/glycolic acid) copolymers (PLGA) are biodegradable drug carriers of great importance, although successful pharmaceutical application requires adjustment of the surface properties of the polymeric drug delivery system to be compatible with the biological environment. For that reason, reduction of the original hydrophobicity of the PLA or PLGA surfaces was performed by applying a hydrophilic polymer poly(ethylene oxide) (PEO) with the aim to improve biocompatibility of the original polymer. PEO-containing surfaces were prepared by incorporation of block copolymeric surfactants, poly(ethylene oxide)–poly(propylene oxide)–poly(ethylene oxide) (Pluronic), into the hydrophobic surface. Films of polymer blends from PLA or PLGA (with lactic/glycolic acid ratios of 75/25 and 50/50) and from Pluronics (PE6800, PE6400, and PE6100) were obtained by the solvent casting method, applying the Pluronics at different concentrations between 1 and 9.1% w/w. Wettability was measured to monitor the change in surface hydrophobicity, while X-ray photoelectron spectroscopy (XPS) was applied to determine the composition and chemical structure of the polymer surface and its change with surface modification. Substantial reduction of surface hydrophobicity was achieved on both the PLA homopolymer and the PLGA copolymers by applying the Pluronics at various concentrations. In accordance with the wettability changes the accumulation of Pluronics in the surface layer was greatly affected by the initial hydrophobicity of the polymer, namely, by the lactide content of the copolymer. The extent of surface modification was also found to be dependent on the type of blended Pluronics. Surface activity of the modifying Pluronic component was interpreted by using the solubility parameters. © 2002 Elsevier Science

Key Words: surface modification; wettability; XPS analysis; polymer blends; Pluronics; PLA; PLGA; drug delivery.

INTRODUCTION

The most often studied potential drug carriers among the biodegradable polymers are poly(lactic acid) (PLA) and its copolymers with poly(glycolic acid) (PGA). These polymers

may be utilized as drug delivery systems because their degradation products, both lactic and glycolic acids, are metabolized in the human body (1). Commonly used biodegradable polymers in the form of nanoparticles suffer a major drawback due to their extensive take up by cells of the mononuclear phagocyte system (MPS) (2). The *in vivo* clearance of the particles by the MPS was reported to increase with increasing hydrophobicity (3), while controlled surface modification, which reduces hydrophobicity, decreases the uptake of nanoparticles by the liver and spleen, assuring their longer presence in the bloodstream (4). These previous experiences showed the need both for further studies and for the control of the surface properties of these polymeric micro- and nanoparticles.

Several research groups applied poly(ethylene glycol) (PEG) or poly(ethylene oxide) (PEO) as a surface modifier (5–15) to create biocompatible or cell-nonadhesive polymeric surfaces. PEO, due to its hydrophilicity, chain mobility, and lack of ionic charge has been shown to have protein repellent activity and hence reduces most cellular interactions when immobilized on various surfaces.

To combine the advantageous properties of PEO and biodegradable polymers, one of the approaches is to incorporate PEO chains into the polymer by forming a block copolymer (16, 17). The presence of PEO chains not only regulates the protein release but also prevents the reabsorption of the already released protein molecules (18). Adsorption of PEO-containing compounds onto polymeric micro- or nanoparticles is an alternative method of surface modification of the polymers. Block copolymers anchor with their hydrophobic (center) part on the particle surface, while the hydrophilic PEO chains protrude into the dispersion medium, rendering the surface hydrophilic (19, 20). In all pharmaceutical applications the stability of such an adsorbed PEO-containing layer is of great importance. Desorption or rather displacement of the adsorbed layer by blood components was recognized as a disadvantage. Improved binding to the carrier surface is expected if the modifier is immobilized by surface gelation and entrapment techniques (7, 21) or is introduced during the manufacturing process of the microspheres (22). Blending of biodegradable polymers with a modifying component was developed to control the water content of

¹ To whom correspondence should be addressed. Fax: 36 1 2090602. E-mail: kissevak@ludens.elte.hu.

the drug carrier material and to regulate the protein release rate (23, 24). The surface properties, however, of that kind of polymer blend has not been investigated systematically.

Our aim in the present work was to utilize the blending process for surface modification of biodegradable polymers. The biodegradable polymers, as possible drug carrier materials, involved in this investigation were PLA and poly(lactic/glycolic acid) copolymers (PLGA) with varied component ratios. Three types of poly(ethylene oxide)–poly(propylene oxide)–poly(ethylene oxide) (PEO/PPO/PEO) triblock copolymers (Pluronic) with different compositions and hydrophobicity were used as modifying additives. Surface properties of the blend films were characterized by wettability measurements, while the chemical composition of the surface layer was determined by X-ray photoelectron spectroscopy (XPS).

EXPERIMENTAL

Materials

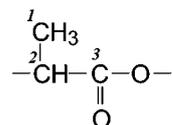
Poly(DL-lactide) (DL-PLA; MW 106,000) and two of its random copolymers with glycolic acid, poly(DL-lactide–coglycolide) (DL-PLGA) with 75/25 (MW 90,000–126,000) and 50/50 (MW 40,000–75,000) component ratios of lactide/glycolide, obtained from Sigma were used in our experiments. PEO–PPO–PEO triblock nonionic surfactants with different compositions, trade named Pluronic PE6100, PE6400, and PE6800 (kindly donated by BASF Hungaria Kft.), were applied for modification of PLA and PLGA. The composition of the Pluronic is characterized by the molecular weight of the central hydrophobic PPO block which is 1750, while the hydrophilic poly(ethylene oxide) contents of the whole molecules are given as 10, 40, and 80% for PE6100, PE6400, and PE6800, respectively (25). Since the PPO blocks are similar in the three Pluronic, the increasing PEO content corresponds to the increasing hydrophilicity of the Pluronic used here. Structural units of the polymers and Pluronic are shown in Fig. 1.

Dichloromethane (p.a., ACS, Merck) was used as solvent for film preparation. Glass plates (microscopic cover glass, 22 × 40 × 0.16 mm; Menzel–Glaser, Germany) were the substrates for casting of the polymer films. All of the chemicals were of analytical grade. Doubly distilled water obtained from a Wagner and Munz Muldestor SE apparatus (München, Germany) checked by conductivity (<5 μS) and surface tension (>72 mN/m at 23°C) was used in sample preparation and also for contact angle measurement.

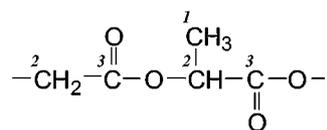
Sample Preparation

The glass surfaces were cleaned in “piranha” solution (3/7 by volume of 30% hydrogen peroxide and concentrated sulfuric acid) for 1 h, rinsed thoroughly with doubly distilled water, and vacuum dried for 16 h at room temperature. The polymer (PLA or PLGA) and the Pluronic were dissolved in a common solvent, dichloromethane, keeping the polymer concentration at 1.0% w/v while the Pluronic concentration varied between 0.01

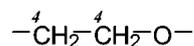
poly(lactic acid), PLA



poly(lactic/glycolic acid), PLGA



poly(ethylene oxide), PEO



poly(propylene oxide), PPO

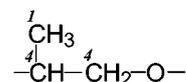


FIG. 1. Structural units of PLA, PLGA, and Pluronic composed of PEO and PPO blocks. (Numbers in italic indicate types of carbons in different chemical environments producing Cls electrons at various binding energies in XPS spectra.)

and 0.1% w/v. The glass slides were coated with 200 μl of the polymer/Pluronic solutions and were allowed to dry slowly by covering the plates with small petri dishes. Final drying was performed in a vacuum at room temperature for 48 h. The Pluronic concentration varied between 1 and 9.1% w/w in the blends.

Wettability

The contact angle of a water droplet on polymer films was measured using the goniometric method (Dataphysics, OCA15, Germany) in a closed chamber saturated with water vapor. Advancing and receding angles were determined by increasing and decreasing the volume of the drop using a motor-driven Hamilton micropipet. Twenty-five to thirty pieces of data were obtained from droplets formed on each surface and a minimum of three films of each composition was used for wettability measurements. The mean values of the advancing contact angles reflecting the original state of the surface were given in all of the figures. (The higher scatter of the receding angles may be related to a limited surface dissolution). Standard deviation of contact angles for a given blend composition did not exceed ±1.5°.

XPS

Chemical composition of the surface layer was determined by XPS (Kratos XSAM800 type spectrometer, using MgK_{α1,2} radiation). Data processing was performed by using the Kratos

VISION 2000 program. The overview spectra were taken between 50 and 1300 eV with an energy step of 0.5 eV, while the detailed spectra of the peaks of interest (O1s, Cls, and Si2p) were recorded with an energy step of 0.1 eV. The overlapping peaks were resolved by the peak synthesis method, applying Gaussian peak components after Shirley type background subtraction. Slight alteration of the Cls intensity was observed at prolonged X-ray exposure. For this reason this spectral range was recorded first.

RESULTS

Wettability Studies

The original polymers, PLA and two different PLGA, were blended with each of the three Pluronics at concentrations of 1, 2, 3.85, 6.5, and 9.1% w/w. Contact angles of water on the polymer films were plotted as a function of the amount of Pluronic additives to PLA in Fig. 2. The contact angle decreased with increasing amounts of Pluronics. These data showed that even a small amount of Pluronic in the blend caused a significant decrease in contact angles; i.e., it decreased the hydrophobicity of the surfaces of the blend films. Unexpectedly, the smallest decrease in contact angle was observed by adding the most hydrophilic Pluronic PE6800 to the polymer. A more pronounced decrease was measured in the presence of PE 6400, while the addition of PE6100, which is the most hydrophobic Pluronic with a low PEO content, resulted in the lowest contact angles below 50° at concentrations of 3.85% w/w and above. A similar trend was observed for PLGA75/25, modified with the same three Pluronics (Fig. 3). For these samples contact angles below 50° were achieved by adding 3.85% w/w of PE6400 and PE6100 or 9.1% w/w of PE6800. The result of the corresponding modification of PLGA50/50 copolymer is displayed in Fig. 4. It is noteworthy, that for this copolymer 1% w/w of the three Pluronics caused a large decrease

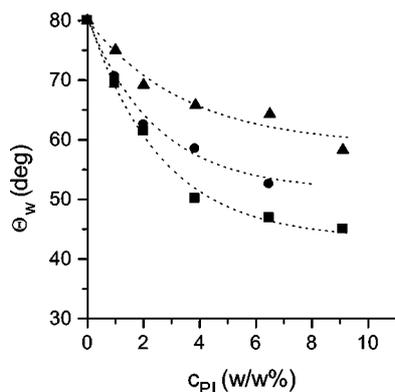


FIG. 2. Advancing water contact angles, Θ_w , on modified PLA surfaces as a function of concentration of various Pluronics (PE6800, ▲; PE6400, ●; and PE6100, ■) in the film c_{PI} (w/w%). Standard deviations of contact angles did not exceed $\pm 1.5^\circ$.

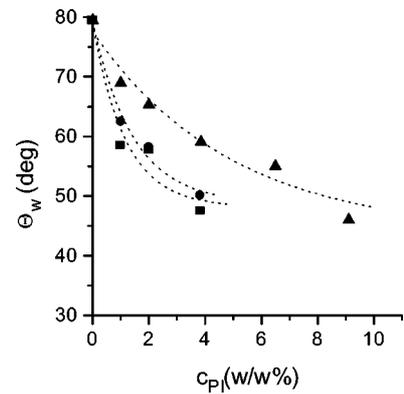


FIG. 3. Advancing water contact angles, Θ_w , on modified PLGA75/25 surfaces as a function of concentration of various Pluronics (PE6800, ▲; PE6400, ●; and PE6100, ■) in the film c_{PI} (w/w%). Standard deviations of contact angles did not exceed $\pm 1.5^\circ$.

(to 60°) in contact angle. Blending PE6800 in higher concentrations decreased further the surface hydrophobicity of the film. Adding higher amounts of PE6400 or PE6100 to PLGA50/50, however, led to heterogeneous film, preventing reliable measurements. As one can see from Figs. 2–4 a considerable hydrophilization of the PLA and PLGA copolymers was achieved by applying Pluronic blends. The surface hydrophilization effect of the various Pluronics, however, was not proportional to their PEO content, as might be expected. On the contrary, the most hydrophobic PE6100 (with only 10% PEO content) proved to be the most effective surface modifier; i.e., it resulted in water contact angles lower than those resulting from the two other Pluronics used at the same concentrations.

The effects of the polymer/copolymer composition on the surface hydrophilization for PLA and the two PLGA copolymers are compared in Fig. 5. Films with PE6800 were chosen for the comparison, because this Pluronic could be blended in the whole concentration range studied with all of PLA and PLGA

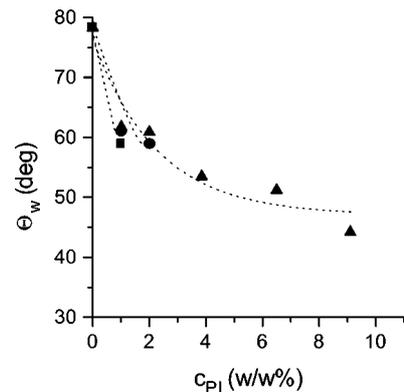


FIG. 4. Advancing water contact angles, Θ_w , on modified PLGA50/50 surfaces as a function of concentration of various Pluronics (PE6800, ▲; PE6400, ●; and PE6100, ■) in the film c_{PI} (w/w%). Standard deviations of contact angles did not exceed $\pm 1.5^\circ$.

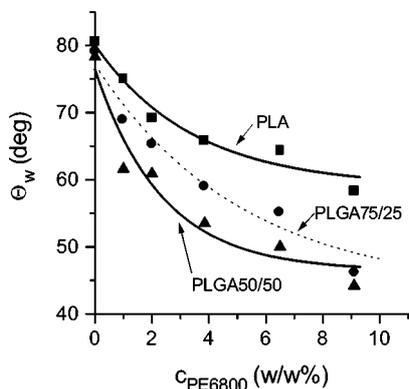


FIG. 5. Advancing water contact angles, Θ_w , on PLA and PLGA copolymer surfaces modified with Pluronic PE6800 at various concentrations. Standard deviations of contact angles did not exceed $\pm 1.5^\circ$.

copolymers. Significant differences in the contact angles were measured depending on the composition of the original polymer/copolymer. The same amount of PE6800 caused increasing wettability in the order of decreasing lactide (increasing glycolide) content of the lactide/glycolide copolymers. The two solid lines in Fig. 5 mark the contact angle range, which can be achieved by modifying the PLA and PLGA surfaces with the Pluronic.

Surface Analysis

XPS analysis was performed on the following polymer blend films: PLA and two copolymers PLGA75/25 and PLGA50/50 modified by 3.85% w/w Pluronic of each type. (The PLGA50/50+PE6100 blend was excluded from the XPS analysis due to the visible heterogeneity of its surface.) The atomic compositions of the surface layers of the blends are given in Table 1. The surface layers contained carbon and oxygen. A small amount of silicon was also detected in some of the samples. From the data it could be concluded that the polymer blend films were generally continuous, fully covering the glass substrates;

TABLE 1
Atomic Composition of the Surface Layer of Polymer+Pluronic Films on Glass Substrates Obtained from XPS Analysis

Samples	Cls at. %	Ols at. %	Si2p at. %
PLA+PE6800	65.6	34.4	0
PLGA75/25+PE6800	61.8	38.2	0
PLGA50/50+PE6800	64.5	35.1	0.4
PLA+PE6400	64.9	35.1	0
PLGA75/25+PE6400	65.8	34.2	0
PLGA50/50+PE6400	64.3	34.8	0.9
PLA+PE6100	69.3	30.6	0.1
PLGA75/25+PE6100	70.3	29.6	0.1

Note. The blends contain 3.85% w/w of Pluronic PE6800, PE6400, or PE6100.

this finding was also supported by the atomic force microscopy measurements. Since the thickness of the film (approx $5 \mu\text{m}$) was 3 orders of magnitude larger than the sampling depth for the XPS signals, the small amount of silicon might be originated from the substrate “seen” through a few pin holes of nanometer range in the films.

The composition of the surface layer of the polymer and Pluronic blends was determined from the detailed analysis of the Cls and Ols peaks of the XPS spectra (Table 2). Carbon signal could be synthesized by four components, while oxygen signal by three components in accordance with the chemical structure of the film-forming compounds. As an example carbon and oxygen signals of PLA+PE6800 blend film are displayed with their components in Fig. 6. The electrons of C–H signal were originating from the carbon in methyl groups of both the lactide units of the polymer and also from the propylene oxide units of the Pluronics (type 1, Fig. 1). This peak may be larger than expected from the composition of the blend due to some CH_x type surface contamination; hence C–H signal was not used in further calculations. Considering the chemical structure of PLA polymer and PLGA copolymers we could assign signals at 288.9 and 286.8 eV to the carbon in carboxylic

TABLE 2
Various Components (in At.%) of Cls and Ols Peaks of XPS Spectra Obtained from the Surface Layer of Polymer+Pluronic Blends

Samples	Cls (type)				Ols		
	C–H (1) 284.8 eV	C–O (2) 286.8 eV	C=OO (3) 288.9 eV	C–O(Pl)(4) 286.1 eV	O=C 532.4 eV	O–C 533.6 eV	O–C(Pl) 531.9 eV
PLA+PE6800	26.7	14.1	14.1	10.7	14.1	14.2	6.1
PLGA75/25+PE6800	19.6	12.5	12.5	17.2	14.2	14.3	9.7
PLGA50/50+PE6800	20.9	11.7	11.8	20.1	11.7	11.8	11.6
PLA+PE6400	21.4	10.6	10.6	22.3	11.7	11.8	11.6
PLGA75/25+PE6400	20.3	10.3	10.3	24.9	10.3	10.3	13.6
PLGA50/50+PE6400	17.6	10.1	10.1	26.5	9.6	9.6	15.6
PLA+PE6100	24.2	7.8	7.8	29.5	7.9	8.0	14.7
PLGA75/25+PE6100	23.0	6.8	6.8	33.7	6.2	6.2	17.2

Note. The compositions of the blends are the same as those in Table 1.

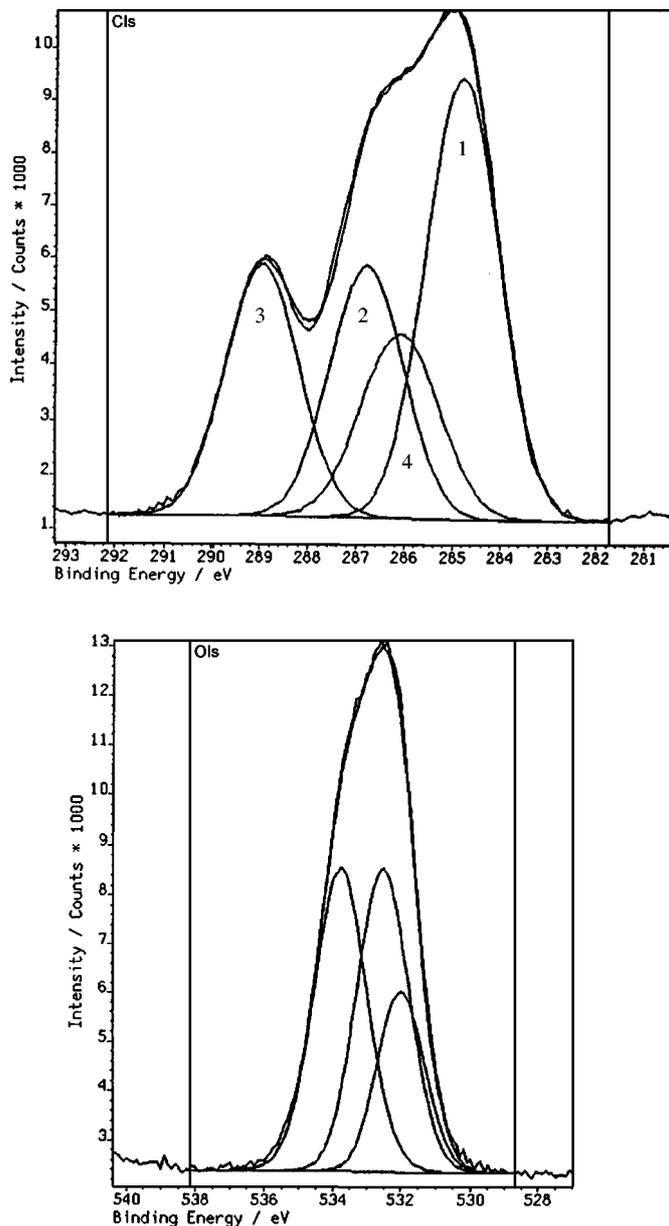


FIG. 6. Carbon and oxygen XPS signals of a PLA film blended with 3.85% w/w of PE6800. Synthetic C1s components correspond to the aliphatic carbon (1) at 284.8 eV, the carbon connected to (2) and constituting ester group (3) of PLA at 286.8 and 288.9 eV, and also the etheric carbon of Pluronic additive (4) at 286.1 eV. Components of oxygen correspond to the two types of oxygen atoms in the ester group at 533.6 and 532.4 eV and also to the etheric oxygen in the Pluronic at 531.9 eV.

group (C=OO) (type 3) and to the neighboring carbon in chain (C–O) of the polymer (type 2), respectively (26). The C–O carbon signal originating from the Pluronic ether units (type 4), named C–O(PI), appeared at a binding energy lower than that of the C–O carbon (type 2) related to the carboxylic group. This highly detectable 0.7 eV difference allowed us to clearly distinguish the (C–O)(2) signals obtained from the PLA/PLGA polymers from those of the Pluronic C–O(PI)(4) in the

surface layer. In accordance with that, the chemical state and, consequently, the binding energy of O1s electrons were also different in the carboxyl group of the polymer (O–C), (O=C) and in the ether group of Pluronic O–C(PI). The chemical shift in binding energy between these components was 0.5 eV, which was smaller than the corresponding C1s shift but still confidently measurable.

The chemical composition of the PLA/PLGA was reasonably well reflected in quantitative XPS analysis: the ratio of the two structurally different carbon atoms, C–O(2) and C=OO(3), and the corresponding oxygen atoms, O–C and O=C, was obtained very close to 1 : 1 : 1 : 1, reproducing the atomic ratio in the structural units of the polymers given in Fig. 1. This also supports the correctness of the deconvolution of the carbon peak into the four components.

The Pluronic content of the surface layer was assigned to the C–O(PI)(4) signal representing the polyether molecules. The concentration of the Pluronic in the surface layer can be expressed by the measured intensities, i.e., C–O(PI)(4) and the C=OO(3) carbon, taking into consideration that one monomeric unit in the Pluronic contains two etheric carbon atoms. Pluronic concentration in monomer ratio is obtained by using the atomic percentage values: $c_{PI}(\text{monomer ratio}) = 0.5C-O(PI)(4)[0.5C-O(PI)(4) + C=OO(3)]^{-1}$. These data can be converted to weight percentage by applying the corresponding monomeric molecular weight data. In the case of copolymers, like PLGA and Pluronic, average values of the monomer molecular weights presented in Table 4 were used. The surface concentrations of Pluronic were summarized for all of the samples in Table 3. Comparison of these data to the bulk concentration of Pluronic in the blend, 3.85% w/w, known from the composition of casting solution, shows that the concentration of Pluronic in the surface layer was much higher than that in the bulk for all of the samples studied here.

TABLE 3
Pluronic Content, c_{PI} , of the Surface Layer—Expressed in Monomer Ratio and Percentage w/w—of Polymer+Pluronic Blends Determined from XPS Data

Samples	c_{PI} in the surface layer		A_s
	Monomer ratio	% w/w	
PLA+PE6800	0.27	20	5.2
PLGA75/25+PE6800	0.41	32	8.3
PLGA50/50+PE6800	0.46	38	9.9
PLA+PE6400	0.51	44	11.4
PLGA75/25+PE6400	0.55	48	12.5
PLGA50/50+PE6400	0.57	51	13.2
PLA+PE6100	0.65	60	15.6
PLGA75/25+PE6100	0.71	67	17.4

Note. The compositions of the blends are the same as those in Table 1. The accumulation ratios, A_s , of Pluronic in the surface layer related to the bulk concentration 3.85% w/w are also given.

The degree of the accumulation of Pluronic in the surface layer was expressed as the ratio of its surface and bulk concentrations, A_s , also given in Table 3. The accumulation ratio ranging from 5 to 18 shows a clear dependence on the composition of the original polymer as well as on the compositions of the Pluronic surfactants.

DISCUSSION

Compatibility of PLA and PLGA with Pluronics

The biodegradable polymers PLA and PLGA were modified with Pluronic block copolymers by applying the solvent casting technique. The compatibility of different polymers in a sense of total miscibility on a molecular scale can be estimated using the Flory–Huggins theory knowing the Hildebrand solubility parameters of the components (27). Although, these calculations give only approximate values and best estimates for high-molecular-weight polymers with similar polarity and hydrogen bonding characteristics, still they can provide valuable help in predicting the behavior of a polymer mixture.

Molecular data of polymers, copolymers, and Pluronics are given in Table 4. Solubility parameters, δ , representing the polarity of the polymer components can be calculated using the Hildebrand equation (27)

$$\delta = \rho_p M_o^{-1} \Sigma F_i,$$

where ρ_p is the density of the polymer, M_o is the molecular weight of the repeat group in the polymer, ΣF_i is the sum of all the molar attraction constants of all the chemical groups in the polymer repeat unit. The solubility parameters of the polymers and also the modifying Pluronics calculated using the Hoy group parameters (28) are also displayed in Table 4. The average

TABLE 4

Molecular Data (Molecular Weight of Polymer, M ; Molecular Weight of Monomer Unit, M_o ; Density, ρ ; Molar Volume of Monomer, \bar{V}) and the Calculated Solubility Parameters (27), δ , for the Polymer/Copolymers and the Pluronics

Polymer	M_o	M	ρ (g/cm ³)	\bar{V} (cm ³ /mol)	δ (J/cm ³) ^{1/2}
PLA	72	106000	1.24 ^a	58.06	19.7
PLGA75/25	68.5	90–126,000	1.27 ^a	53.94	20.3
PLGA50/50	65	40–75,000	1.30 ^a	50.00	21.3
PGA	58	—	1.55 ^a	37.42	25.1
PE6800	46.8	8340	1.06	44.15	20.3
PE6400	52.4	2880	1.05	49.90	18.6
PE6100	56.6	2000	1.02	55.49	17.3
PEO	44	—	1.20 ^b	36.67	21.1
PPO	58	—	1.00 ^b	58.00	16.9

Note. The monomer unit molecular weight given for copolymers (italic) is an average value calculated using the known composition ratio.

^a Measured.

^b From Merck Index.

molecular weight of the monomer for a given copolymer was calculated according to the known composition of the polymers. The solubility parameters of the PLGA copolymers were derived from this monomer molecular weight, M_o , the related density, and group parameters considering the chemical composition of the macromolecule. For random copolymers, such as PLGA, this approach seemed to be reasonable. However, for Pluronics, which are block copolymers, another way of calculation was followed: in this case the weight average solubility parameters were calculated from δ values obtained for homopolymer components and then the length of the PPO and PEO blocks were taken into account to get the overall δ values for the Pluronics.

The Flory–Huggins interaction parameter χ between the two polymers of interest can be calculated using their solubility parameters and average molar volume of the monomers:

$$\chi = V/RT (\delta_1 - \delta_2)^2.$$

The results obtained for the blends are summarized in Table 5, indicating that the compatibility (corresponding to low χ values) with Pluronics decreases with the decreasing PEO content of the Pluronic and is also effected by the composition of the polymers. The compatibility of polymer with Pluronic additive decreases with increasing glycolide content of the polymer.

The concentration range of phase separation could also be estimated using the value of the interaction parameters at the spinodal points, χ_{sp} . These values calculated for the different Pluronic concentrations are presented in Table 5. Blends characterized with χ_{sp} higher than the interaction parameter, χ , were supposed to be stable, while those with smaller χ_{sp} values probably formed phase-separated films. Those concentrations where the polymer mixture was supposed to be phase separated or incompatible, $\chi_{sp} < \chi$, are indicated by bold χ_{sp} values in Table 5. These values are concentrated in the lower right corner of the table reflecting that both the increasing glycolide content of the copolymers and the decreasing hydrophilicity of the Pluronic additives reduced the compatibility of the components. From these data it can be concluded that 1 or 2% w/w of Pluronic could be blended with the polymer or any of the copolymers without phase separation. Formation of a one-phase, homogeneous blend was also expected when the most hydrophilic Pluronic, PE6800, was applied to PLA or the two copolymers in the concentration range of 1–9.1% w/w Pluronic.

The above estimation of the compatibility of polymers with Pluronics is in good agreement with the experimental findings. Those polymer+Pluronic systems for which phase separation was predicted produced indeed opaque heterogeneous films not suitable for wettability measurements.

Surface Activity in the Blend

Two conclusions could be drawn from the solubility parameters, δ , of the polymers and Pluronics (Table 4), which represent the overall polarity of the molecules. The δ parameters of PLA

TABLE 5
Flory–Huggins Interaction Parameters, χ , Calculated (27) for PLA/PLGA+Pluronic Pairs and the Interaction Parameters at Spinodal Points χ_{sp} within the Concentration Range of 1.0–9.1% w/w Pluronic in the Blend

Polymer pair	χ	χ_{sp} at concn.(% w/w) of Pluronic				
		1.0	2.0	3.85	6.5	9.1
PLA+PE6800	0.0058	0.2398	0.1161	0.0607	0.0369	0.0268
PLGA75/25+PE6800	0.000	0.2140	0.1161	0.0607	0.0364	0.0263
PLGA50/50+PE6800	0.0209	0.2142	0.1163	0.0597	0.0353	0.0259
PLA+PE6400	0.0283	0.6872	0.3575	0.1903	0.1163	0.0854
PLGA75/25+PE6400	0.0591	0.6871	0.3575	0.1903	0.1163	0.0838
PLGA50/50+PE6400	0.1493	0.6874	0.3577	0.1905	0.1122	0.0818
PLA+PE6100	0.1320	1.0687	0.5559	0.2838	0.1762	0.1290
PLGA75/25+PE6100	0.1908	1.0687	0.5559	0.2838	0.1718	0.1255
PLGA50/50+PE6100	0.3368	1.0690	0.5561	0.2900	0.1700	0.1235

Note. Polymer+Pluronic mixtures that are supposed to be phase separated, $\chi_{sp} < \chi$, are indicated by bold χ_{sp} values.

and PLGA covered a range from 19.7 to 21.3, increasing with higher glycolide content of the copolymers. The δ values of the Pluronics represented a range of 17.3 to 20.3. Considering these values PE6800 (with $\delta = 20.3$) was expected to be the most compatible among the three Pluronics with the copolymers. This expectation is expressed quantitatively by the χ_{sp} data and also supported by the properties of the blend films.

Solubility parameters, in other respects, could be used to estimate the surface activity of the components in the blend (29). Since the solubility parameter reflects the relative hydrophobic or hydrophilic character of the compound, it is presumable that the component with the lower solubility parameter will show surface activity in the blend. For polymer/copolymer+Pluronic systems some surface accumulation of Pluronics was expected because the Pluronics had solubility parameters lower than those of the base polymer/copolymer (except one case, see Table 4). Comparing the experimental surface accumulation data to the differences in solubility parameters a clear trend could be observed as is shown in Fig. 7. The higher the $\Delta\delta$ of the film-forming materials the larger the surface accumulation ratio of the Pluronics.

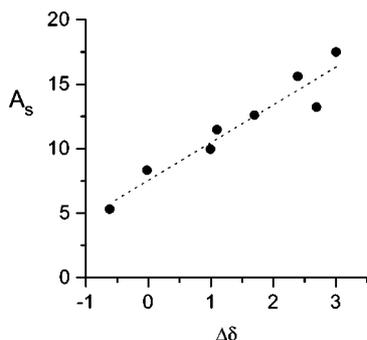


FIG. 7. Accumulation ratio of Pluronic in the surface layer of polymer blend films, A_s , as a function of difference in solubility parameters of polymer and the modifying Pluronic, $\Delta\delta$.

SUMMARY

Biodegradable lactide and lactide/glycolide copolymers were blended with poly(ethylene oxide)–poly(propylene oxide)–poly(ethylene oxide) triblock copolymers (Pluronics) in order to affect the surface hydrophobicity of the original polymer. Wettability of the modified films by water was considerably increased compared to that of the PLA or PLGA surfaces.

- Improvement of wettability was found to be proportional to the concentration of Pluronics in the surface layer derived from the XPS measurements.
- Water contact angles indicated that the increase in wettability was also dependent on the polarity of the polymer/copolymers. It was shown that the appropriate blending composition could be found for any of the polymers to obtain highly reduced surface hydrophobicity.
- XPS measurements revealed a considerable accumulation of Pluronics in the surface layer of the blend films. The extent of surface accumulation was dependent on the polymer/copolymer composition and also on the type of Pluronic. The guide in that respect is the surface activity originating from the difference in polarities of the film forming compounds. The surface activity in PLA+Pluronic or PLGA+Pluronic systems can be reasonably estimated from the difference in the solubility data of the blend components.
- Pluronic additive with a high-molecular-weight and a high solubility parameter and polarity similar to that of the polymer was found to be the most effective in increasing the wettability, i.e., decreasing the hydrophobicity of the surface layer of the polymer. Although, other Pluronics with lower molecular weights and smaller solubility parameters can be more effective in the reduction of surface hydrophobicity, they tend to be phase separated when applied at higher concentrations.

Results obtained here by combining the wettability study with the surface analysis and the solubility data might contribute to a

better understanding of the properties of a certain biodegradable polymer/copolymer blended with a surface-active modifying agent. Those systems could be utilized to design effective drug delivery systems.

ACKNOWLEDGMENTS

E. Kálmán (Chemical Research Center, Hungarian Academy of Sciences) is acknowledged for AFM measurements. The research was supported by the Ministry of Education, Hungary FKFP 0156/1997, by the Natural Sciences and Engineering Research Council of Canada (NSERC) through Grant OGP 0037393, and by the Merck Frosst Centre for Therapeutic Research (Canada).

REFERENCES

- Chasin, M., and Langer, R., "Biodegradable Polymers as Drug Delivery Systems." Dekker, New York, 1990.
- Allemann, E., Rousseau, J., Brasseur, N., Kudrevich, S. V., Lewis, K., and vanLier, J. E., *Int. J. Cancer* **66**, 821 (1996).
- Norris, D. A., Puri, N., Labib, M. E., and Sinko, P. J., *J. Controlled Release* **59**, 173 (1999).
- Blunk, T., Hochstrasser, D. F., Sanchez, J.-C., and Müller, B. W., *Electrophoresis* **14**, 1382 (1993).
- Nagaoka, S., Mori, Y., Takiuchi, H., Yokota, K., Tanzawa, H., and Nishiumi, S., in "Polymers as Biomaterials" (S. W. Shalaby, A. S. Hoffman, B. D. Ratner, and T. A. Horbett, Eds.), p. 361. Plenum, New York, 1984.
- Gölander, C.-G., and Kiss, É., *J. Colloid Interface Sci.* **121**, 240 (1988).
- Desai, N. P., and Hubbell, J. A., *Biomaterials* **12**, 144 (1991).
- Tiberg, F., Malmsten, M., Horbett, T. A., and Hoffman, A. S., *Langmuir* **7**, 2723 (1991).
- Harris, J. M. (Ed.), "Poly(Ethylene Glycol) Chemistry." Plenum, New York, 1992.
- Shen, M. S., Hoffman, A. S., Ratner, B. D., Feijen, J., and Harris, J. M., *J. Adhes. Sci. Technol.* **7**, 1065 (1993).
- Li, J. T., Caldwell, K. D., and Rapoport, N., *Langmuir* **10**, 4475 (1994).
- Schroën, C. G. P. H., Cohen Stuart, M. A., van der Voort Maarschalk, K., van der Pad, A., and van't Riet, K., *Langmuir* **11**, 3068 (1995).
- Kiss, É., Samu, J., Tóth, A., and Bertóti, I., *Langmuir* **12**, 1651 (1996).
- Chittur, K. K., in "Biopolymers at Interfaces" (M. Malmsten, Ed.), p. 143. Dekker, New York, 1998.
- Holmberg, K., and Quash, G. A., in "Biopolymers at Interfaces" (M. Malmsten, Ed.), p. 597. Dekker, New York, 1998.
- Morlock, M., Kissel, T., Li, Y. X., Koll, H., and Winter, G., *J. Controlled Release* **56**, 105 (1998).
- Zange, R., Li, Y., and Kissel, T., *J. Controlled Release* **56**, 249 (1998).
- Bouillot, P., Petit, A., and Dellacherie, E., *J. Appl. Polym. Sci.* **68**, 1695 (1998).
- Li, J. T., and Caldwell, K. D., *Colloids Surf. B* **7**, 9 (1996).
- Caldwell, K. D., in "Chemistry and Biological Applications of Polyethylene Glycol" (J. M. Harris and S. Zalipsky, Eds.), pp. 400–419. ACS Symposium Series 680, Am. Chem. Soc., Washington, DC, 1997.
- Quirk, R. A., Davies, M. C., Tendler, S. J. B., Chan, W. C., and Shakesheff, K. M., *Langmuir* **17**, 2817 (2001).
- Coombes, A. G. A., Scholes, P. D., Davies, M. C., Illum, L., and Davis, S. S., *Biomaterials* **15**, 673 (1994).
- Cleek, R. L., Ting, K. C., Eskin, S. G., and Mikos, A. G., *J. Controlled Release* **48**, 259 (1997).
- Park, T. G., Cohen, S., and Langer, R., *Macromolecules* **25**, 116 (1992).
- BASF Technische Information, Pluronic PR Marken, TI/ES 1026d, 1995.
- Beamson, G., and Briggs, D., "High Resolution XPS of Organic Polymers: The Scienta ESCA300 Database." Wiley, Chichester, England, 1992.
- Krause, S., in "Polymer Blends" (D. R. Paul and S. Newman, Eds.), p. 15. Academic Press, New York, 1978.
- Hoy, K. L., *J. Paint Technol.* **42**, 76 (1970).
- Van Oss, J. C., "Interfacial Forces in Aqueous Media." p. 272. Dekker, New York, 1994.