The in vitro blood compatibility of poly(ethylene oxide)-grafted polyurethane/polystyrene interpenetrating polymer networks

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Abstract—Poly(ethylene oxide) (PEO) grafting polyurethane (PU)/polystyrene (PS) interpenetrating polymer networks (IPNs) were synthesized. The effects of the mobile pendant PEO chains with their microphase separated structure on blood-compatibility were investigated. The morphology of both the fracture surface as well as the top surface indicate that the size of the dispersed domains of the PS-rich phase decreased as the grafting with the PEO was increased. The swelling ratio also decreased as the grafting with the PEO was increased. However, the dynamic contact angle and the interfacial energy between IPN surface and water decreased, due to the structural reorganization of the pendant PEO chains. PU/PS IPNs have an excellent mechanical property as compared with PU homopolymers. The adsorption of bovine plasma fibrinogen (BPF) onto the PU/PS IPNs and PU homopolymers was effectively suppressed by the PEO-grafting. In the platelet adhesion test, the amount of platelets was reduced, activated, and/or conglutinated upon the PEO-grafted PU/PS IPNs were reduced when compared with the ungrafted PU homopolymers.

Key words: Polyurethane/polystyrene interpenetrating polymer networks (PU/PS IPNs); poly(ethylene oxide) (PEO) grafting; blood-compatibility; fibrinogen adsorption; platelet adhesion; microphase-separated structure.

INTRODUCTION

Since Okano et al. reported in 1976s that block copolymers having hydrophilic–hydrophobic microdomain structures exhibited nonthrombogenicity due to their marked suppression of the activation of adherent platelets [1–3], many efforts to develop new blood compatible materials having a microdomain structure have

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been made [4–10]. Polyurethanes (PUs) having microdomain structures, including segmented polyurethane proposed by Cooper and his coworkers, exhibited excellent blood compatibility, compared with other polymeric materials. Therefore, they are extensively used in blood-contacting and organ re-construction applications [11–14]. However, PUs are also known to be prone to surface cracking, stress induced degradation, biodegradation, and calcification [15]. So, in 1994, Kim reported that hydrophilic PU/hydrophobic PS IPNs exhibit good blood compatibility as well as excellent mechanical properties. They also investigated the effect of the degree of phase separation on blood compatibility, with controlled morphology [16–18]. The reaction temperature, composition of monomers, and cross-link density, considerably affected blood-compatibility since the size of the dispersed PS-domain was affected by those conditions. As a result, protein adsorption and platelet adhesion decreased as the size of PS-domains decreased.

During the same period, Nagaoka and Mori proposed the use of a hydrated dynamic surface for better blood compatibility in a study of grafting PEO onto polyvinyl chloride [19]. They demonstrated that the excluded volume effect, and the dynamic motion of the water-soluble PEO chains on the surface, suppressed protein adsorption and platelet adhesion. The movement of hydrated PEO chains induces the microflow of water, and inhibits surface adsorption. They said that the PEO chains might be called ‘molecular cilia’. Andrade et al. were stimulated by that work, and also found that pendant PEO chains on the surfaces of materials had an important role in reducing the adsorption of blood proteins onto the surfaces [8]. In their succeeding works, the protein resistance character of polyethylene oxide chains terminally attached on the substrate was investigated experimentally and also theoretically [20–23]. They considered the steric repulsion effect of PEO, van der Waals attraction between PEO and protein, and hydrophobic interaction between substrate and protein, and found that the protein resistance character of PEO was dependant on the chain length and surface density of PEO, and a high surface density and long chain length of terminally attached PEO exhibited optimal protein resistance.

In this study, both the effects of the pendant PEO chains, and the microphase separated structure on the blood compatibility of PU/PS IPNs, were simultaneously considered by introducing the mobile pendant PEO chains to the PU/PS IPNs. The amphiphilic microphase-separated structure of PU/PS IPNs may suppress cellular activation resulting from the redistribution of glycoproteins and reorganization of cytoskeletal components adhering in the blood cells. Also, the pendant PEO chains on the surface at the hydrated state may prevent the adsorption of proteins and platelets by their dynamic motion
MATERIALS AND METHODS

Materials
Poly(ethylene glycol) (PEG, $M_n = 1000$), poly(ethylene glycol) methylether (PEGME, $M_n = 350$), 1,4-butanediol (1,4-BD) and trimethylolpropane (TMP) as a cross-linking agent for the PU network were degassed at 65°C for 12 h under vacuum to remove moisture before use. Styrrene monomer (SM) was purified by the conventional method [24]. Hexamethylene disiocyanate (HDI), divinylbenzene (DVB) as a cross-linking agent for PS network, and benzoin as an initiator for the polymerization of styrene were used without further purification.

Synthesis and characterization
The disiocyanate-terminated PU prepolymer is (Fig. 1) was prepared by reacting 1 equiv. of PEG with 2 equiv. of HDI at 65°C for 2 h under N2 atmosphere. 0.05 wt% dibutyltin dilaurate (T-12) as a catalyst was added to poly(ethylene glycol) before reaction. HDI was poured into a four-neck flask held at 65°C by a heating-mantle, and then the degassed PEG was added dropwise to HDI through a dropping funnel with vigorous stirring of the mixture. The completeness of the reaction was identified by the di-n-butylamine titration method [25], and the product was kept below 0°C after N2 purging. The molecular structure of PU prepolymer was investigated by NMR spectroscopy.

Isocyanatemethoxy-terminated poly(ethylene oxide) (IMPEO) is was prepared by reacting 1 equiv. of PEGME with 1 equiv. of HDI. The dihydroxymethoxy-terminated poly(ethylene oxide) (DHMPEO) is was prepared by reacting 1 equiv. of IMPEO with excess trimethylolpropane (TMP). The unreacted TMP would be used as the cross-linking agent in PU/PS IPN synthesis. The molecular structure of IMPEO and DHMPEO was investigated by NMR spectroscopy, and their monodispersity of molecular weight was identified by GPC analysis.

Ungrafted PU homopolymers were prepared by reacting the disiocyanate-terminated PU prepolymer with 1,4-butanediol (1,4-BD) as a chain extender, and trimethylolpropane (TMP) as a cross-linking agent. 0.05 wt% of dibutyltin dilaurate (T-12) was added as a catalyst. 1,4-BD and TMP were mixed and degassed before reaction. After PU prepolymer and 1,4-BD/TMP mixture were mixed vigorously by a high-torque stirrer in a 250-ml beaker, the air bubbles entrapped during the mixing were then removed under vacuum for about 3 min. The mixture was cast in a glass plate mold, with a silicon spacer of 1 mm thick. The cast mixture was polymerized at 60°C for 5 h, and then postcured at 100°C for 2 h in a convection oven. 10 wt% PEO-grafted PU homopolymers were prepared in the same way as in the preparation of the ungrafted PU, but a 10 wt% DHMPEO (based upon the total weight of the cast mixture) was used instead of 1,4-BD. In the case of the preparation of 18 wt% PEO-grafted PU homopolymers, 18 wt% DHMPEO was used instead of 1,4-BD.
PEO-grafted PU/PS IPNs were also prepared. PU prepolymer, 1,4-BD, TMP, SM, DVB, and benzoin were mixed by a high-torque stirrer in a 250-ml beaker for about 5 min. PU/PS/IPNs with PEO grafted side chains were prepared by replacing part of the 1,4-BD chain extender by DHMPEO. The mixture was degassed under vacuum for about 3 min, and then cast in a glass plate mold with a silicon spacer.
First, the PU network was formed in a convection oven at 60 °C for 5 h, and then a PS network was formed in a refrigerator equipped with an UV polymerization chamber, by exposing the reaction mixture to UV light (λ_{max} = 350 nm) at −25 °C for 48 h.

**Measurement of the bulk properties**

**Morphology.** The morphology of the fracture surface and the top surface of the PU/PS IPNs was investigated by using both the scanning electron microscopy (SEM, Philips 535M) as well as the scanning probe microscopy (SPM, DI NanoScope IIIa), respectively. SPM measurement was performed in air with an etched silicon probe of which the length was 125 μm, and the spring constant was from 20 to 100 N m⁻¹. Scanning was carried out in the Tapping™ mode, and its frequency was about 0.5 Hz.

**Swelling ratio.** PU/PS IPN sample specimens were dried at room temperature for 24 h under a vacuum, and then immersed in distilled water until equilibrated with water. The weight of the sample was measured every 15 min, and the swelling ratio was calculated by the following equation:

\[
\text{Swelling ratio} = \frac{W_s - W_d}{W_d} \times 100
\]

where \( W_s \) is the weight of swollen sample and \( W_d \) is the weight of dried sample.

**Mechanical property.** The stress–strain properties were measured by a tensile tester (Instron Model 4202) with a cross-head speed of 10 mm min⁻¹ at room temperature. The samples were cut into dumbbell-shaped specimens of which the size was standardized by ASTM D638 (Type V) [26].

**Measurement of surface properties**

**Dynamic contact angle with water.** Dynamic contact angles of PU homopolymers and PU/PS IPNs with water were measured by using an ATI Cahn DCA series 300 analyzer to investigate the hydrophilicity of the surfaces. Stage speed was 150 μm s⁻¹ and the calibration weight was 500 mg.

**Interfacial energy between surface and water.** Interfacial energy between the surfaces of PU/PS IPNs, PU homopolymers and the water was measured by an underwater captive bubble technique [27]. The samples were equilibrated with distilled water for more than 24 h, and the static bubble contact angles of the surface–water–air and the surface–water–octane were then measured by a contact angle goniometer (Erma model C-I type) equipped with an oil droplet apparatus in the water. The interfacial energy between the surface and the water was calculated from the geometric mean equation.
Blood compatibility

Bovine plasma fibrinogen (BPF) adsorption test [28]. The BPFs (ICN Biomedicals, Inc.) was dissolved in phosphate buffer saline (PBS) in concentration of 30 mg ml⁻¹. Samples (5 × 1 × 20 mm) were immersed in the solution at 37°C under mild shaking. To consider the adsorption of BPF's on the wall of the vial, a blank test was performed. After a series of immersion time (10, 20, 40, 60 min), samples were removed, and the changes of the concentration in the solution were investigated by using an UV-spectrophotometer.

In vitro platelet adhesion test (PAI) [29]. The adhesion and activation of the platelets on the surfaces of PU homopolymers and PU/PS IPNs were observed. After samples (10 × 10 mm²) were equilibrated with PBS overnight, they were then immersed in platelet rich plasma (PRP), which was obtained from Chungnam Red Cross, at 37°C with mild shaking in an incubator. After 10 h, the samples were taken out from the solution and rinsed five times with PBS to remove the weakly adsorbed platelets. Then the strongly adsorbed platelets were fixed on the surfaces by immersing the sample in 2 v/v% glutaraldehyde PBS solution at room temperature for 2 h. After that fixation, the samples were dehydrated with a series of ethanol solutions (50, 60, 70, 80, 90, 100 v/v%) for 15 min per each step. Then they were dried in atmosphere overnight and under vacuum for 5 h. The dried samples were coated with evaporated gold, and the adherent platelets were observed with Philips 535M SEM.

Whole blood coagulation test. The amount of blood coagulants adsorbed on the PU homopolymers and PU/PS IPNs was investigated. After the dimension and the weight of four dried specimens (7 × 1 × 20 mm) of each sample were measured, they were equilibrated with PBS overnight, and then immersed in human whole blood, which was obtained from Chungnam Red Cross, at 37°C with mild shaking (90 rpm) in an incubator. After 30 min, 1, 3, and 10 h, each sample was removed and dried in atmosphere overnight and under a vacuum for 5 h. The dried samples were weighed, and then the amount of blood coagulants per unit area of the sample was calculated by using the equation as follows.

\[ W_{BC} = \frac{W_A - W_B}{A} \]

where \( W_{BC} \) is the weight of blood coagulant per unit surface-area, \( W_A \) is the weight of sample after blood-coagulation, \( W_B \) is the weight of sample before blood-coagulation, and \( A \) is the surface area of sample.

Sample notation

The prepared PU homopolymers and PU/PS IPNs were denoted as follows
**RESULTS AND DISCUSSION**

**Characterization**

**NMR spectroscopy.** The molecular structures of PU prepolymer, IMPEO, DHMPEO were identified by a 300 MHz 1H-NMR, which indicated that the products were synthesized very successfully without any side-reactions. The products were characterized as follows: PU prepolymer (δ, ppm): 4.8–4.9 (2H, m, NH–COO), 4.1–4.3 (4H, s, NH–COO–CH₂), 3.5–3.6 (8H, m, O–CH₂–CH₂–O), 3.2–3.3 (4H, q, CH₂–NCO), 3.0–3.1 (4H, q, CH₂–NH–COO), 1.3–1.6 (16H, m, CH(CH₃)₂), IMPEO (δ, ppm): 4.8–4.9 (1H, m, NH–COO), 4.1–4.2 (2H, t, NH–COO–CH₂), 3.5–3.6 (28H, m, O–CH₂–CH₂–O), 3.3–3.4 (3, s, CH₃–O), 3.2–3.3 (2H, q, CH₂–NCO), 3.0–3.1 (2H, m, CH₂–NH–COO), 1.3–1.6 (8H, m, CH₃–CH₂), DHMPEO (δ, ppm): 5.1–5.2 (4H, m, NH–COO–OH), 4.1–4.2 (4H, t, NH–COO–CH₂), 3.5–3.6 (32H, m, O–CH₂–CH₂–O, C–CH₂), 3.3–3.4 (3, s, CH₃–O), 3.0–3.1 (4H, m, CH₂–NH–COO), 1.4–1.5 (2H, m, C–CH₃), 1.3–1.4 (8H, m, CH₃–CH₂), 0.7–0.8 (3H, m, CH₃–CH₃).

**GPC analysis.** The monodispersity of the molecular weight distributions of IMPEO, DHMPEO was investigated by GPC based upon the monodisperse polystyrene standard. A 200-μl sample of each specimen was injected into a THF mobile phase pumped at 1.0 ml min⁻¹. The molecular weight distributions of IMPEO and DHMPEO were very monodispersed, of which the polydispersity indices were 1.012 and 1.014, respectively.

**Morphology**

**Fracture surfaces.** All the PU/PS IPN samples show microphase separated structures in which the hydrophobic PS-rich phase domains are dispersed in the hydrophilic PU-rich phase matrix, and the diameter of the domains in each sample is smaller than 1 μm (Fig. 2). The size of the domains of the PS-rich phase decreases as the content of the PEO-side chains increases. The dispersed domain size decreases from about 0.2 μm to about 0.1 μm, as the content of pendant PEO chain increases from 0 to 18 wt%.
Figure 2. SEM photographs of the fracture surfaces of PU/PS IPNs: (a) IPN0; (b) IPN10; and (c) IPN20.

Top surfaces. The morphology of the top surfaces of PU/PS IPNs was very similar to that of the fracture surfaces (Fig. 3). The PS-rich phase domains were observed higher than PU-rich phase matrix. The average diameter of the PS-rich phase domains is smaller than 0.2 μm, and it decreased from 0.13 to 0.05 μm as the grafting with PEO increased. The surface also became smoother by PEG-grafting (Table 1), because the sphere domains of PS-rich phase became smaller.
Figure 3. SPM images of the top surfaces of PU/PS IPNs: (a) IPN0, (b) IPN10, and (c) IPN18.

The difference of height between the PU-rich phase and PS-rich phase became smaller by the PEO grafting, because the isolated PEO chains grafted on the PU-rich phase increased the height of PU-rich phase matrix. In the morphology of
Table 1.
Roughness of the surfaces of PEO-grafted PU/PS IPNs

<table>
<thead>
<tr>
<th>Sample</th>
<th>*IMS, ( R_g ) (nm)</th>
<th>*Mean roughness, ( R_a ) (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPN0</td>
<td>4.513</td>
<td>3.356</td>
</tr>
<tr>
<td>IPN50</td>
<td>3.426</td>
<td>2.720</td>
</tr>
<tr>
<td>IPN18</td>
<td>2.776</td>
<td>2.131</td>
</tr>
</tbody>
</table>

\[ R_g = \frac{1}{N} \sum_{i=1}^{N}(H_i - H_{ave})^2, \]

where \( H_i \) is the height of \( i \) point and \( H_{ave} \) is the average height of the surface.

\[ R_a = \frac{1}{L_x L_y} \int_{a}^{b} \int_{c}^{d} \sqrt{f(x,y)} \, dx \, dy, \]

where \( f(x,y) \) is the surface relative to the center plane and \( L_x \) and \( L_y \) are the dimensions of the surface.

the surface of IPN18, the scan-line, scratched by the stiff crystal silicon probe, was observed, and the interface of PS-rich domains was not clear because the soft matrix of PU-rich phase was pussed over the PS-rich domains by the probe. It indicates that the surface was very mobile and soft, compared with the ungrafted surface.

Mechanical property

The tensile strength, the elongation at break, and tensile modulus of PU homopolymers, and the PEO-grafted PU/PS IPNs were investigated. Figure 4 shows the effect of the PEO chains on the mechanical behavior of PU homopolymers, and PU/PS IPNs. The tensile strength and the elongation at break decreased as the content of PEO grafted was increased, because the crosslinking density of the PU network became less uniform, as the content of the side chains increases. DHI-PEO used instead of 1,4-BD in the preparation of the grafted samples, was also less mobile than TMP used as the cross-linking agent. So the mobile TMPs reacted with both the isocyanate end-groups in PU prepolymer ahead of less mobile DHI-PEO, and the highly cross-linked network may have been partially formed. That non-uniformity of the cross-link density became more prominent as the use of DHI-PEO increased in the preparation of the higher grafted sample. The tensile modulus of PU homopolymers was about 6.6 MPa, and this value is not sufficient to be used as biomaterials, except for coating application. In general, polyurethanes, used as biomaterials, have the hard segments in their structures, but the PU homopolymers, synthesized in this study, are only comprised of the soft segments, so they are more hydrophilic and flexible than other polyurethanes having the hard segments. These soft-segmented polyurethanes can be coated on a supporting material, such as PE tubes, and then this supported material may be used as the material for the artificial blood vessel.

For the case of PU/PS IPNs, the tensile strength and the elongation at break decreased as the content of PEO side chain was increased. The PU/PS IPNs had
the microphase separated structure composed of PU-rich phase matrix, and the PS-rich phase domains of which the diameter was smaller than 1 μm. So, the matrix of the PU-rich phase had a dominant effect on the mechanical behavior of PU/PS IPNs. As the content of the PEO side chain was increased, the network was less uniformly formed, that is, the non-uniformity of the cross-link density became more prominent, so the tensile strength and the elongation at break decreased. The tensile modulus of PU/PS IPNs was about 32 MPa, which was about five times bigger as compared with PU homopolymers. This result indicates that the PU/PS IPNs, synthesized in this study, have an excellent mechanical property, and can be used as biomaterials in a broad range of applications.

Hydrophilicity

Swelling ratio. Figure 5 shows the swelling behavior measured at 25°C for the PU/PS IPNs. Generally, it has been known that the swelling behavior of the
Figure 5. Swelling behavior of PU/PS IPNs with water. ●: IPN0; ■: IPN10; ▲: IPN18.

Figure 6. The effect of PEO side chains on the dynamic contact angle of PU homopolymers and PU/PS IPNs with water. ○: Advancing contact angle of PU homopolymers; □: Receding contact angle of PU homopolymers; ●: Advancing contact angle of PU/PS IPNs; ▲: Receding contact angle of PU/PS IPNs.

polymer blend is strongly influenced by its heterophase structure. When the IPNs of hydrophilic and hydrophobic components are swollen in water, the water diffuses through the hydrophilic phase. At a fixed composition, the swelling ratio in water decreases as the degree of intermingling increases. In Fig. 5, the swelling ratio decreases with increase of the content of the PEO side chains, due to an increase in the degree of intermixing as shown in the morphology of the fracture surface.

Surface energy. The hydrophilicity of the surfaces of PU/PS IPNs and PU homopolymers was investigated by measuring the advancing and the receding dynamic contact angles with water. Figure 6 shows that both the advancing and the receding contact angles of PU/PS IPNs and PU homopolymers with water decrease with increase of grafting the PEO, which indicates that the surface becomes more
<table>
<thead>
<tr>
<th>Sample notation</th>
<th>Underwater contact angle (deg)</th>
<th>Interfacial energy, γ_{sw} (dyn cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Water–octane–solid</td>
<td>Water–air–solid</td>
</tr>
<tr>
<td>IPN0</td>
<td>57.1</td>
<td>48.9</td>
</tr>
<tr>
<td>IPN10</td>
<td>49.2</td>
<td>39.7</td>
</tr>
<tr>
<td>IPN18</td>
<td>43.3</td>
<td>38.9</td>
</tr>
<tr>
<td>PU0</td>
<td>23.8</td>
<td>19.1</td>
</tr>
<tr>
<td>PU10</td>
<td>19.8</td>
<td>17.2</td>
</tr>
<tr>
<td>PU-10</td>
<td>16.4</td>
<td>16.6</td>
</tr>
</tbody>
</table>

hydrophilic. Since the mobile hydrophilic pendant chains are stretched and migrated toward the interface between the surface of the sample and the water, the surface becomes more hydrophilic.

The interfacial energy between the surfaces of the PU/PS IPNs and the water decreases. That is, the surface becomes more hydrophilic at the hydrated state, as the grafting with PEO chain increases (Table 2). The surface–water interfacial energy decreases from 4.32 to 1.75 dyn cm⁻¹ with the increase of the pendant PEO chain from 0 to 18 wt%. The interfacial energy between the surfaces of PU homopolymers and water also decreased as the grafting with PEO chains increased.

**Blood compatibility**

The BPFs adsorption. Fibrinogen is one of the most important globular proteins circulating in the blood. It plays a central role in the regulation of hemostasis and thrombosis by participating in blood coagulation and facilitating adhesion and aggregation of platelets. Fibrinogen is a relatively large (340 kD) glycoprotein composed of two each of three non-identical polypeptide chains (Aα2,Bβ2,γ2). The molecule is folded in such a way that all six amino termini are clustered in a central domain (E domain), but the three different carboxyl ends are located at opposite ends of distended molecule (D domain), which are connected to the central domain by three-stranded ‘coiled coil’. These D domains can be split and displaced from the molecular axis, and each coiled-coil rod was interrupted by a small globular region to form an added globular region adjacent to the central E domain through the folding of Aα chains. This macromolecular dimensions and conformation of hydrated fibrinogen considerably affects surface-dependant interaction [30–32]. In this test, BPF was adsorbed rapidly within a few minutes, and then reached equilibrium. Large amounts of BPF’s were adsorbed upon the PS homopolymer surface, as compared with the PU homopolymer and PU/PS IPNs (Fig. 7). Fibrinogen resistance character of PEO chains terminally attached to a solid substrate has been studied in many group [33–41], and it was found that the steric repulsion effect of PEO, van der Waals attraction, and hydrophobic
interaction were highly related to the fibrinogen resistance character of pendant PEO chains. Specially, the steric repulsion force is very important when the pendant PEO chains are relatively longer and overlapped each other, and such force is about ten times stronger than other forces, van der Waals force, and hydrophobic interaction. However, the pendant PEO chains observed in this study was relatively very short, of which the Flory radius \( R_f \) was only about 0.96 nm, and their surface density was very low. (The pendant PEO chains were all separate coils, \( \sigma < N^{-1/3} \), \( \sigma \) is fraction of surface sites grafted, and \( N \) is the number of monomer per chain.) Therefore, the van der Waals interaction, hydrophobic interaction became considerable as the steric repulsion effect. From the results of contact angle measurement, we found that the surfaces of PU/PS IPNs and PU homopolymers became hydrophilic by PEO grafting, which indicate that the hydrophobic interaction between the surface and the fibrinogens was reduced. Dimer, trimer, and macromer of the hydrated fibrinogen have linear conformations predominantly, and increased affinity for the hydrophobic surface compared with monomeric fibrinogen [31]. Therefore, the hydrophobic interaction became important more as the immersing time of samples in the fibrinogen solution was getting longer, because the amount of dimers, trimers and macromers of fibrinogen formed was increased. The pendant PEO chains diminished the hydrophobic interaction between the surface and fibrinogens, and such effect became stronger as the content of pendant PEO increased. As a result, the total amount of BPFs adsorbed decreased, as the grafting of the PEO chains was increased.

The adhesion of human platelets. The interaction of platelets with the surfaces of PU homopolymers and PU/PS IPNs was investigated by using PRP prepared from human whole blood. Unstimulated platelets have a 2-μm discoid shape,
Figure 8. SEM photographs of the platelets adhered on the PU homopolymers after 10 h incubation:
(a) PU0; (b) PU10; (c) PU18; (d) IPN0; (e) IPN10; and (f) IPN18.

and functioning platelets are divided into three zones: the peripheral, sol-gel, and
granule [44]. The peripheral zone consists of the platelet membrane, the open
canalicular system, and the exterior coat of the platelet (rich in glycoproteins).
Platelet glycoproteins form the basis of the platelet receptor system for activation,
and the sol-gel zone contains a fibrillar contractile system that allows shape change,
Figure 9. Effect of the microtome separated structure of PU/PS IPN — SEM photographs of the platelets adhered: (a-1) PU0 (low magnification); (a-2) PU0 (high magnification); (b-1) IPN0 (low magnification); (b-2) IPN0 (high magnification).

pseudopod formation, and contraction. In the platelet adhesion test, platelets initially react with the surface by pseudopod formation, and then form aggregates through the binding of glycoproteins. The SEM photographs of the adhered platelets onto the surfaces are shown in Figs 8 and 9. Figure 8 shows that the platelets were less attached on the surfaces of PEO-grafted PU homopolymers than on the ungrafted ones. On the IPN0, ungrafted PU/PS IPN surface, large amounts of platelets were adhered, spread, and then deployed pseudopodia, compared to the IPN18, PEO-grafted PU/PS IPNs, which indicated the activation of the adhered platelets. However, the adhesion and the shape change in the platelets were significantly suppressed on the surface of IPN18. For the PEO-grafted samples, the mobile PEO side chains had an important role of reducing the adhesion, and aggregation of platelets by the steric repulsion, and by diminishing the hydrophobic interaction between glycoproteins and surfaces. Therefore, the grafting with PEO chains enhanced the blood compatibility of the samples. On the other hand, the mural thrombosis, which means the aggregation of the platelets, occurred so actively on the ungrafted PU homopolymers, as compared with the ungrafted PU/PS IPN (Fig. 9). On the PU/PS IPNs, the expression of the platelet glycoproteins was suppressed by regulating the excessive assembly of them, and the formation of platelet aggregates was indeed diminished. This means that the secondary
thrombosis was extensively suppressed by the effect of the microporous-separated structure of IPN.

The coagulation of human whole blood. Figure 10 exhibits the changes in the amounts of blood-coagulants on the surfaces of both PU homopolymers and PU/PS IPNs during the immersion of samples in human whole blood. The coagulation of the blood occurred within a moment of contact with the foreign surface. After that time the coagulation of blood proceeded gradually until the blood could not flow. The weight of blood coagulants per unit area of surface increased with time, and larger amounts of blood coagulants were adsorbed on the less PEO-

(a)

(b)

Figure 10. Weight of blood coagulant on the surfaces: (a) PU homopolymers. •, PU10; □, PU100; ▲, PU50; (b) PU/PS IPNs. ●, IPN0; ■, IPN10; ▲, IPN18; ○, IPN18.
grafted surface. Although the possibility that unattached blood clots may have been present cannot be considered, we can know that the mobile pendant PEO chains play an important role in the suppression of blood-coagulation on both the PU homopolymers and PU/PS IPNs. When the PEO-grafted samples are in contact with blood, the mobile hydrophilic pendant PEO chains stretched and migrated toward the interface. They suppressed the coagulation of blood on the surface by suppressing the adsorption of globular proteins, and platelets, owing to their steric repulsion effect, and reduced hydrophobic interaction effect. On the other hand, the blood coagulation is suppressed more on the PU/PS IPNs, as compared with on the PU homopolymers, which indicates that its microphase-separated structure also suppressed the coagulation of blood.

CONCLUSION
PU homopolymers and PU/PS IPNs were synthesized changing the content of the pendant PEG chains. All the PU/PS IPNs had the microphase-separated structures in which the PS-rich phase domains were dispersed in the matrix of the PU-rich phase. The domain size decreased a little, as grafting with PEO chains was increased, which indicates an increase in the incompatibility between the PU-rich phase and the PS-rich phase. The tensile strength decreased as the contents of the pendant PEG chains were increased. The PU/PS IPNs showed excellent mechanical properties, as compared with the PU homopolymers. Both the water swelling ratio, and the contact angle measurement for the PEO-grafted PU/PS IPNs indicated that the surfaces were more hydrophilic than the bulk at the hydrated state, since the mobile hydrophilic pendant PEG chains were stretched and migrated toward the interface, when contacted with water. This reorganization of the structure affected the blood compatibility. Based upon the results of BPF adsorption tests, platelet adhesion tests, and the measurements of the weight of blood coagulants, blood compatibility was enhanced by grafting with PEO chains. Especially the PEO-grafted PU/PS IPN shows an excellent thromboresistance. This material can be used as a material for blood-contacting devices in a broad-range of bio-related applications, owing to its excellent blood compatibility, as well as its good mechanical and thermal properties.

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