Novel Blood-Compatible Polyurethanes Containing Poly(butadiene) Soft Segments and Phosphatidylcholine Analogues for Biomedical Applications

Yu-Jun Li,[†] Kerr H. Matthews,[‡] Tian-Ming Chen,[†] Yan-Feng Wang,[†] Makoto Kodama,[‡] and Tadao Nakaya*[,†]

[†]*Department of Bioapplied Chemistry, Faculty of Engineering, Osaka City University, 3-3-138 Sugimoto, Sumiyoshi-ku, Osaka 558, Japan;* [‡]*Bionic Design Group, National Institute for Advanced Interdisciplinary Research, 1-1-4 Higashi, Tsukuba, Ibaraki 305, Japan*

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New segmented polyurethanes (SPUs) based on stearyl and phosphatidylcholine analogues were synthesized. The soft segments used in this study were the poly(butadiene) (PBD) glycol, the hard segments of these SPUs were composed of 4,4′-methylenediphenyl diisocyanate (MDI), 2-[bis(2-hydroxyethyl)methylammonio]ethyl stearylphosphate (BESP), and 1,4-butanediol (BD). The bulk and surface characterization was investigated by differential scanning calorimetry (DSC), X-ray diffraction, attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR), and contact angle measurements. The mechanical properties were investigated by dynamic viscoelasticity and tensile property experiments. The blood compatibilities of the new SPUs were evaluated by platelet-rich plasma (PRP) contact studies and viewed by scanning electron microscopy (SEM). The results show that this new material has good mechanical strength with an elongation at break of 252%, and the blood compatibilities of the SPUs have a great difference between the glass contact side and air-exposed side for the same cast films. The hot-pressed films, having same polyimide contact surface, show that the phospholipid SPU is a favorable surface in terms of platelet adhesion and that the morphology of adhered platelets undergoes a relatively low degree of variation. The clotting time of the cast films contacting with PRP was more than 240 s for the new polymers and 122 and 86 s for polystyrene and glass, respectively.

Introduction

There is no doubt that synthesizing phospholipid polymers and investigating their properties are very useful in the course of mimic membranes. Since the first phospholipid vinyl polymer containing 2-(methacryloyloxy)ethyl 2-aminoethyl hydrogen phosphate and a very useful vinyl monomer containing a phosphatidylcholine analogue, 2-(methacryloyloxy)ethyl-2-(trimethylammonium)ethyl phosphate were reported,[1,2] more and more attention has been paid to synthesis of phospholipid polymers and investigation of their properties for possible applications.[3,4] We have recently reported some new phospholipid polyurethanes, and preliminary results showed that these phospholipid polyurethanes may be regarded as a new kind of hopeful biomaterial.[5−10] Some other phospholipid biomaterials have also been made either by introducing phosphatidylcholine derivatives as plasticizers into polymers such as PVC and polyurethane[11] or by copolymerizing phosphatidylcholine monomers into the polymer backbone of polyurethane and polyesters.[12,13] The phosphatidylcholine polar head groups can be attached on many surfaces by a number of different ways, and large improvements in blood compatibility have been observed.[14−17]

On the other hand, it has been reported that alkyl-grafted SPUs show a high affinity for albumin adsorption and low platelet reactivity,[18−20] and introducing long alkyl side chains onto a polyurethane has been shown to reduce platelet deposition and enhance in vitro albumin adsorption.[21−25] More recent studies suggest

* To whom correspondence should be addressed at the Osaka City University. Tel: +81-6-605-2782. Fax: +81-6-605-2769. E-mail: yujun@bioa.eng.osaka-cu.ac.jp.

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that the blood compatibilities of the polyurethanes containing long-chain alkyl groups and phosphatidylcholine analogues are very exciting.[26] Because no evidence of *any* blood platelet attachment was apparent from the PRP contact studies and from scanning electron microscopy evaluation for the phospholipid polyurethanes, the excellent blood compatibilities of the new phospholipid polyurethanes have become a very promising candidate for clinical trials. However, the mechanical strength of the films prepared from these polyurethanes is almost too weak to prepare real films. To improve the mechanical strength of this material for practical biomedical application, introducing some suitable soft segments and investigating the blood compatibility of this prosthesis have attracted our interest.[27,28]

The polyurethanes introduced into soft segments are termed segmented polyurethanes (SPUs). During the past decade, SPUs have been widely used for various commercial and experimental blood-contacting applications such as vascular prostheses, endotracheal tubes, pacemaker lead wire insulation, catheters and artificial hearts due to their generally favorable physical and mechanical properties, together with fairly good biocompatibility and antithrombogenicity characteristics.[29,30] SPUs are multiblock copolymers consisting of hard and soft segments. The properties of SPUs are mainly influenced by hard and soft segment structure, the molecular weight of the soft segment, and the state of microphase separation.[31,32] For most cardiovascular products, in which polyurethanes are incorporated as a structural or coating material, it is essential that the polymer be designed to be not only stable in vivo for a prolonged period but also biocompatible.

To date, although a variety of commercial biomedical polyurethanes does exist, only a few have been applied extensively.[29] The SPUs targeted for use in biomedical applications are usually based on polyether polyols; perhaps the most popular polyurethanes used in past years have been Biomer or Biolon, which originated from DuPont under the trade name of Lycra, a linear polyurethane used to make the elastic fiber Spandex.[33] Biomer and Biolon are reported to be composed of soft

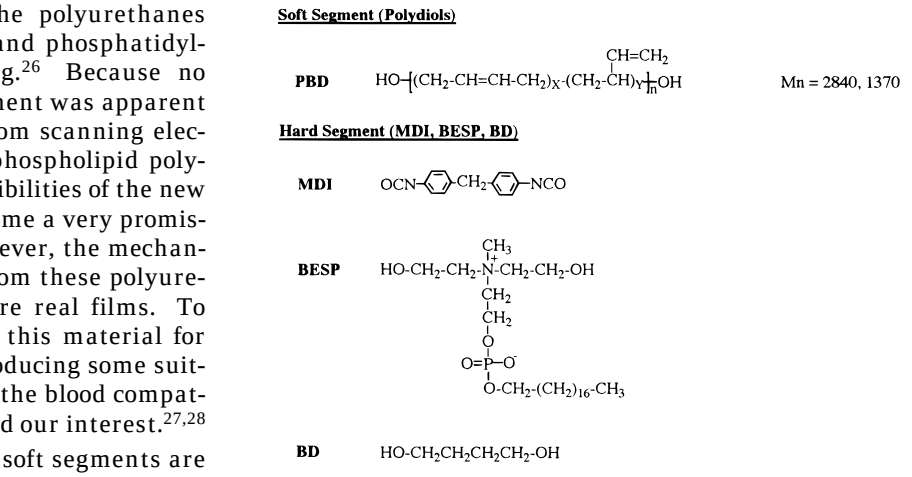

Figure 1. Chemical structures of the phospholipid SPUs components.

segments derived from poly(tetramethylene glycol) (PTMG) and hard segments from MDI, ethyldiamine (ED), and other multifunctional amines.[34] The segmented poly(ether urethane)s have long been considered to have good biostability.[35−37] However, recent investigations have revealed that polyurethanes are subject to significant degradation under certain specific conditions of mechanical or chemical action of implanted devices.[38−41] One of the major causes of degradation is oxidation of the polyether chain. It has been suggested that major causes of degradation are calcification, environment stress cracking, hydrolysis, and oxidation.[30,38,42−45]

To develop polyurethane biomaterials which are more stable in vivo, it may be desirable to prepare SPUs without ether-containing polydiols. Takahara et al.[46] have used several non-ether polydiols such as PBD, hydrogenated poly(butadiene) (HPBD), and poly(dimethylsiloxane) (PDMS) chain segments to synthesize SPUs. They have demonstrated that the SPUs based on these hydrophobic polydiols showed distinct microphase separation between hard and soft segments. Moreover, these SPUs containing hydrophobic polydiols are also interesting for their interfacial chemistry. Due to the large difference in surface free energy between their hard and soft segments, the polydiol soft segment may be enriched at the air−solid interface. However, after immersing the specimen in water, surface reorganization may occur in response to the system's requirement

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Table 1. Synthesis of the Phospholipid SPUs[a]

	first step				second step		third step			
polymers	polydiols (M_n) (4.0 g)	MDI (g)	reaction solvents (20 mL)	reaction time at 75 °C (h)	BESP/solvent (g/15 mL)	reaction time at 95 °C (h)	BD/solvent (g/15 mL)	reaction time at 100 °C (h)	precipitated solvent	yield (%)
SPU **1**	PBD(2840)	0.706	DMAc/THF(1/1)	1	0.349	3	0.064	1	methanol	86
SPU **2**	PBD(1370)	1.462	DMAc/THF(1/1)	1	0.724	3	0.132	1	methanol	82
SPU **3**	PBD(2840)	1.059	DMAc/THF(1/1)	1	0.699	3	0.127	1	methanol	87

[a] SPU, segmented polyurethane; PBD, poly(butadiene) glycol; MDI, 4,4′-methylenediphenyl diisocyanate; BESP, 2-[bis(2-hydroxyethyl)methylammonio]ethyl stearylphosphate; BD, 1,4-butanediol; DMAc, *N*,*N*-dimethylacetamide; THF, tetrahydrofuran.

Table 2. Bulk Property Characterization of the Phospholipid SPUs

			IR spectral data (cm^{-1})				elemental analysis[a]			
polymers	stoichiometry polydiol:MDI:BESP:BD	hard segment (%)	$-CH_2-$	$-NHCOO-$	$-P{=}O$	$-PO-CH_2-$	C	H	N	M_w[b]
SPU **1**	1:2:0.5:0.5	21.8	2900				82.9 (83.4)	10.0 (10.1)	2.0 (1.7)	37 000
SPU **2**	1:2:0.5:0.5	36.7	2840	1710	1220	1060	79.3 (80.2)	9.4 (9.4)	3.3 (2.9)	35 000
SPU **3**	1:3:1:1	32.0	1440				79.9 (81.0)	9.5 (9.8)	2.6 (2.4)	43 000

[a] Values in parentheses are calculated data. [b] Determined by GPC using polystyrene as standard.

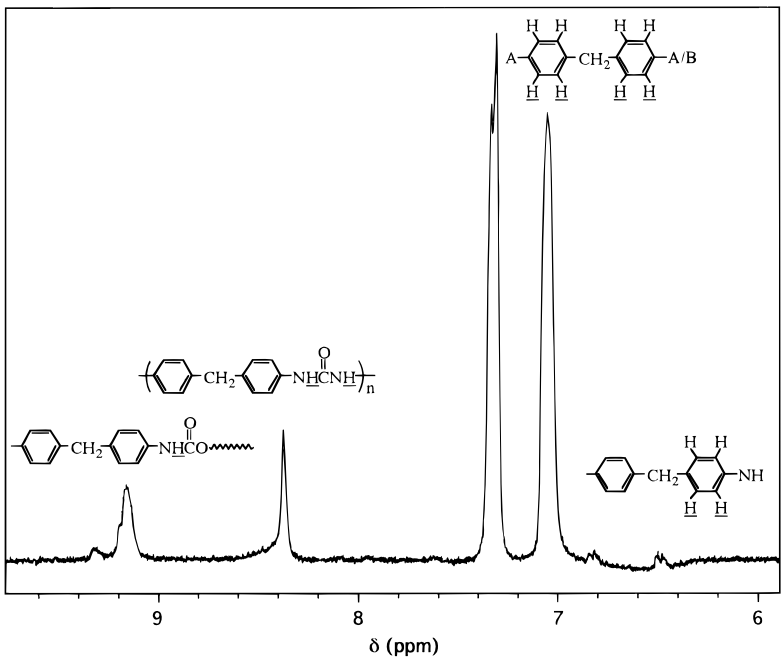

Figure 2. High-field ^1H NMR spectrum of the phospholipid SPU **2** based on PBD1370.

to minimize its interfacial free energy. It was concluded that polyurethanes with aliphatic hydrocarbon-based polyol components are stable against oxidative degradation. In addition, recent investigation shows that SPUs which do not contain the ether linkage in the polyol component do not inhibit metabolic cooperation and might be less prone to cause tumor formation than polyether-based polyurethane.[47]

An objective of our current research is to synthesize new SPUs based on non-ether soft segments and phospholipids. Furthermore, to investigate the relationships between ex vivo blood-contacting properties and surface and bulk structure, the synthesized phospholipid SPUs were evaluated before characterizing the polymers stability in the biological environment. The characterization tests for bulk characterization of the polyurethanes included IR, ^1H NMR, gel permeation chromatography (GPC), elemental analysis, DSC, and X-ray diffraction measurements. The mechanical property investigation included dynamic viscoelasticity and tensile measurements. In general, tensile behavior depended on the size and concentration of the hard segment domains, the strength of the hard segment aggregation, the ability of the segments to orient in the stretch direction, and the ability of the soft segment to crystallize under strain. Surface characterization was performed by contact angle measurements and ATR-FTIR analyses. The blood compatibility of the SPUs was evaluated by describing the platelet state and shape variation for the attached platelets, as well as the clotting time.

Experimental Section

General Method. The IR spectra were recorded on a Jasco A 202 spectrometer and ^1H NMR spectra were obtained over 128 scans at a sample temperature of 80 °C on a JEOL GSX 270 MHz instrument. Chemical shifts are reported in δ values relative to TMS ($\delta = 0$) for proton spectra. GPC measurements were performed on a HLC802UR GPC instrument with G4000H8 + G2000H8 columns; the samples were dissolved in THF or mixed solvent of THF and DMAc and using polystyrene as standard. Elemental analysis was performed by Osaka Gas Co. Ltd. (Osaka, Japan). The thermogram were recorded by DSC using a Rigaku thermoflex apparatus DSC-

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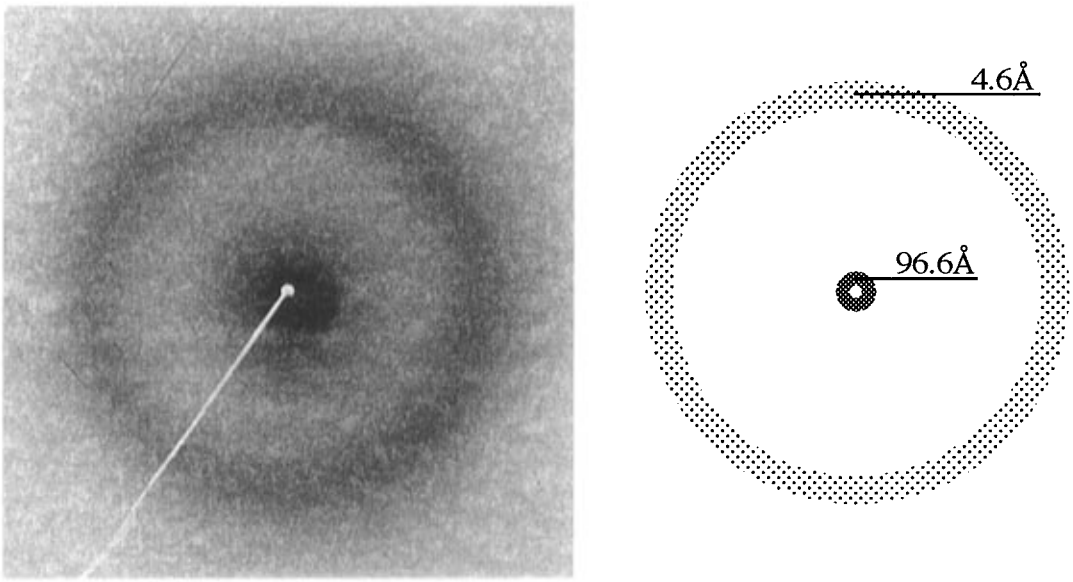

Figure 3. X-ray diffraction patterns of the phospholipid SPU **3** based on PBD2840 obtained with a flat camera by Ni-filtered X-rays of Cu Kα (camera length 7.21 cm).

8230B. The sample quantity was 5 mg with a 10 °C min^{-1} rate of heating. For an X-ray diffraction measurement, the film specimen was completely sealed with mica in the sample holder. The X-ray film diagram was photographed with nickel-filtered Cu Kα radiation (37.5 kV, 20 mA), using a flat-plate camera of 7.21 cm passage at room temperature. The temperature dependence of the dynamic viscoelasticity of the sample was obtained using a microprocessor-controlled Rheovibron DDV-III-EP under a dry nitrogen purge. The sample (223 μm thick, 4 mm wide) was cooled to −150 °C, and data were subsequently taken at a test frequency of 11 Hz and a heating rate of 3 °C min^{-1}. The stress−strain properties were measured by an Instron type tensile tester (Tenshiron Model UCT-30T) with a crosshead speed of 12 mm min^{-1} at room temperature. The sample was cut into a dumbbell-shaped specimen using an ASTM D638 (Type V) standard die. ATR-FTIR was performed on the surfaces of the cast films. The spectrum was collected at 4 cm^{-1} resolution using a Jasco Micro FT/IR-200 microsampling spectrometer over 50 scans. The sampling area was 25 μm^2, coupled with an ATR accessory and 45° KRS-5 crystal.

Contact Angle Measurements. The values quoted are the average of 12 measurements of each sample taken at 3 min contact of the water droplet on both the air-exposed side and the glass contact side, using a face contact angle meter. Moreover, the receding contact angle for hydrated SPUs films on both sides and water absorption of the polymers were also estimated. The hydrated samples were prepared by immersing the films into distilled water at 25 °C for 24 h and then drying them naturally; the receding contact angle for hydrated samples was measured using the same procedure. The water absorption of the polymers was estimated using the procedure described by Shin et al.[48] The procedure of blood compatibility evaluation for blood platelet adhesion and shape variation was the same as that described previously.[26]

Clotting Time. 10% phospholipid SPUs solutions in THF and DMAc mixed solvent (volume ratio 1:1) were poured into glass vials; after remaining in the vials at 23 °C overnight, the excess solutions were poured out, and the inner surface coated vials were then dried at 70 °C overnight under nitrogen atmosphere, following another 30 h of drying at 60 °C under vacuum. The glass vial coated with 10% polystyrene solution in THF and the vial without coating were used as control experiments. The fresh PRP was prepared by mixing 8.1 mL of the blood of human and 0.9 mL of 3.13% sodium citrate solution, following the centrifugation at 1000 rpm for 20 min. The vials were washed with saline and incubated at 37 °C for 10 min. Then, 0.1 N calcium chloride solution was added into the vials, and the clotting time was measured.

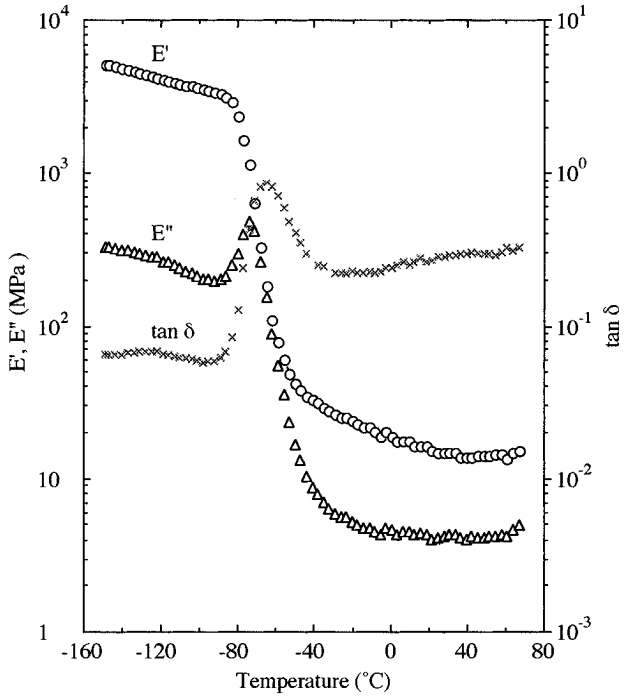

Figure 4. Temperature dependence of the storage modulus (E'), loss modulus (E''), and loss tangent (tan δ) for the phospholipid SPU **3** based on PBD2840 at 11 Hz.

Materials. Tetrahydrofuran (THF) was distilled from lithium aluminum hydride to ensure dryness. *N,N*-Dimethylformamide (DMF) and *N,N*-dimethylacetamide (DMAc) were dehydrated over calcium hydride for 2 days and then vacuum distilled. Methanol was distilled in the presence of magnesium methoxide to ensure dryness, BD and MDI were commercially obtained and purified by vacuum distillation. All purified solvents were dried over Molecular Sieves 4A (Wako Pure Chemical Ind. Ltd., Japan), and other solvents were best commercial grades and used as received, unless otherwise noted. PBD was kindly provided by Nippon Oil and Fats, Co., Ltd. One PBD had a number average molecular weight of M_n = 2840 and 20% of 1,2-vinyl, 60% of 1,4-trans, and 20% of 1,4-cis structure components; the other PBD had a number average molecular weight of M_n = 1370, 92% of 1,2-vinyl and 8% of 1,4-trans structure components. The synthesis of BESP has been described in detailed previously.[26]

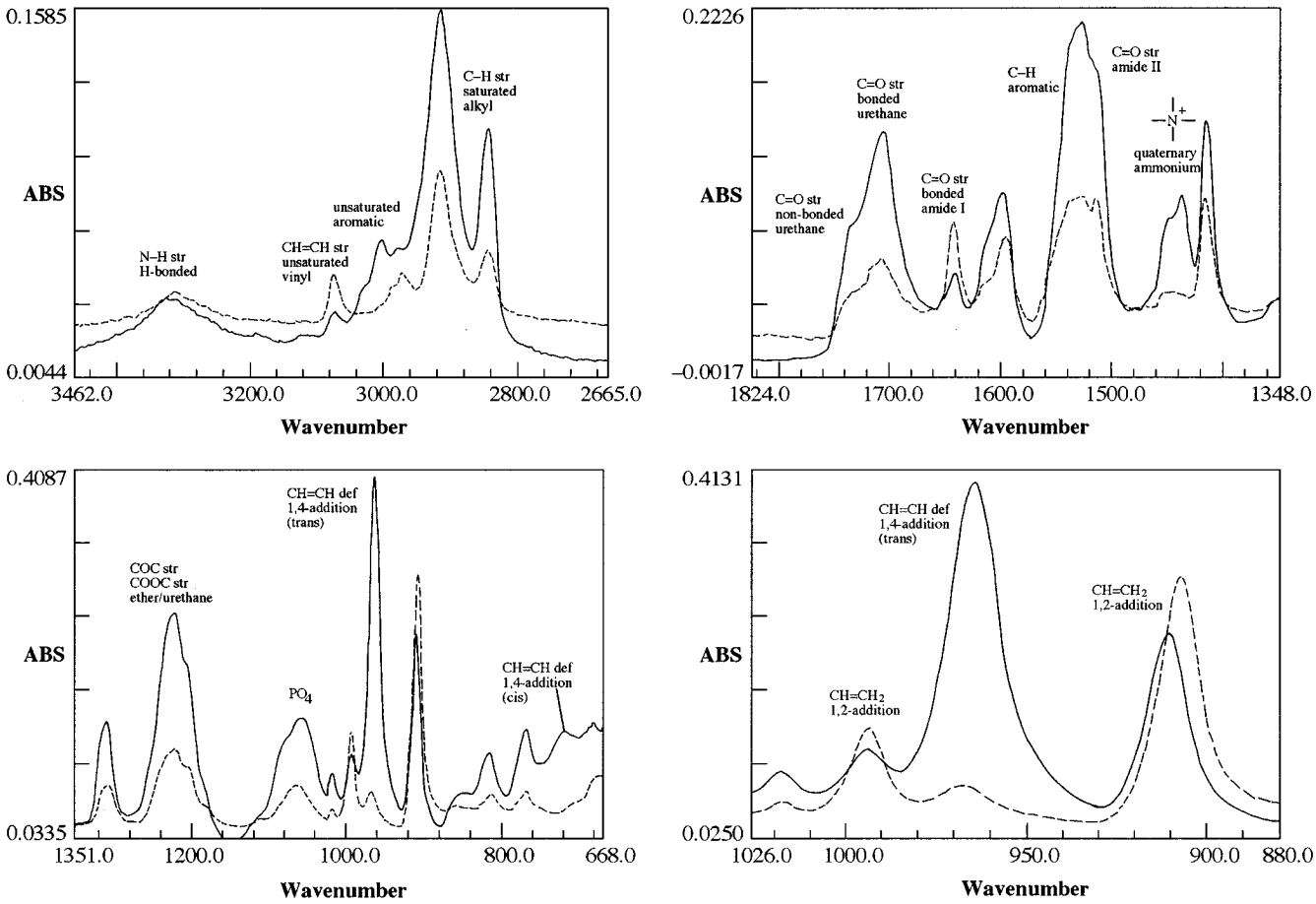

Figure 5. ATR-FTIR spectra of the phospholipid SPU **1** based on PBD 2840 (—) and SPU **2** based on PBD 1370 (- - -).

Table 3. Mechanical Properties of the Phospholipid SPU 3 Cast Film

sheet thickness (μm)			modulus (MPa)			100% modulus (MPa)			ultimate strength (MPa)			elongation at break (%)		
run 1	run 2	ave	run 1	run 2	ave	run 1	run 2	ave	run 1	run 2	ave	run 1	run 2	ave
221	225	223	7.41	7.58	7.50	2.58	2.73	2.66	38.2	42.7	40.4	243	261	252

Synthesis of Phospholipid SPUs. The phospholipid SPUs containing PBD polydiol soft segments were synthesized by a three-step addition polymerization reaction; refer to the conventional two-step solution polymerization procedure under a nitrogen atmosphere.[49] The polymers were based on 1/2/0.5/0.5 or 1/3/1/1 molar ratio of PBD/MDI/BESP/BD, and the reaction was carried out in a 1:1 mixture of THF:DMAc without catalyst. The phospholipid SPUs were all synthesized by similar methods; therefore, a representative synthesis is shown.

Synthesis of PBD2840-MDI-BESP-BD (SPU1). In the first step, 0.706 g (2.82 mmol) of MDI dissolved in 10 mL of the mixed solvent was added to a stirred solution of 4.0 g (1.41 mmol) of PBD (M_n = 2840) in 10 mL of the same mixed solvent under a dry nitrogen atmosphere. After 1 h at 70−75 °C the solution was cooled to room temperature slowly. In the second step, 0.349 g (0.705 mmol) of BESP, which was previously dissolved in 15 mL of the mixed solvent, was slowly added into the reaction solution over 20 min. Stirring was continued at 90−95 °C for 3 h. For the last step, using the same procedure, 0.064 g (0.705 mmol) of BD, which was previously dissolved in 15 mL of the same solvent, was added dropwise over another 10 min to the reaction mixture with stirring. The stirring was continued at 100 °C for 1 h. The resulting phospholipid SPU was precipitated in methanol. Following this, the polymer was washed with methanol, and the washing procedure performed three additional times with methanol. The polymer was dried in a vacuum oven at 70 °C for at least 48 h. A pale yellow elastomer of the polymer SPU**1** (4.4 g, 86%) was obtained. IR (film): 2900, 2840 (−CH_2−), 1710 (−NHCOO−), 1590 (aromatic), 1220 (P=O), 1060 cm^{-1} (P−O−CH_2−). Anal. Calcd for $C_{505}H_{732}N_9O_{20}P$: C, 83.4; H, 10.1; N, 1.7. Found: C, 82.9; H, 10.0; N, 2.0. M_w = 37 000.

The other phospholipid SPUs were synthesized by procedures similar to those described above. The chemical structures of the SPUs components, detailed synthesis conditions, and chemical compositions for the synthesized phospholipid SPUs are summarized in Figure 1 and Table 1.

Preparation of Casting Films. To obtain a solution suitable for casting on test surfaces, after briefly drying under vacuum to remove residual methanol, the resulting SPUs were dissolved in mixed DMAc and THF (volume ratio 1/1) solution by ultrasonic generator. The obtained SPUs solutions were defoamed by evaporator in a desiccator and then cast onto glass plate to create films for bulk property testing or surface property experiments. In casting procedure, the casting films were first dried in an oven at 70 °C under a flowing nitrogen for at least 48 h to remove most of the solvents. The final drying stage involved drying the sheet in a vacuum oven at 70 °C for at least 48 h to remove residual solvents.

Preparation of Hot-Pressed Films. To eliminate the effect of different contact surface, the SPU **3** cast film was placed between two thin polyimide sheets, and the materials were subjected to a pressure of 100 kg cm^{-2} and a temperature of 150−170 °C for 15 min in a mechanical hot-press. After the polyimide films were cooled and removed, SPU **3** produced a successful hot-pressed film.

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Table 4. Water Contact Angle of Nonhydrated and Hydrated Cast Films of Phospholipid SPUs

	air-exposed side (deg)		glass contact side (deg)	
samples	nonhydrated	hydrated	nonhydrated	hydrated
SPU **1**	102.2 ± 2	86.2 ± 5	92.5 ± 2	89.9 ± 3
SPU **2**	104.2 ± 4	100.4 ± 1	90.9 ± 1	90.2 ± 2
SPU **3**	89.3 ± 2	89.4 ± 5	89.8 ± 2	88.4 ± 3

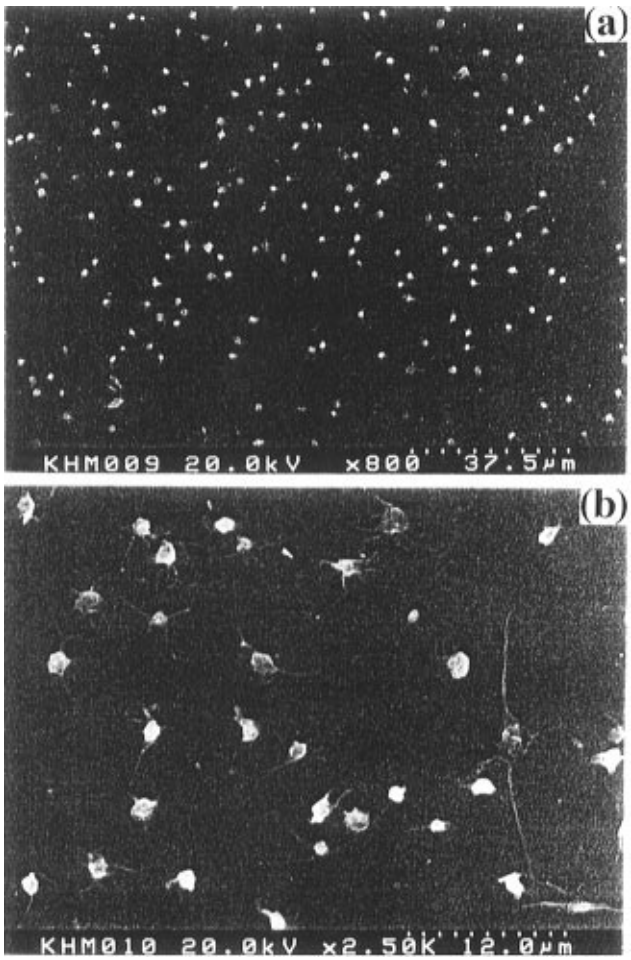

Figure 6. SEM photographs of the surface of reference glass after 60 min of PRP exposure. Actual magnification: (a) 800; (b) 2500.

Results and Discussion

Bulk Property Characterization. Bulk property characterization data are summarized in Table 2. The stoichiometry of the reaction was 1:2:0.5:0.5 or 1:3:1:1 for PBD:MDI:BESP:BD, respectively. The designed hard segment was in the range 21.8−36.7%. The IR spectral analyses of the polymers were taken on cast films. All phospholipid SPUs are related with the inclusion of MDI, BESP, and BD. This is clear from the complete IR spectrum of each material, which shows adsorption bands due to −NH− band at 3300 cm^{-1}, −NHCOO− band at 1710 cm^{-1}, $-CH_2-$ band at 2900, 2840, and 1440 cm^{-1}, aromatic linkage at 1590 cm^{-1}, P═O at 1220 cm^{-1}, and $P-O-CH_2-$ at 1060 cm^{-1}.

The results of elemental analyses for C, H, and N confirmed that the proper phospholipid groups had been incorporated into the controlled polyurethane samples.

The weight-average molecular weights (M_w) of the polymers were characterized by GPC based on a polystyrene standard. From the relationship between retention time and molecular weights derived for narrow-distributed standard polystyrene, the weight average molecular weights (M_w) of SPUs **1**−**3** were 37 000, 35 000, and 43 000, respectively. Corresponding polydispersity (M_w/M_n) of SPUs **1**−**3** was 1.7, 1.6, and 1.8. The relative low M_w may contribute to the water absorbed in the phospholipid diol BESP. Nevertheless, these molecular weights are sufficient for most biomedical applications.

Although the synthesized SPUs is not sufficiently soluble in DMSO-d_6, evidence for substantial arylurethane was obtained from the high-field ^{1}H NMR spectra of the SPUs. Figure 2 represents a typical high-field ^{1}H NMR spectrum of SPU **2**. This result indicates that protons were associated with MDI-derived moieties.

To further investigate properties and prospective applications of the synthesized phospholipid SPUs, using the SPU **3** as an example, we further examined the other properties. The DSC thermal transition data were obtained from the first heating of the sample. The glass transition temperature (T_g) of the SPU **3** was observed near 5 °C. Moreover, when heated to 250 °C, the sample melted, and the color of the sample changed from pale yellow to brown.

A further investigation of X-ray diffraction analysis for the film samples of SPU **3** was carried out with nickel-filtered Cu Kα radiation. Figure 3 shows the X-ray diffraction pattern of the film sample of the SPU **3**. As can be seen from the figure, a ring with strong intensity in the small-angle region together with a weak diffuse scattering in the wide-angle region was observed. The 96.6 Å of intense scattering in the small-angle region corresponds to the length of the soft segments, the hydrophobic PBD layer. This result indicates that the PBD hydrophobic layer may be arranged in a coil, because the theoretical length of the hydrophobic PBD layer was estimated to be 231.2 Å. On the other hand, the dimension of the weak diffuse scattering in the wide-angle region was 4.6 Å. This value should be the distance between the hydrophobic PBD layers, based on our earlier report.[50]

The result of dynamic viscoelasticity experiment for the SPU **3** film sample is displayed in Figure 4. The storage modulus (E') was slowly decreased from 5.0 × 10^3 MPa at −150 °C to 2.4 × 10^3 MPa at −80 °C, following a rapid decrease with about 3-order. The material was followed into the elastomer region with 15 MPa near −10 °C. The peak of tan δ at −65 °C, together with the peak of loss modules (E'') at −74 °C was observed. At 37.2 °C, 13.6 MPa, 4.15 MPa, and 0.305 for E', E'', and tan δ were observed.

The tensile property data for the SPU **3** film sample are summarized in Table 3. When the film sheet thickness was 223 μm, this elastomer had a 7.50 MPa modulus, 2.66 MPa 100% modulus, and 40.4 MPa ultimate strength. Moreover, this elastomer had a good mechanical strength with an elongation at break of 252%.

Surface Property Characterization. To characterize the surface properties of the SPUs, the ATR-FTIR measurements were carried out. Figure 5 shows the ATR-FTIR spectra of SPU **1** and SPU **2**. The analyses for absorption bands are also shown in Figure 5. The spectra of the SPUs give evidence of unsaturated C═C

(50) Sakurai, I.; Kawamura, Y.; Suetsugu, T.; Nakaya, T. *Macromolecules* **1992**, *25*, 7256.

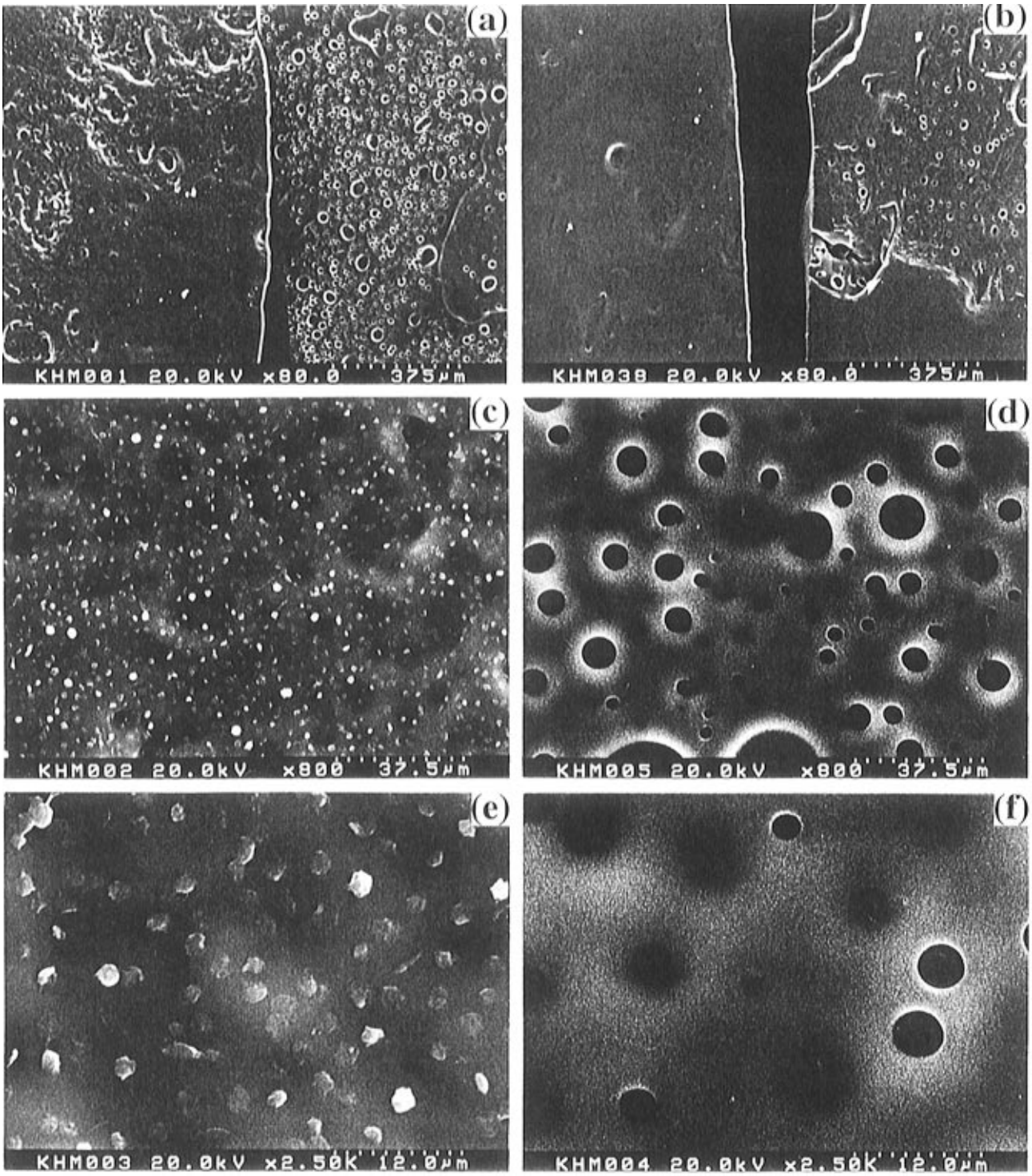

Figure 7. SEM photographs of the surface of SPU **1** films cast from mixed DMAc and THF (volume ratio 1/1) solution after 60 min of PRP exposure. (b) As a reference without PRP contact and without ethanol treatment; (a and b) Air-exposed side on right and glass contact side on left. (c and e) Glass contact side. (d and f) Air-exposed side. Actual magnification: (a and b) 80; (c and d) 800; (e and f) 2500.

double bonds, PO_4-, N−H, C═O bonds, quaternary ammonium, nonbonded and bonded urethane, and unsaturated aromatic bonds (as indicated). The results indicate that the obtained SPUs contain PBD, MDI, BESP, and BD. This is in agreement with the designed structures. Bonded and nonbonded urethane bands presented at 1704 and 1728 cm^{-1} and a relatively weaker band at 1639 cm^{-1} owing to amide I and a strong band at 963 cm^{-1} due to trans-1,4 addition of HC═CH were observed on the ATR-FTIR spectrum of SPU **1**.

SPU **2** was completely soluble in DMF to a clear solution at room temperature but not completely soluble in DMSO-d_6. The structure of SPU **2** was consistent with the intended formulation. PBD bands appeared at 3073 and 910 cm^{-1}, bonded and nonbonded urethane bands were present at 1704 and 1728 cm^{-1}, and relatively strong amide I was present at 1639 cm^{-1}. All bands associating with MDI-based urethanes were present. Differences between the spectra of SPU **1** and SPU **2** are attributed to PBD2840 and PBD1370,

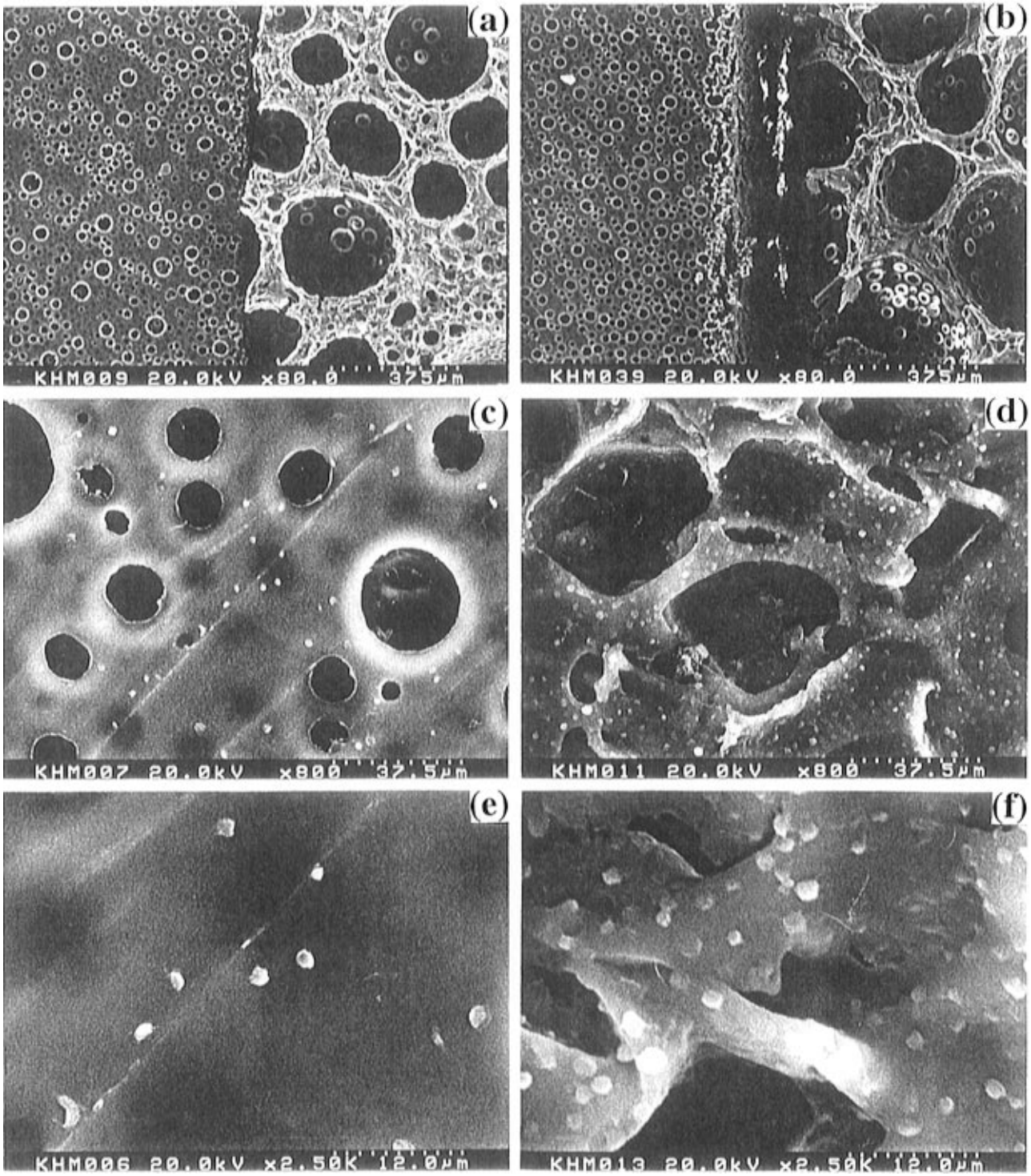

Figure 8. SEM photographs of the surface of SPU **2** films cast from mixed DMAc and THF (volume ratio 1/1) solution after 60 min of PRP exposure. (b) As a reference without PRP contact and without ethanol treatment. (a and b) Air-exposed side on right and glass contact side on left. (c and e) Glass contact side. (d and f) Air-exposed side. Actual magnification: (a and b) 80; (c and d) 800; (e and f) 2500.

respectively, such as bands at 3073, 3006, and 967 cm^{-1}.

To obtain information on the hydrophilicity−hydrophobicity, different roughness and surface morphology of the two opposite surfaces of the SPUs, water contact angle measurements for the SPU films were performed on both the air-exposed side and glass contact side. Moreover, since the SPUs as biomaterials should "work" in aqueous media, receding contact angle analysis of hydrated samples was also performed. The results are shown in Table 4. As expected, the relatively big contact angles indicated that these SPUs had hydrophobic surfaces for both the air-exposed side and glass contact side. For nonhydrated films, the air-exposed side of SPUs **1** and **2** had relatively bigger contact angles than did the glass contact side, and the SPU **3** had almost the same contact angle for both sides. For hydrated films, both the air-exposed side and glass contact side showed the trend of decrease of contact angle; however, only SPU **1** on the air-exposed side showed a great difference before and after the sample was hydrated, and other samples had only a little change. This result may be attributed to the following: after the sample was

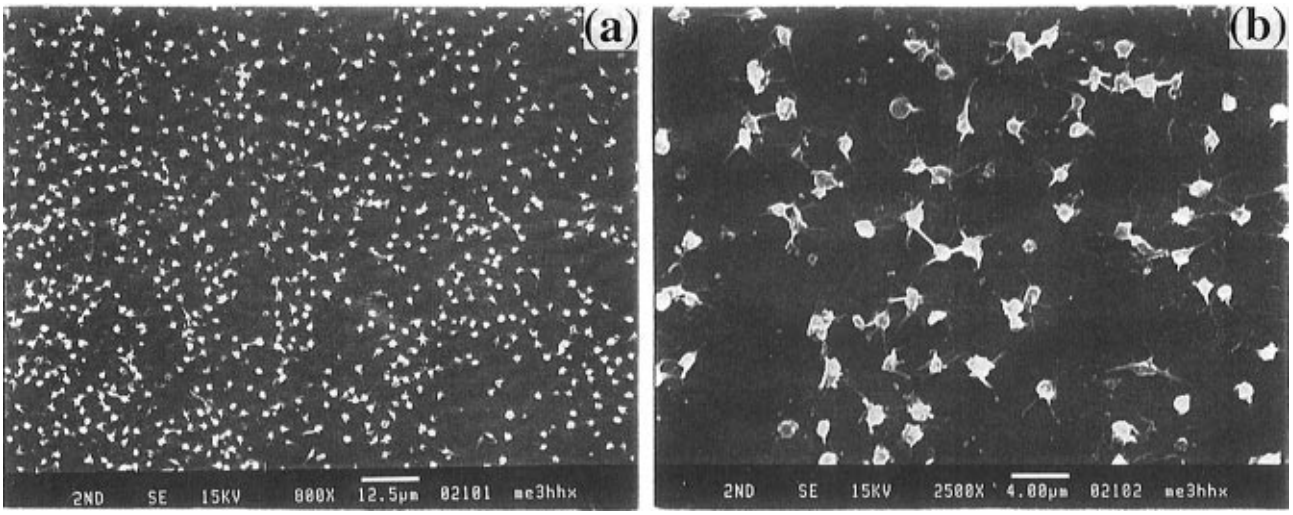

Figure 9. SEM photographs of the surface of SPU **3** hot-pressed films after 60 min of PRP exposure. Actual magnification: (a) 800; (b) 2500.

immersed in water, the surface reorientation may occur in response to the system's requirement to minimize its interfacial free energy. It should be noted that the great change of the contact angle on the air-exposed side for SPU **1** may be owing to the surface roughness during the preparation of the cast films. In addition, the water absorption of the polymers was estimated using the procedure described by Shin et al.[48] After the cast films of SPUs **1**−**3** were immersed in distilled water for 24 h and then the surfaces of the films were dried naturally, the swell ratio was 1.16%, 0.72%, and 0.74% for SPUs **1**−**3**, respectively. However, after the samples were further dried in a desiccator at room temperature for another 24 h, the weight of the samples was almost unchanged compared to the original samples without immersal in water. This result also indicated that the materials were very hydrophobic and almost did not absorb the water.

Blood-Compatibility Evaluation. The synthesized SPUs were assessed as biomaterials mainly by the degree and nature of blood platelet adhesion resulting from exposure to PRP for 60 min. The specimens incubated in PRP were viewed by SEM. The typical SEM photographs of glass reference and SPU **1** and SPU **2** are shown in Figures 6−8.

For glass reference, substantial adhered platelets greatly changed their shape. For PBD 2840 based phospholipid SPU **1**, the side in direct contact with the glass surface, used as a substrate on which the SPU solutions in a solvent mixture of DMAc and THF were cast, adhered a large number of platelets and also slightly changed their shape, whereas the air-exposed side had *no* detectable platelets. SPU **2** based on PBD1370 adhered few platelets on the glass contact side, whereas there were extensive platelets on the air-exposed side. The shape of the attached platelets also changed for both sides of the SPU **2**. Generally, it seemed that the blood compatibility of PBD2840 based SPU **1** was better than that of PBD1370 based SPU **2**. This may contribute to the effect of the molecular weight and the structure of the soft segments.

Why did the glass contact side and air-exposed side as opposite sides for these SPUs produce such contrasting results in the level of platelet adhesion and shape variation? ATR-FTIR analysis could not detect any differences between both sides. The only differences were in fact attributed to the different soft segment components used in construction of polymer backbone. This could have been a consequence of the generally rough surface texture created by the method of solvent casting, especially on the air-exposed side. On the other hand, the receding contact angle values measured on the hydrated samples (in Table 4) may in turn explain partially their different behavior in terms of platelet adhesion and morphology changes, since the platelets see the water-exposed surface.

Table 5. Clotting Time (seconds) of the Phospholipid SPUs, Polystyrene, and Glass

SPU **1**	SPU **2**	SPU **3**	polystyrene	glass
>240	>240	>240	122	86

To eliminate the effect of different contact surface, PBD 2840 based SPU **3** cast film was placed between two thin polyimide sheets, and the materials were subjected to a pressure of 100 kg cm^{-2} and temperature of 150−170 °C for 15 min in a mechanical hot-press. SPU **3** produced successful hot-pressed film. The SPU **3** hot-pressed film was exposed to PRP for 1 h and treated for SEM observation. The SEM photographs of the surface for the SPU **3** hot-pressed films are shown in Figure 9.

On the basis of the SEM observation, the number of adhered platelets in an area of 10 μm × 10 μm was 0.3 for phospholipid SPU **3**, and the adhered platelets showed some degree of shape variation. The shape variation of adhered platelets may affect the accuracy of the estimated number of adhered platelets; however, a further investigation on the clotting time of the new materials on polystyrene and glass suggested that it was apparent that the trend of blood compatibility of the new polymer was better than that of polystyrene and glass (Table 5). The clotting time of the cast films contacting with PRP was more than 240 s for the new polymers SPUs **1**−**3** and 122 and 86 s for polystyrene and glass, respectively. Combined with the good mechanical properties of the new phospholipid SPU, this new polymer may be regarded as a hopeful biomaterial. Direct-comparison experiments on blood compatibilities between these new phospholipid polyurethanes and bio-

medical polyurethanes that are in clinical use are in progress.

Conclusion

In summary, SPUs containing hydrophobic poly(butadiene) non-ether soft segment and phospholipids have been synthesized. The preliminary results suggest that the poly(butadiene) ($M_n = 2840$) based phospholipid SPU may be regarded as a hopeful biomaterial for its favorable blood compatibilities and good mechanical properties. Moreover, it has been suggested that the blood-contacting properties of the polymers are not solely dependent on the structure of hard segments such as phospholipid. The combination of factors including the molecular weight of soft segment, microphase separation, surface heterogeneity, and surface hydrophilicity determined the polymers blood-contacting response. We are trying to introduce the different phospholipid into the polyurethanes and trying to investigate the effect of the phospholipid contents in SPUs. Moreover, we are trying to further develop these new segmented polyurethanes for possible bioapplications such as heart valves, vascular prostheses, pacemaker lead wire insulation, catheters, etc.

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