Study on Thermoplastic Polyurethane/Polypropylene (TPU/PP) Blend as a Blood Bag Material

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ABSTRACT: Blends with different ratios of thermoplastic polyurethane/polypropylene (TPU/PP) were prepared by melt mixing using an internal Haake mixer. Properties of the blends were investigated using SEM micrographs of cryofractures and measurement of the mechanical strength, water absorption, cell culture, and platelet adhesion *in vitro* tests, which were compared with those of PVC blood bags. The effect of the addition of the ethylene–vinyl acetate (EVA) copolymer on the TPU/PP blend properties was investigated. The results indicated that a TPU/PP/EVA = 80/20/5 blend can be used as a new blood bag material. It was observed that the blend is homogeneous with higher mechanical strength than that of the commercial PVC blood bag. This blend also showed a compatible cell response in contact with L929 fibroblast cells and fewer tendencies to interaction with platelets compared to the PVC blood bag. Although the blends were immissible and no chemical reaction at the interface could be found, the blood compatibility of the blends were improved. © 2003 Wiley Periodicals, Inc. J Appl Polym Sci 89: 2496–2501, 2003

Key words: poly(propylene) (PP); blends; biomaterials

INTRODUCTION

The blood bag system is a disposable biomedical device used for the collection, storage, transportation, and transfusion of human blood and blood components.[1] Until now, most widely used blood bag material has been plasticized poly(vinyl chloride) (PVC).[2] PVC is a relatively rigid and brittle polymer. Plasticizers are added to PVC to facilitate processing and increase flexibility and toughness in the final product by internal modification of the polymer molecule.[3] The main plasticizer used in blood bags is di-2-ethylhexyl phthalate (DEHP).[2] It is a lipophilic or fat-loving compound and so it tends to concentrate in fatty tissues.[4] *In vivo* and *in vitro* research links DEHP or its metabolites to a range of adverse effects on the liver, reproductive tract, kidneys, lungs, and heart. It also appears to pose a relatively low risk of hepatic cancer in humans.[3] As a result of such problems, several efforts have been made to develop plastic materials suitable for storing blood components from non-PVC plastics.[5] Among the materials investigated were polymers such as thermoplastic polyurethanes, silicone–polycarbonate block copolymers, ethylene–vinyl acetate copolymers, flexible polyesters, and various thermoplastic elastomers and polyolefin blends.[6] We also tried to solve the problem of the toxicity of plasticized PVC by use of a polyurethane (PU) and polypropylene (PP) blend as a blood bag material. PUs are one of the few synthetic materials with good biocompatibility and other performance characteristics, which make them suitable for a wide range of medical application such as for blood bags and surgical gloves and for a wide range of high-risk applications such as catheters, synthetic veins, and, more recently, wound dressings.[7] PP is also one of the polymeric biomaterials that is extensively used for biomedical application such as sutures and finger-joint implants due to its good mechanical properties and inertness in living systems.[8]

PP, as a dispersed phase in a thermoplastic polyurethane/polypropylene (TPU/PP) blend, may play two roles: It can improve the physical properties of the blend as a blood bag material and it can also balance the hydrophilicity/hydrophobicity of the blend, which plays a vital role in blood compatibility.[9] The presence of PP in the blend reduces the concentration of hard-segment domains of PU at the blend surface and it becomes less attractive to blood platelets.[10]

The resultant blends are autoclavable and RF-sealable. Additionally, the material of the present study is extrudable, injection-moldable, and blow-moldable. Because it is a non-PVC, non-DEHP material, it eliminates the environmental concerns of acid rain and the alleged carcinogenic properties of DEHP. Further, with respect to tubing, the resultant tubing is kink-resistant.

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In this study, TPU/PP blends were prepared and their properties were examined to compare them with those of commercially available blood bags. An *in vitro* cell culture experiment was done to evaluate the cell compatibility of the blend materials, and the behavior of platelet adhesion onto the best sample surface was also compared with that of the PVC blood bag surface.

EXPERIMENTAL

Materials

TPU (LARIPUR 7025) was obtained from the Coim Co. (Milan, Italy) with a Shore A hardness of 70. It is a block copolymer consisting of hard segments and polyester soft segments.

PP was supplied by the Arak Petrochemical Co. (Arak, Iran), known as V30GA type with a nominal melt-flow index (MFI) = 16. The ethylene–vinyl acetate copolymer with 18% vinyl acetate was supplied by the Hyundai Co. (Seoul, South Korea). Blood bag samples made from plastcized PVC were purchased from the Green Cross Medical Co. (Seoul, South Korea).

Preparation of blends

Before processing, the TPU was dried for at least 3 h in a vacuum oven at 100°C. The blending of components was done in a Haake mixer (Buchler Rhecord 90) at 190°C with a rotor speed of 60 rpm for 5 min.

Pressure molding was used to produce specimens for tests. The residence time in the molten state was to 5 min at 190°C. The molding pressure was about 100 bar and the rate of cooling was 5°C/min. The molds employed were Teflon-coated to provide a nonadhesive surface.

Physical properties of blends

Morphology studies were done using a scanning electron microscope (SEM) Model XL30 made by the Philips Co. The prepared blends were cryogenically broken and the fractured surface was coated with a gold–platinum alloy and scanned. The mechanical strength of the PP, PU, and blends were evaluated at room temperature in a tensile testing machine (Instron 6025) at a crosshead speed of 200 mm/min and compared with those of the commercial blood bags.

The swelling properties of the blends were examined by measuring the water-absorption content. The prepared samples were weighed after drying (dry weight) and immersed in double-distilled water. The swollen films were taken out of the water after 72 h, the surfaces wiped with filter paper, and weighed (wet weight).The swelling capacity was calculated as follows:

$$\% \text{ Swelling} = [(\text{wet weight} - \text{dry weight}) \div \text{dry weight}] \times 100 \quad (1)$$

All swellings are the mean value of five measurements of the films.

Evaluation of cytocompatibility

The cytocompatibility of the prepared films were evaluated by an *in vitro* cell culture test. The mouse L929 fibroblast cells were used as a test model in this study. The cell suspension of 4×10^5 cells/mL was prepared before seeding. The duplicate specimens of each sample were sterilized in 96% ethanol and washed in a culture medium before the cell culture procedure. They were placed in a multiwell tissue culture polystyrene plate with a 5 mL cell suspension, with one well kept as a negative control and then maintained for 48 $\pm$ 1 h in a CO_2-controlled incubator at 37°C. After incubation, the samples were washed with a phosphate-buffered saline solution (PBS). The cells were fixed and dehydrated in graded ethanol (60, 70, 80, 95%) and stained with 5% Giemsa. The cells were observed with light microscopy (Zeiss).

Platelet adhesion

Venous blood from healthy human volunteers was collected with a vacuum syringe containing 5% citric acid. The blood was centrifuged at 800 rpm for 10 min at 25°C and the platelet-rich plasma (PRP) was withdrawn with a polyethylene (PE) pipette and placed in clean vials. The residue of the blood was centrifuged at 3000 rev min^{-1} for 10 min to obtain platelet-poor plasma (PPP). The platelet count of PRP was determined with a Coulter counter (type 4) and adjusted to 150,000 platelets in mm^3. PRP (1 mL) was placed on each of the samples of 1 cm^2 and allowed to stand for 1 h at 37°C. The samples were then vigorously washed with PBS and fixed with 2.5% glutaraldehyde in saline at 20°C overnight. The samples were then dehydrated with ethanol (50–100 %) and dried to the critical point and stained with 5% Giemsa. The platelets were observed with light microscopy (Zeiss).

RESULTS AND DISCUSSION

Morphology

TPU/PP blends are highly incompatible because of large differences in their polarities and high interfacial tension.[11] The differences in the surface free energies induce an incompatibility.[12] Due to this fact, SEM micrographs of cryofractures have revealed no sign of interfacial adhesion (Fig. 1). As shown in these figures,

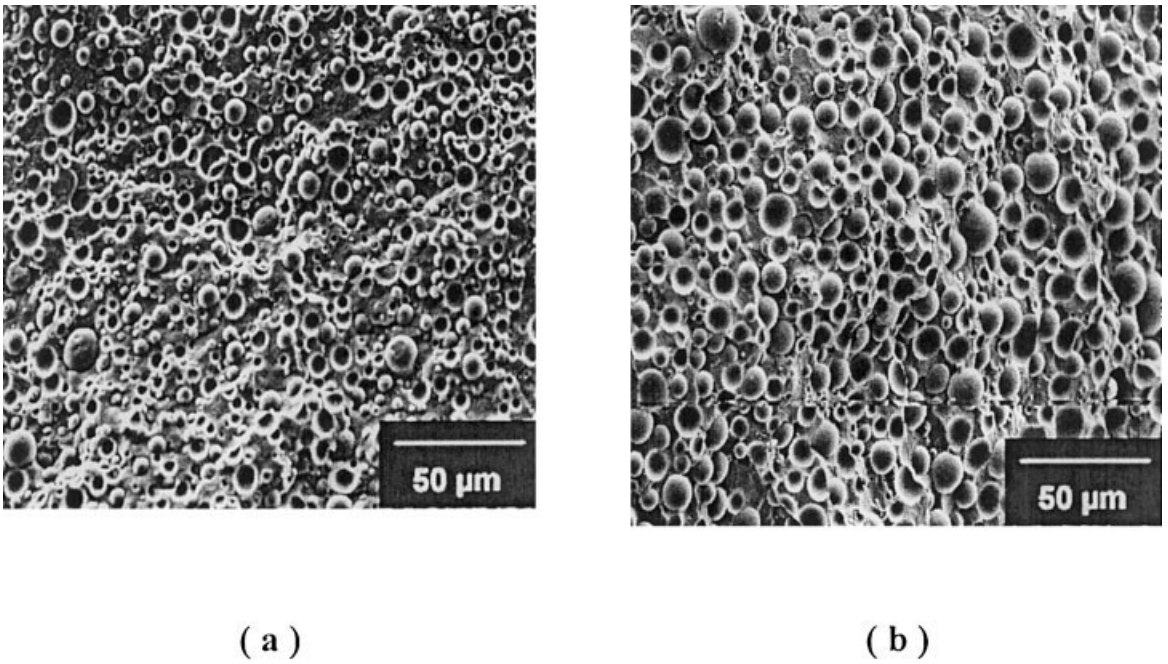

Figure 1 SEM photomicrographs of (a) TPU/PP = 80/20 blend and (b) TPU/PP = 70/30 blend.

the blends exhibited a two-phase morphology. The size of the dispersed particles (PP) became coarser in the TPU/PP = 70/30 blend than in the TPU/PP = 80/20 blend. This is caused by coalescence, which has been previously observed at concentrations lower than 1% of PP.[11] Coalescence in the first blend is more than that the second one due to the higher probability of collision.[13]

Since these immiscible blends are thermodynamically unstable, they must be stabilized to prevent coalescence during melt processing.[14] The stability of polymer blends is enhanced by addition of a useful block copolymer.[15] The influence of the EVA copolymer on the blend is shown in Figure 2. With addition of EVA, the relatively finer dispersity of the PP phases was found, and the distribution of particle sizes also improved. So, in this case, the homogeneity of the blend is better than is that of the blend without EVA.

Mechanical properties

The mechanical behavior (tensile strength and modulus) of the blends and commercial blood bags are shown in Table I. All blends except TPU/PP = 50/50 have a higher tensile strength and modulus than those of the blood bag.

As shown in Figure 3, the samples have shown a U-shaped curve for the dependence of the tensile strength on the blend composition. Usually incompatible blends show this typical U-shaped curve and a decrease in tensile strength with the addition of a second polymer.[11] This phenomenon depends on the phase inversion from PP to TPU that happens at 50% by weight of each polymer.

The extent of the reduction in properties is related to the blend morphology; blends having a finer dispersity show less reduction in properties.[11] Due to this fact, the TPU/PP = 80/20 blend had a higher tensile strength than that of the TPU/PP = 70/30 blend. It is found from Table I that the addition of the EVA copolymer to the blend reduced its tensile strength. This can be related to the dispersion of some extent of EVA in the TPU matrix, which leads to a reduction of the

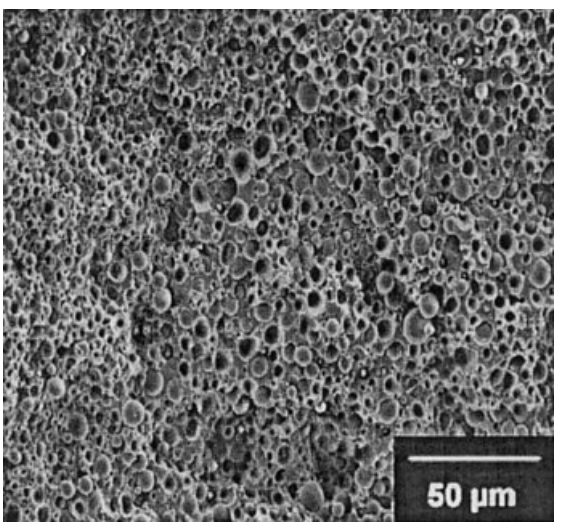

Figure 2 SEM micrograph of TPU/PP/EVA = 80/20/5 blend.

TABLE I
Tensile Strength and Modulus of Prepared Samples (n = 3)

Sample	PP	TPU/PP (50/50)	TPU/PP (70/30)	TPU/PP (80/20)	TPU/PP/EVA (80/20/5)	TPU	PVC (blood bag)
Tensile strength at break (MPa)	31.32 ± 4.64	3.59 ± 0.96	13.02 ± 4.47	18.23 ± 2.51	14.21 ± 1.94	32.80 ± 3.34	13.11 ± 0.81
Modulus (100%) (MPa)	458 ± 48	101 ± 10.2	16.7 ± 2.46	12.6 ± 2.15	11.9 ± 1.83	6.1 ± 1.37	7 ± 1.55

Values are means ± standard deviation.

cohesive energy density in this phase.[16] However, the tensile strength and modulus of the blend with EVA is higher than that of the blood bag.

Water absorption

The swelling property of the TPU/PP blends and commercial blood bag films was evaluated by measuring the water-absorption content after immersion in distilated water for 72 h. As can be seen in Figure 4, the water absorption of TPU is higher than that of PP, which relates to the polar nature and hydrophilicity of PU.[17] Due to this fact, the water absorption of the prepared films was reduced with the addition of PP to the TPU matrix. The high swelling of TPU/PP = 50/50 blend in water is due to the intensive surface roughness of the blend, because of a bicontinuous phase structure at this ratio.[11]

The addition of the EVA copolymer to the TPU/PP blend increased the water-absorption content compared with original blend, which is probably due to the flexibility of the copolymer chains (T_g = 10°C) that leads to the molecular rearrangment of polar groups on the surface in contact with water. So, the addition of the EVA copolymer is good for our purposes, because of the higher water-swelling property than that of the blend, which reduces the friction of the film surface, reducing damage to the blood cells and platelet adhesion.[17]

Biocompatibility results

In the cell culture method, the performance of a cell is investigated by comparing it with a negative control. A negative control [tissue cell culture polystyrene (TCPS) in this experiment] is a sample thoroughly compatible with cells and is cultured with the main samples. For this type of test, a material is considered to be biocompatible if it supports cell attachment and growth.[18] Figure 5(a–d) shows optical photomicrographs of the L-929 fibroblast cell attachment onto the control, PP, TPU, and TPU/PP/EVA (80/20/5) blend surfaces, respectively. As can be seen, both the shapes and the numbers of the attached cells are different depending on the substrate. The comparative results show that cell adhesion and spreading is better with the control sample (PS) than with the PP surface (hydrophobic surface). Cells on the control sample appeared flattened with small peripheral filopodia and ruffled edges. The PP surface causes a significant decrease in the cell attachment, which was attributed to the high hydrophobic surface.[19] Figure 5(c,d) shows the appearance of L-929 cells grown onto the TPU and TPU/PP blend. Cell growth and all four stages (at-

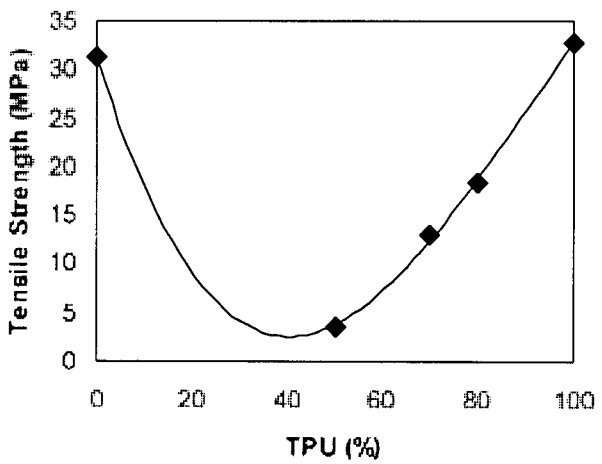

Figure 3 Tensile strength of TPU/PP blends versus TPU (% wt).

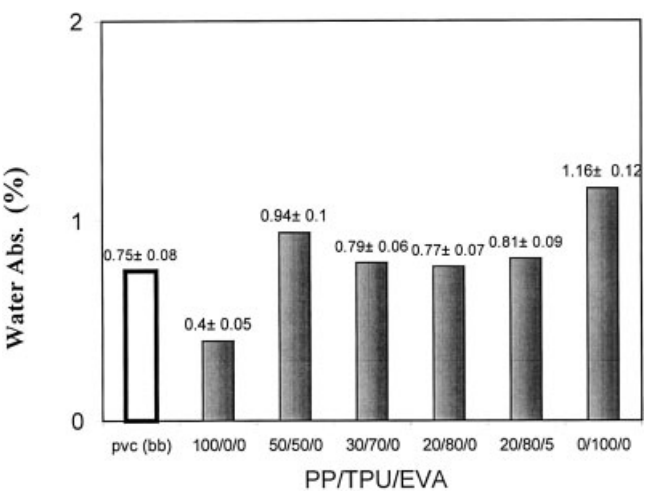

Figure 4 Water absorption of the samples after 72 h (n = 3).

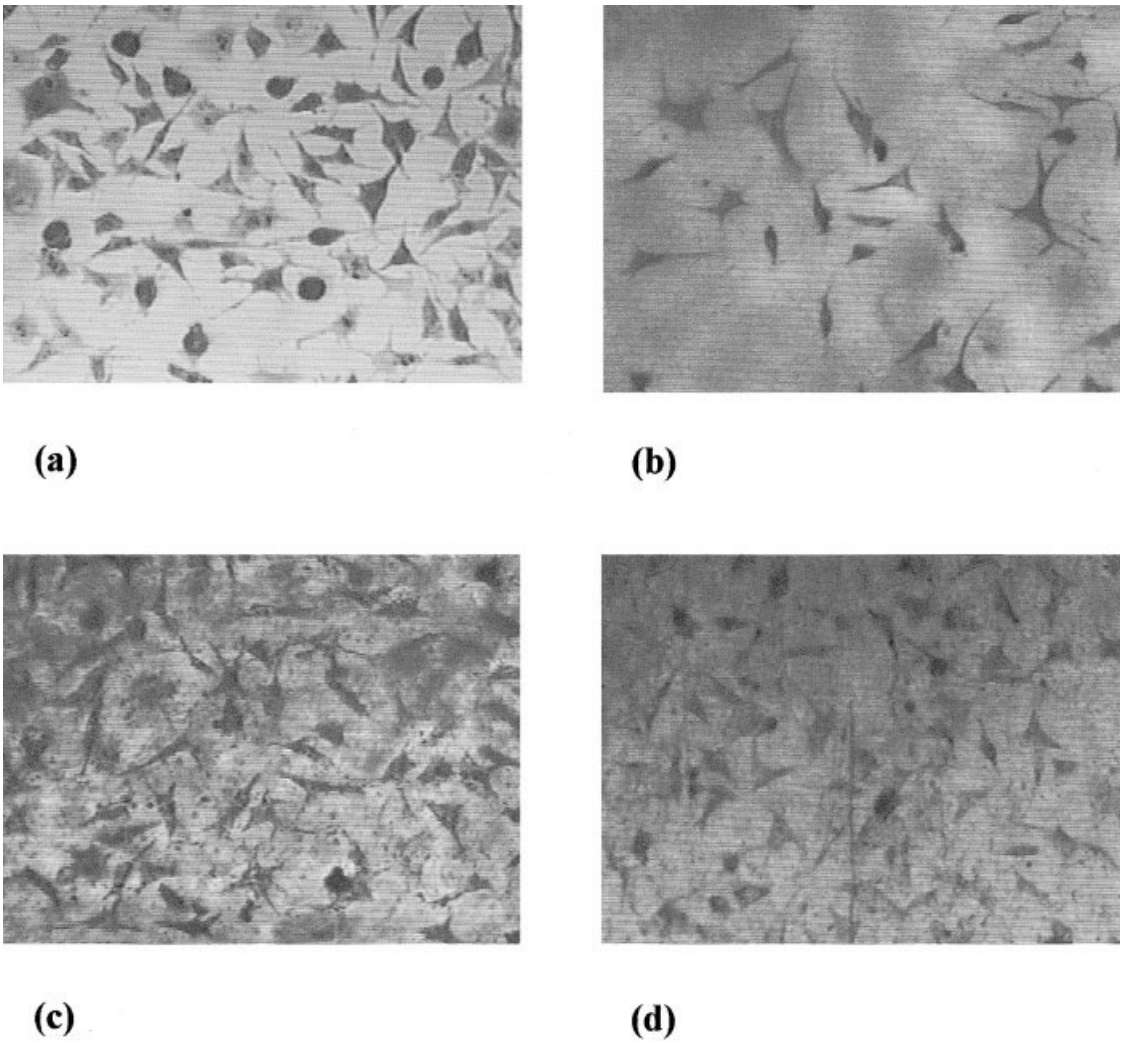

Figure 5 Cellular response of L929 fibroblast cells to the surface film: (a) negative control; (b) PP; (c) TPU; (d) TPU/PP/EVA (80/20/5) after 48 h incubation (magnification: 400×).

tachment, filopodia, webbing, flattening) appear but the number of cell adhesions on these surfaces is a little lower than that of the control. It was found that the extent of the cellular adhesion is considerably affected by the physical and chemical properties of the substrate, that is, the chemical composition, surface charge, surface tension, microstructure, and rigidity.[20,21] This cell response is a sign of the cytocompatibility of PP, TPU, and TPU/PP/EVA = 80/20/5 blend.

Platelet adhesion study onto the film surfaces

Platelet adhesion experiments were carried out *in vitro* using the platelet-rich plasma (PRP) method.[22,23] An optical microscope was used to study the morphology of the adherent platelets. One of the possible routes to the formation of blood clotting is adhesion, activation, and aggregation of platelets at the foreign interface.[24] Figure 6(a,b) shows the morphology of platelets attached onto the polymer films. As can be seen in Figure 6, the platelet adhesion on the blend [Fig. 6(a)] is significantly lower than that onto the PVC blood bag surface [Fig. 6(b)]. Complete activation and aggregation of the attached platelets were observed on the PVC blood bag film as a control [Fig. 6(b)]. However, small platelets were attached onto the surface of the blend. The excellent blood compatibility of PU was discovered by Boretos and Pierce.[25,26] They also noticed the excellent mechanical properties of PU and applied it to a blood pump for an artificial heart system. However, little attention has been paid to the relationship between the blood compatibilitty and the structure of PU. However, as reported, the grafting of long alkyl side chains onto PU has been shown to reduce platelet deposition.[27] The poor blood-contacting properties of hydrophobic polymers may be ascribed to the absence of specific interactions between

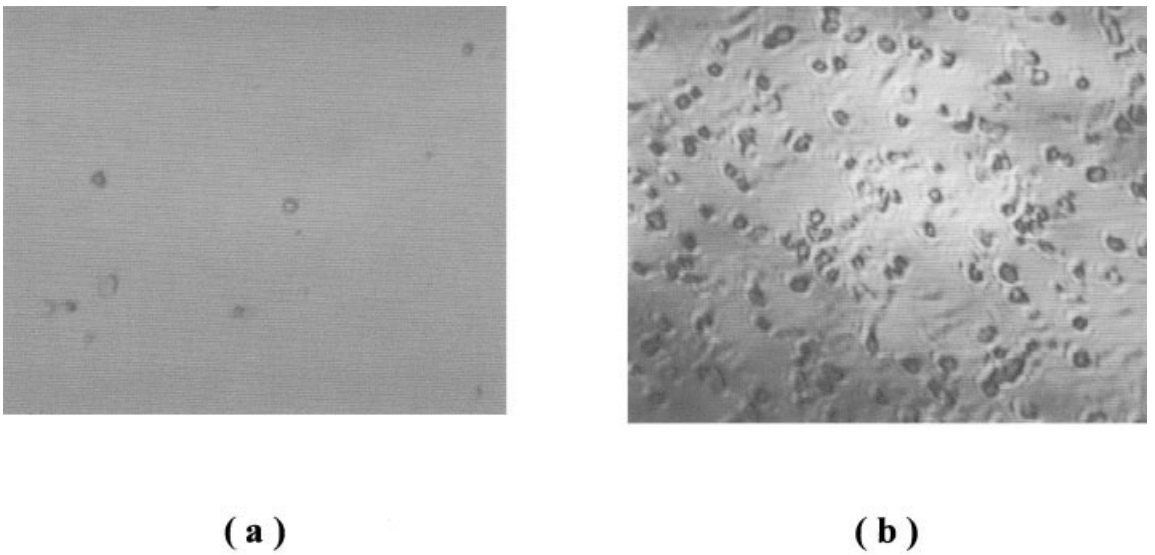

Figure 6 Optical micrographs of platelets adhering on the (a) TPU/PP/EVA = 80/20/5 and (b) commercial blood bag film surfaces (magnification: 400×).

the surface and platelet due to the alkyl branch length. Therefore, PP chains play a similar role to that of the grafting of alkyl chain on PU that was described. The combination of factors including microphase separation, surface heterogeneity, and surface hydrophobicity determined the polymer blood-contacting response. Therefore, these factors that are different between the blend and the PVC blood bag affect the reduction of platelet adhesion (Fig. 6) and the spreading on the prepared blend film in comparision with the PVC commercial blood bag film.

CONCLUSIONS

Blend systems were immissible and no chemical reaction at the interface between PP and TPU was found. The blend with the EVA copolymer has a finer dispersed morphology than that of the others. All the blends except TPU/PP = 50/50 have a higher tensile strength than that of the PVC blood bag. Cell culture experiments also showed no sign of toxicity for the blend materials.

From the results of this study, the most suitable blend for blood bag application seems to be TPU/PP/EVA = 80/20/5, because of its appropriate mechanical strength, slightly higher water swelling, and significantly less interaction with blood platelets than with the PVC blood bag.

References

1. Carmen, R. Transfus Med Rev 1993, 7, 1.
2. Lee, J. H.; Kim, K. O. J Biomed Mater Res 1999, 48, 328.
3. Tickner, J. A.; Schettler, T.; Guidotti, T.; McCally, M.; Rossi, M. Am J Ind Med 2001, 39, 100.
4. Bruck, S. D. In Encyclopedic Handbook of Biomaterials and Bioengineering; Wise, D. L.; Trantolo, D. J.; Altobelli, D. E.; Yaszemeski, M. J.; Gresser, J. D.; Schwartz, E. R., Eds.; Marcel Dekker: New York, 1967; Part 1, Vol. 1, p 300.
5. Leaversuch, R. D. Mod Plast 1999, 76.
6. Czuba, L . MDDI Mag 1999, 28.
7. Reed, D. Urethane Technol Mag 1999, 22.
8. Poole-Warren, L.; Martin, D. J.; Schindhelm, K.; Meijs, G. F. Polym Biomater Mater Forum 1997, 21, 241.
9. Mathew, J.; Liu, S. Q.; Komada, M. Biomaterials 1993, 14, 57.
10. Lenk, T. J.; Chittur, K. K.; Ranter, B. D. Biomaterials 1989, 15, 134.
11. Potschke, P.; Wallheinke, K.; Fritsche, H.; Stutz, H. J Appl Polym Sci 1997, 64, 749.
12. Walheinke, K.; Potschke, P.; Stuts, H. J Appl Polym Sci 1997, 65, 2217.
13. Petrovic, Z. S.; Budinski-Simendic, J.; Divjakovic, V. J Appl Polym Sci 1991, 42, 779.
14. Walheinke, K.; Potschke, P. Polym Eng Sci 1990, 39, 1022.
15. Macosko, C. W.; Guegan, P.; Khandpur, A. K. Macromolecules 1996, 29, 5590.
16. Folkes, M. J.; Hope, P. S. Polymer Blends and Alloys; Chapman & Hall: London, 1993; p 46.
17. Lamba, N. M. K.; Woodhouse, K. A.; Cooper, S. L . Polyurethanes in Biomedical Applications; CRC: Boca Raton, FL, 1998; p 205.
18. Sheikhi , N.; Mirzadeh, H.; Katbab, A. A. Iran J Polym Sci Tech 2001, 10, 3.
19. Dekker, A.; Reitsma, K.; Beugeling, T.; Banjes, A.; Feijen, J.; Van Aken, W. G. Biomaterials 1991, 12, 130.
20. Massia, S. P.; Stark, J.; Letbetter, D. Biomaterials 2000, 21, 2253.
21. Hunter, A.; Archer, C. W.; Walker, P. S.; Blunn, C. W. Biomaterials 1995, 16, 287.
22. Mathew, J.; Liu, S. Q.; Kodama, M. Biomaterials 1992, 13, 1051.
23. Park, K.; Mao, F.; Park, H. Biomaterials 1990, 11, 24.
24. Cooper, S. T.; Peppas, N. A.; Hoffman, A. S.; Ratner, B. D. Biomaterials: Interfacial Phenomena and Applications; American Chemical Society: Washington, DC, 1982; p 87.
25. Boretos, J. W.; Pierce, W. S. Science 1967, 158.
26. Boretos, J. W. Pure Appl Chem 1980, 52.
27. Takahara, A.; Okkema, A. Z.; Cooper, S. L.; Cory, A. J. Biomaterials 1991, 12, 324.