Structure–Protein Adsorption Relationships of Polyurethanes

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ABSTRACT: A series of hydroxyl-terminated polybutadiene (HTPB) and 4,4′-dicyclohexylmethane diisocyanate (H_{12}MDI)-based polyurethanes (PUs) with different molecular weight, hard-segment content, or 4-vinyl pyridine content (4-VP content) were synthesized by solution polymerization. Protein adsorption ratio of fibrinogen to albumin (F/A molar ratio), which was adopted as the indicator of blood compatibility, was measured. The F/A molar ratio on the film's surface was affected by surface composition. The surface composition was quantified by carbonyl group to butadiene group (C=O/C=C) adsorption ratio on FTIR-ATR spectra and oxygen to carbon atom (O/C) ratio, which was determined by ESCA. PUs with more hard-segment content on the surface (i.e., high C=O/C=C ratio) possess more fibrinogen adsorption and less albumin deposition (i.e., high F/A molar ratio). The C=O/C=C ratio, hydrogen-bonding index (HBI value), frequency shift and difference ($\Delta\nu$), glass transition temperature of soft segment (T_gs) as a measure of homogeneity, average strength of interpolymer hydrogen bonds, and interpenetrating networks (IPNs) were utilized to study the surface composition, intermolecular attraction, and IPN formation of the prepared PUs. The effect of hard-segment content, molecular weight or 4-VP content on the F/A molar ratio were investigated. The results of FTIR and ESCA explain well the surface composition, and hence, the F/A molar ratio as well. © 1999 John Wiley & Sons, Inc. J Appl Polym Sci 74: 297–305, 1999

Key words: protein adsorption; polyurethane; interpenetrating network

INTRODUCTION

Polyurethanes (PUs) are multiblock copolymers usually consisting of hard segments and polyether or polyester soft segments. The soft segment is typically with a molecular weight between 400 to 3000. The hard segment unit is normally a diisocyanate, which is chain extended with diol or diamine of low molecular weight to form a urethane or urethane–urea segment. PUs are widely used as biomaterial due to their good biocompatibility and mechanical properties.[1,2] Many studies have aimed at discussing the effect of surface composition of PUs on the protein adsorption and the platelet adhesion.[3–5] The adsorption of fibrinogen on the material's surface increases the platelet adhesion.[6] It is observed that the albumin-coated surfaces exhibit remarkable inhibition of platelet adhesion.[7] It is believed that the ability of a polymer surface to promote platelet adhesion and activation is correlated to the adsorbed or deposited concentration ratio of fibrinogen to albumin.[8,9] In the study of Hoffmann et al.[10] it was reported that there is a strong

interaction between blood and material's surface of biomaterial with more hydrogen bonding or polar groups that cause higher coagulation of thrombocytes. Many investigations have been carried out to gain an understanding of the surface composition–protein adsorption relationships of PUs.[11–13] It is reported that PUs with more C—H bonds or soft segment dispersed on the surface show a high affinity for albumin adsorption and low platelet reactivity.

Hydroxyl-terminated polybutadiene (HTPB) is composed of about 80 wt % of the butadiene component, 20 wt % of the vinyl group, and hydroxyl terminated. This nonpolar, low-energy polyol of HTPB prevents the formation of hydrogen bonding and crystallization in PUs studied.[14] In this study, PUs with nonpolar soft-segment domains derived from HTPB and polar hard-segment domains derived from a diisocyanate and a chain extender were prepared. H_{12}MDI, which is a hydrogenated compound of 4,4′-diphenylmethane diisocyanate (MDI), was used in this study due to its linear structure and its compatibility with HTPB. HTPB was used in this study due to its nonpolar property and subsequent change of composition on the air–polymer interface of these PUs. Polymer chains at the air–polymer interface are in an unsymmetrical environment in comparison with that within the polymer.[15] It is reported that the surface composition of poly(urethane urea)s with polybutadiene as soft segment is high in butadiene soft-segment content.[16]

This study attempted to characterize the surface structure to clarify the factors influencing the protein adsorption of a polymeric surface. A study of surface composition of low surface energy HTPB-based PUs should be of primary importance for their application as biomaterials. The purpose of this study was to synthesize HTPB-based PUs and to investigate the surface composition of these PUs, which were presented by the change of C=O/C=C ratio and measured by FTIR-ATR. Intrinsic viscosities of PU solutions were used as an indication for the molecular weight of these PUs, and were assumed to be the size of the molecular chain. The O/C ratio measured by ESCA was utilized to determine the surface composition of the PUs. The C=O/C=C ratio, HBI values, IR frequency difference and shift, glass transition temperature, and decomposition temperature were used for the identification of surface composition, intermolecular attraction, IPN formation, and hence, the effect on the F/A adsorption molar ratio.

EXPERIMENTAL

Materials

The chemicals used in this study were 4,4′-dicyclohexylmethane diisocyanate (H_{12}MDI, Desmodur W of Mobay Co.) and hydroxyl-terminated polybutadiene (HTPB, equivalent weight of 1333 with approximate 60 wt % of *trans*-1,4, 20 wt % of *cis*-1,4, and 20 wt % of vinyl-1,2, R-45M of Arco Co.). 1,4-Butane diol (1,4-BD) was used as chain extender. The 4-VP monomer was purified by vacuum distallation. Dibutyltin dilaurate (DBTDL) was used as a catalyst. Divinylbenzene (DVB) was used as crosslinking agent for the preparation of IPNs. Toluene and dimethylformamide (DMF) were used as solvents for the preparation of PU solutions. Benzoyl peroxide (BPO) was used as a crosslinker for the preparation of crosslinked PU and an initiator for the preparation of 4-VP/PU IPNs. Fibrinogen from human plasma of M.W. 341,000 and albumin from human serum of M.W. 68,000 (Sigma Chemical Co.) were used.

Preparation of Polyurethane

The two-stage polyurethanes with different equivalent ratios were polymerized first by a NCO-terminated prepolymer and then chain extended with 1,4-BD to give a 25 wt % solid content in about 30 min to 1 h. It was then diluted to a 15–20 wt % solid content for a predetermined viscosity. Detailed procedures for polymerization have been reported in a previous publication.[17] In this study, PUs were made with different equivalent ratio of HTPB/H_{12}MDI/1,4-BD = 1/4/3, 1/8/7, and 1/12/11, which possess 33.08, 50.56, and 60.79 wt % of hard-segment content, respectively. PUs with different intrinsic viscosity, which was measured by an automatic viscometer of Schott AVS 310, were prepared by HTPB/H_{12}MDI/1,4-BD = 1/12/11. Finally, the samples were kept under a vacuum at room temperature for at least 5 days prior to the test.

4-Vinyl pyridine (4-VP) is a pyridine containing vinyl monomer, which possesses hydrophilic or polar property. IPNs of HTPB/H_{12}MDI/1,4-BD = 1/4/3-based PU and poly(4-VP) were synthesized by sequential polymerization. Initially, crosslinked films were prepared by adding 1.0 wt % (based on the PU solid content) of BPO to the HTPB/H_{12}MDI/1,4-BD = 1/4/3-based PU solution and then reacted at 65°C for 6 h and then cooled to room temperature immediately. Addition of

BPO (0.5 wt %), DVB (1.0 wt %) and different 4-VP contents of 2.63, 8.44, 10.86, and 17.42 wt % into the above BPO-crosslinked PU solution were mixed homogeneously for about 20 min at room temperature, respectively. All the following film-preparation steps were the same as those described in the above section.

Infrared Spectroscopy

Infrared spectra of PU were obtained by using a JASCO FTIR-310E spectrometer. Spectra were collected at a resolution of 2 cm^{-1}. The peak due to hydrogen-bonded C=O stretching is centered at about 1700 cm^{-1} and that due to free C=O stretching is centered at about 1717 cm^{-1}, while the peak of bonded —NH stretching is at 3320 cm^{-1} and that of free —NH stretching is at 3442 cm^{-1}. Hydrogen-bonded carbonyl (or —NH) bands will correspond to those groups that are in the interior of hard segments, while the free bands may correspond to those groups in the hard segment domains or in the soft domains or at the interface.[18] In these butadiene-containing PUs, hydrogen bonding occurs only between urethane segments because the carbonyl group in the urethane linkage and the urethane alkoxy oxygen are the only proton acceptors. The extent of the carbonyl group participating in hydrogen bonding is expressed by the hydrogen bonding index (HBI), which is the relative absorbances of the hydrogen bonded carbonyl peak ($A_{C=O,bonded}$) to that of free hydrogen bonded carbonyl peak ($A_{C=O,free}$).[19] The frequency difference is defined as $\Delta \nu = \nu_f - \nu_b$, where ν_f and ν_b are the frequencies of maximum absorption for the free and hydrogen bonded —NH group, respectively. The frequency difference in the stretching frequency is considered as a measure of the strength of the hydrogen bond between molecules.

The infrared absorbance of carbonyl group measured by FTIR-ATR is calculated by the addition of the respective hydrogen bonded C=O absorbance peak height and free C=O absorbance peak height. The infrared absorption band of butadiene soft segment are the *trans*-1,4 form at 972 cm^{-1}, the 1,2 form at 912 cm^{-1} and the *cis*-1,4 form at 685 cm^{-1} [20]. The C=O/C=C ratio on the surface is the ratio of total C=O absorbance peak height with *trans*-1,4 form absorbance peak height. Larger value of C=O/C=C ratio indicates that more hard segment materials are dispersed on the surface.

ESCA Measurements

ESCA data were obtained by using a Perkin-Elmer PHI 590 SAM/ESCA instrument, equipped with Digital PDP 11/04 computer. The spectra were collected using exciting radiation from MgKα (hν = 1253.6 eV) operated at a pressure lower than 5×10^{-8} Pa, 250 W. A survey scan (0–1000 eV binding energy) to determine the elemental composition of PU elastomer was conducted at an analyzer pass energy of 1000 eV. For high resolution studies, the pass energy was reduced to 25 eV. The atomic sensitivity factors (ASF) of the elements were taken into account to calculate atomic ratios.

Molar Ratio of Fibrinogen to Albumin Adsorption

The films with 8 cm^2 surface area were immersed into CPBS buffer solution (0.01 M sodium citrate, 0.01 M sodium phosphate, 0.12 M sodium chloride, PH 7.40) for 12 h.[21] The concentrations of albumin and fibrinogen were 1.0 and 0.2 mg/mL, respectively, in CPBS buffer solution. The film surface was then quickly blotted with absorbent paper to remove surface buffer solution. The films were then filled with 2 mL of protein solution at 30°C for 1 h. After desorption, the films were rinsed with deionized water. The absorbed proteins were desorbed with 1% Triton X-100 and 1% dodecyl sodium sulfate in 0.01 N NaOH at 30°C with agitating at 100 rpm for 1 h.[22] Afterwards, the boric buffer solution was added into the desorbed proteins. A 0.5-mL fluorescamine solution with a 3:2 volume ratio in acetone (20 mg/100 mL) was added to the mixture with vigorous stirring. The protein quantity was determined by a fluorescence spectrophotometer (Hitachi Co., F-2000) and the fluorescence intensity was measured at 392 nm with excitation and at 491 nm with emission.

RESULTS AND DISCUSSION

Effect of Hard-Segment Content

For the study of the effect of PU composition on the protein adsorption, PU solutions were prepared with the same intrinsic viscosity but with different hard-segment contents varying from 33.02 (1/4/3) to 50.56 (1/8/7) and 60.79 (1/12/11) wt %. Figures 1 and 2 show that the F/A molar ratio and C=O/C=C ratio decrease with an increase of the hard-segment content in contradic-

Figure 1 Effect of hard-segment content on the F/A molar ratio of PUs with the same intrinsic viscosity of 1 dL/g.

Figure 3 Relationship between the C=O/C=C ratio and the F/A molar ratio of PUs with the same intrinsic viscosity of 1 dL/g.

tion to the conventional behavior. Figure 3 shows that F/A molar ratios are increased with the increase of the C=O/C=C ratio. This phenomenon is in agreement with many previous reports, which indicates that PUs containing more soft-segment content on the surfaces possess more

albumin adsorption and less fibrinogen deposition.[11–13]

To determine the polymer surface composition, an ESCA analysis was carried out to calculate the ratio of oxygen atom to carbon atom (O/C ratio).[4] A large O/C ratio indicates that more hard segments are present on the polymer surface. Figure 4 shows that the O/C ratio at the surface de-

Figure 2 Effect of hard-segment content on the C=O/C=C ratio of PUs with the same intrinsic viscosity of 1 dL/g.

Figure 4 Effect of hard-segment content on the O/C ratio of PUs with the same intrinsic viscosity of 1 dL/g.

creases with the increase of hard-segment content. PUs with a higher hard-segment content possessing a lower $C=O/C=C$ ratio, as shown in Figure 2, possess a lower O/C ratio, as shown in Figure 4. It was suspected that two explanations might be investigated by the change of hard-segment content of PUs with the same intrinsic viscosity. One is that PU with a lower hard-segment content has less hard segments forming aggregates, and contain more hard segments dispersing in the soft-segment region. This is consistent with the fact that a PU with a 33.02 wt % of the hard-segment content has the smallest HBI value (Fig. 5) compared with the other two types of PUs. Lower HBI value indicates that PU molecules possess fewer hydrogen bonds. On the other hand, hydrogen bonding occurs only between urethane segments of these butadiene-containing PUs. As a result, a PU with a low hard-segment content contains more free hydrogen-bonded hard segments, and hence, the length of hard-segment aggregations is small. The other is that the polymerization time of PUs with a low hard-segment content for the same intrinsic viscosity must be much longer than that with a high hard-segment content. The results may be the increase of the destruction of $C=C$ double bonds in the polymerization reaction, and hence, will increase the crosslinkage between polymer molecules. This will increase the entanglement of molecular chain

Figure 6   Effect of intrinsic viscosity on the F/A molar ratio of PUs with an equivalent ratio of HTPB/H$_{12}$MDI/1,4BD = 1/12/11.

and homogeneity of the whole polymer and the restriction of the soft-segment moving toward the surface. These two effects may be the reason for the high $C=O/C=C$ ratio of PUs with a low hard-segment content. When the hard-segment content exceeds 50 wt %, the enlargement of the hard-segment aggregation in the bulk of the polymer and the restriction of the soft segment moves toward the air–polymer interface will be largely increased. This may be the reason for the slow decrease of the $C=O/C=C$ ratio and the HBI value at the air–polymer interface, which reaches a maximum as the hard-segment content exceeds 50 wt %.

Effect of Intrinsic Viscosity

PUs with a hard-segment content of 60.79 wt % (1/12/11) were used in this section due to the low F/A adsorption ratio as described in the above section, and can be easily prepared with different viscosity of these PUs. Figures 6 and 7 show that both the F/A molar ratio and $C=O/C=C$ ratio are decreased with an increase of intrinsic viscosity. The increase in intrinsic viscosity indicated an increase in molecular weight. There are two effects on the $C=O/C=C$ ratio due to the increase of molecular weight. One effect is the increase of the degree of entanglement between molecular chains and the enlargement of the hard domain's aggregation with the increase of molecular

Figure 5   Effect of hard-segment content on the HBI values of PUs with the same intrinsic viscosity of 1 dL/g.

Figure 7   Effect of intrinsic viscosity on the C=O/C=C ratio of PUs with an equivalent ratio of HTPB/H$_{12}$MDI/1,4BD = 1/12/11.

Figure 8   Relationship between the C=O/C=C ratio and the F/A molar ratio of PUs with an equivalent ratio of HTPB/H$_{12}$MDI/1,4BD = 1/12/11.

weight. In these butadiene-containing PUs, hydrogen bonding occurs only between urethane segments due to the fact that there is no any polar group in the HTPB soft segment. The domain of the hard segment will aggregate more easily with an increase in the degree of molecular entanglement (or the increase of molecular weight), and hence, the migration of the hard segment moving toward the air–face will be more difficult.[23] The other effect is that the restriction of the movement of soft segments with the increase of intrinsic viscosity, and hence, the increase of the hard-segment content on the surface. The competition of the above two effects shows that the former has the superior influence on the C=O/C=C ratio, which decreases with the increase of molecular weight. This change of C=O/C=C ratio may be the reason for the variation of the F/A molar ratio, as shown in Figure 8. This indicates that PUs contain more hard segments on the surface, possessing less albumin adsorption and more deposition of fibrinogen.[11–13]

To confirm the surface composition, an ESCA analysis was carried out to calculate the ratio of oxygen to carbon (O/C ratio). Figure 9 shows that the O/C ratio decreases with the increase of intrinsic viscosity. This result indicates that the surface composition of these PUs with a higher intrinsic viscosity possess a lower C=O/C=C ratio, as shown in Figure 7, and a lower O/C ratio.

Effect of the Interpenetrating Network of PU and 4-VP

4-VP/PU IPNs were prepared by the addition of an electronegative group containing the monomer of 4-VP to the BPO crosslinked PUs, which was studied in a previous report.[24] The PU with an

Figure 9   Effect of the intrinsic viscosity on the O/C ratio of PUs with an equivalent ratio of HTPB/H$_{12}$MDI/1,4BD = 1/12/11.

equivalent ratio of HTPB/H$_{12}$MDI/1,4-BD = 1/4/3 was used in this IPN study due to its larger content of soft segments and the enhancement of the interpenetrating network by the addition of 4-VP. 4-VP can form hydrogen bonds with a proton-donating group through sharing the valence electrons of pyridine nitrogen atoms. The association between —NH groups and pyridine prevails over those with a carbonyl association.[25] Four PUs were prepared for the study of the effect of 4-VP content on the surface composition and F/A molar ratio.

Figures 10 and 11 show that the F/A molar ratio and the C=O/C=C ratio are all decreased as the 4-VP content increased up to 8.44 wt % of the 4-VP content and then increased for a higher 4-VP content. These results possess the same trend, indicating that PUs containing more soft segments on the surface possess more albumin adsorption and less fibrinogen deposition.[11–13] The introduction of the 4-VP monomer will enlarge the hard domain's aggregation due to the strong interaction between pyridine and the hard segment of the —NH or C=O group. The difficulty for the polar hard segments to move toward the air–face are increased with increasing the 4-VP content, and hence, the C=O/C=C ratio decreases as the 4-VP monomer added up to 8.44 wt %. As the addition of the 4-VP content is higher than 8.44 wt %, some of the 4-VP monomer

Figure 11 Effect of 4-VP content on the C=O/C=C ratio of PUs with an equivalent ratio of HTPB/H$_{12}$MDI/1,4BD = 1/4/3.

may act as a crosslinker between the HTPB soft segment. The degree of entanglement between the HTPB soft segment and molecular chain of the poly(4-VP) are then increased. This shows that the polymer homogeneity and the restriction of soft-segment movement are increased as the 4-VP content increased. The enlargement of the hard domain and the increase of molecular entanglement and polymer homogeneity show a increase of the C=O/C=C ratio on the surface, because the 4-VP content is higher than 8.44 wt %.

Frequency difference ($\Delta\nu$) and shiftment were utilized in this study to discuss the interaction between 4-VP and PU. The IR spectra indicates the interaction between the pyridine group and the —NH group of these 4-VP/PU IPN films. Coleman and coworkers[26] used the frequency difference ($\Delta\nu$) between hydroxyl groups and those of the hydrogen bonded hydroxyl groups as a measure of the average strength of the hydrogen bond between the —NH groups and pyridine groups of 4-VP. The frequency differences of these 4-VP/PU IPNs increase from 124 to 133, 136.5 and 142 cm^{-1} as the 4-VP content changes from 2.63 to 8.44, 10.36, and 17.42 wt %. The increase of frequency difference indicates that the intermolecular average strength of these IPNs are increased as the 4-VP content increased. On the other hand, the infrared study of the bonded —NH group frequency of these 4-VP/PU IPNs shifts to the lower

Figure 10 Effect of 4-VP content on the F/A molar ratio of PUs with an equivalent ratio of HTPB/H$_{12}$MDI/1,4BD = 1/4/3.

frequency, which changes from 3321 to 3316, 3308, and 3300 cm^{-1} as the 4-VP content increases from 0 to 2.63, 8.44, 10.86, and 17.42 wt %. Upon hydrogen bonding of the —NH groups with the pyridine groups, the energy and force constant of the bonded —NH group absorption decrease, and the absorption band shifts to a lower frequency. From the above discussions, we can confirm that the increase of 4-VP content will enhance the intermolecular attraction of these IPNs.

Characterization of 4-VP/PU IPN

The existence of 4-VP in the 4-VP/PU IPNs can be evidenced by the infrared spectra, which are detected by FTIR. Figure 12 shows the characteristic spectra of the pyridine group at 1643 and 1600 cm^{-1} in the pyridine containing the PU polymer.

In most cases, the thermogram of the IPN falls in between those of the two component-based ho-

Figure 13 TGA thermogram of BPO-crosslinked PU and 4-VP/PU IPNs: (a) crosslinked PU; (b) IPN-2.63; (c) IPN-8.44; (d) IPN-10.86; (e) IPN-17.42.

Figure 12 Infrared spectra of BPO-crosslinked PU and 4-VP/PU IPNs: (a) crosslinked PU; (b) IPN-8.44; (C) IPN-10.86; (d) IPN-17.42.

mopolymers.[27] TGA curves can be used to manifest the formation of 4-VP/PU IPNs, as reproduced in Figure 13. A rapid weight loss starts at approximately 300 to 500°C. The main quantity of gaseous components, for example, water, carbon monoxide, and methane, are split off. Decomposition of step 2 corresponds to the urethane bond breaking, and step 3 is polyol decomposition.[28] Almost complete decomposition was observed at about 500°C. PU with no 4-VP content has a lower second decomposition temperature and a higher third decomposition temperature. The second decomposition temperature of 4-VP/PU IPNs increases as the 4-VP content increases, due to a higher thermal degradation temperature of 4-VP.

The influence of the 4-VP content in the 4-VP/PU IPNs can be indicated by the change of glass transition temperatures of the soft segment. Figure 14 presents the DSC data for a number of different 4-VP/PU IPNs. It shows that the glass transition temperatures of soft segments (T_gs) increased as the 4-VP content increased. The introduction of 4-VP induces the restriction of soft segment mobility and the increase of entanglement of molecular chain, and hence, the increase of T_gs with the increase of 4-VP content.

Figure 14 Effect of 4-VP content on the T_gs of 4-VP/PU IPNs.

CONCLUSIONS

The surface composition was revealed by the C=O/C=C ratio. F/A molar ratios decrease with the increase of hard-segment content or molecular weight. F/A molar ratios of 4-VP/PU IPNs decrease to a minimum with the film with 8.44 wt % of the 4-VP content, then increase as the 4-VP content increases further. All the above results can be explained by the change of the C=O/C=C ratio on the polymeric surface. It is that PUs with more C—H bonds or soft segments dispersed on the surface show a high affinity for albumin and a low deposition for fibrinogen (i.e., a low F/A molar ratio). This study implies that change of surface composition of these HTPB-based PUs will affect the adsorption of fibrinogen and albumin.

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