Sequential Surface Derivatization of PET Films

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ABSTRACT: The present study describes the surface tailoring of a polymeric substrate by a multistep process using two consecutive plasma treatments, followed by derivatization reactions. The chemical concept of this approach is presented in this paper, using a poly(ethylene terephthalate) (PET) substrate. In the first step, tetrafluoroethylene (TFE) was plasma polymerized, generating a highly cross-linked perfluoric surface layer. The next step introduced amine groups into the plasma polymer, by exposing the surface to plasma of ammonia. The reactive amine moieties were then used as anchoring sites for further derivatization. Finally, poly(ethylene glycol) (PEG) chains were grafted onto the surface via a hexamethylene diisocyanate (HDI) spacer. The ESCA spectrum of treated PET revealed that the surface chemistry obtained after plasma polymerizing TFE was one clearly dominated by CF_2 and CF moieties, as demonstrated by the large peaks appearing at 291.1 and 289.5 eV, respectively. As expected, substantial amounts of nitrogen could be seen after exposing the surface to a plasma of ammonia, as revealed by the large N 1s peak at 402.0 eV. ESCA also demonstrated the presence of PEG chains bound to the surface. These findings were confirmed by FTIR spectroscopy and supported by water contact angle measurements. Special attention was given to the absorption bands of the CF groups and ether bonds belonging to the fluorinated plasma polymer and the PEG chains, respectively, as well as to the characteristic N═C═O band (2272 cm^{-1}). While the water contact angle of untreated PET was 76°, it increased sharply after the fluorinated layer was created (93°), decreasing drastically (to less than 20°) once the highly hydrophilic PEG chains were grafted on the surface.

Introduction

The interface generated between implants and their physiological environment plays a crucial role in determining their biological performance. This pertains to complex chemical, physical, and biological phenomena taking place at the surface of the implanted system. In the case of blood-contacting implants, their surface thrombogenicity and long-term biodurability are of special concern.

Protein adsorption and cell adhesion processes play a fundamental role in determining the hematological response elicited by prostheses implanted in the cardiovascular system. It is due to its effect on these phenomena that the biomaterial's surface chemistry largely dictates the hemocompatibility of the implant's blood-facing surface.[1,2]

The in vivo degradation of implanted polymers has been attributed[3−9] to diverse mechanisms such as stress cracking, enzymatic attack, oxidative degradation, metal ion induced oxidation, and simple hydrolysis. Since the different degradation mechanisms initiate at the prosthesis−biological environment interface, modifying the surface of the implanted material, so to prevent these processes from taking place, is crucial.

Clearly, therefore, tailoring the prosthesis surface plays a focal role in minimizing the thrombogenicity and enhancing the long-term biodurability of blood-contacting implants, these two being fundamental issues which largely affect their biological performance.

Enhancing the hemocompatibility of polymeric surfaces by means of glow discharge treatments has been investigated, its versatility being reflected by the different approaches pursued.[10−14a,b] Plasma treatments using polymer-forming perfluoromonomers such as tetrafluoroethylene (TFE), have been reported.[15,16] Glow discharge was also used to introduce various functional groups into different polymeric substrates, by using ammonia,[17] allylamine, and allyl alcohol[18] plasma treatments, or by creating a plasma-induced free radical-containing substrate, subsequently exposed to decylamine hydrochloride[19] or SO_2 gas.[20]

This article describes the chemical concept of a multistep sequential surface tailoring process aimed at enhancing the biostability and blood compatibility of biomedical polymers. The surface modification scheme presented comprises two consecutive plasma treatments, followed by specific derivatization reactions. The purpose of the first plasma treatment is to enhance the substrate's biodurability by creating an inert perfluoro protective layer, while the second plasma treatment as well as the subsequent reactions aim at minimizing the thrombogenicity of the material by grafting poly(ethylene glycol) chains, via diisocyanate spacers onto its surface. This article illustrates the working concept on poly(ethylene terephthalate) (PET).

Experimental Section

Plasma treatments were performed by placing 10 μm thick PET films (Du Pont), into a cylindrical Pyrex plasma chamber connected to a radio frequency generator (13.56 MHz) (HFS 501 S) and a matching unit MN 500 (RF Plasma Products Inc.). The dimensions of the PET samples were 2 cm × 3 cm. The tetrafluoroethylene (TFE), purchased from PCR, and ammonia plasma treatments were performed at 50 W and 0.65 mbar, for periods of 10 and 7 min, respectively.

The reaction between the amine groups present on the fluorinated surface and hexamethylene diisocyanate (HDI) supplied by Aldrich was carried out by immersing the samples in 3 mL of HDI at room temperature for 45 min. The polymer was then thoroughly rinsed in dry dioxane (Frutarom). The remaining free isocyanate groups were then reacted with dry poly(ethylene glycol) chains (PEG_{1000}) (Aldrich), in excess, at 70 °C for 1 h, with dibutyl tin dilaurate (DBTDL) (Aldrich) as catalyst (15 mg of DBTDL per gram of PEG). After the reaction, the polymer was rinsed with a 2:1 mixture of ethanol/acetone (Frutarom) and dried.

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The surface composition of the treated PET samples was investigated by ESCA using a Perkin-Elmer (Physical Electronics Division) XPS PHI 555 apparatus, equipped with an Al Kα anode.

KBr (Fluka) grains were coated with a very thin layer of PET, for the purpose of increasing the sensitivity of the FTIR analysis. This was performed by adding 10 mL of a 0.02% PET solution in hexafluoro-2-propanol (HFIP) (Fluka) to 5 g of ground and dried KBr. The solvent was then evaporated while rotating the mixture under vacuum, further removal of the solvent being performed in a vacuum oven at 50 °C, overnight. Plasma treatments were then performed by placing glass Petri dishes containing a thin layer of the PET-coated KBr grains (amounting to a total of about 400 mg) in the reaction chamber. The reaction between the amine groups and HDI and between the remaining isocyanate groups and the poly(ethylene glycol) chains were conducted in the same manner as described before for the films.

FTIR analyses of each of the surface treatments were performed using KBr pellets (around 200 mg) containing 40 mg of the PET-coated KBr grains, using a Nicolet 510 FTIR spectrometer.

Contact angle determinations were performed with distilled water on a Ramé-Hart NRC C.A. (model 100-00-230) goniometer. The data presented are the average of at least five measurements.

The thickness of the layers obtained by the plasma treatments was measured using a thin-film thickness monitor (Inficon XTC, model 751-001-G1).

Results and Discussion

Various surface tailoring techniques have been investigated, including both physical and chemical methods. Plasma is a powerful and versatile technique which is able to dramatically alter the surface chemical composition and morphology of a substrate, without affecting its bulk properties.[21,22] Plasma treatments can be divided into two general categories, depending on whether the gas used is polymer-forming or not. In the latter category, the modification of polymeric surfaces can be effected by various processes which, by adding, abstracting, or rearranging surface species, result in the functionalization, etching, or cross-linking of the material's surface layer. Alternatively, if a polymer-forming gas is used, plasma polymerization processes take place. In this case, smooth, ultrathin, pinhole-free coatings can be generated, covering a wide range of surface chemistries, often displaying unique characteristics.

The objective of this study is to tailor the surface of PET samples by a multistep process using two consecutive plasma treatments, the first of which created an inert perfluoric protective layer, while the second introduced amine groups, covalently bound to the fluorinated layer. With the purpose of minimizing the surface thrombogenicity of the substrate, poly(ethylene glycol) (PEG) chains were reacted with the amine groups via an hexamethylene diisocyanate (HDI) bridge. PEG molecules are known to enhance blood compatibility by minimizing cell and blood proteins adsorption to the surface.[23−28] The four layers of the surface modification scheme are shown schematically in Figure 1. It is worth mentioning that while the sole purpose of performing the second and third steps was to respectively provide anchoring sites and binding bridges for the molecules used in the fourth step, the first and last layers were specifically chosen for a particular type of performance and biological environment. The nature of these two layers may vary for different types of performances or biological environments.

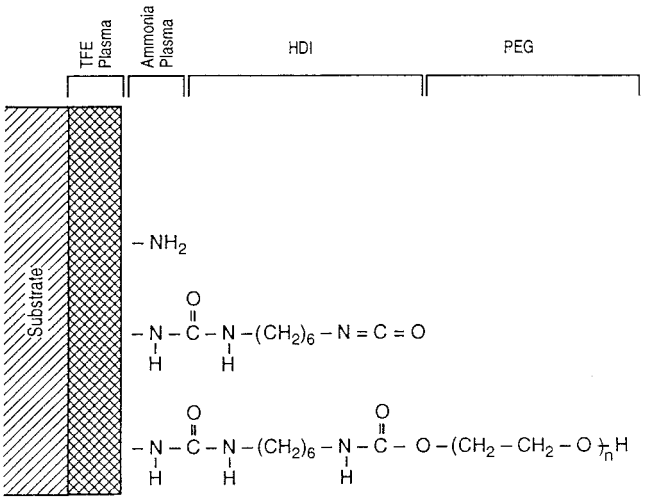

Figure 1. Surface modification scheme.

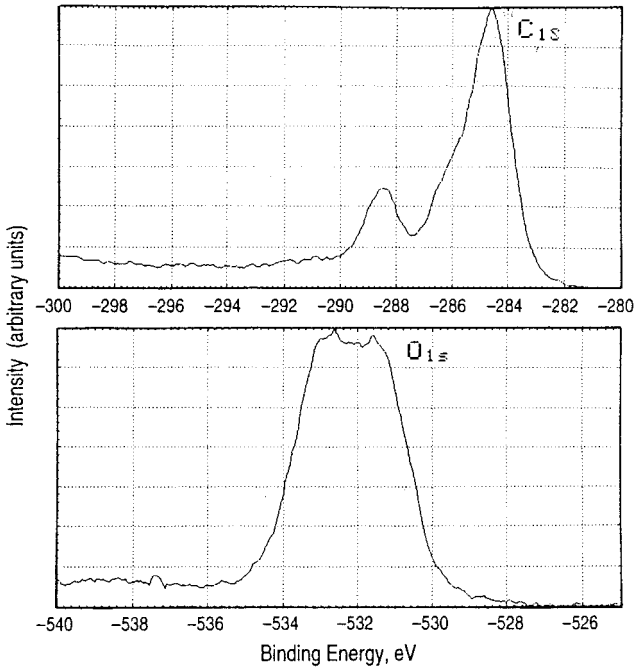

Figure 2. ESCA spectra of PET: upper, C 1s peak; lower, O 1s peak.

The actual occurrence of the various reactions and the composition of the new surfaces created at the different stages of the tailoring process were investigated by ESCA, FTIR spectroscopy, and contact angle studies.

ESCA Studies. The ESCA spectrum of untreated PET showed the carbon and oxygen peaks only, the 2.43 (C/O) ratio measured being very close to the theoretical 2.50 value. These findings are indicative of an essentially uncontaminated substrate surface. The characteristic carbon 1s peaks at 285.0, 286.4, and 288.9 eV, assigned to the aromatic, ether, and ester carbon atoms, respectively, as well as the oxygen 1s peaks at 532.0 and 535.5 eV, are shown in the spectra presented in Figure 2.

The first glow discharge treatment generated a highly cross-linked TFE plasma polymer. This extremely intractable and highly effective diffusion barrier was intended to affect both the chemistry and the transport properties of PET's surface layer, aiming at rendering it with superior biostability. The surface chemistry obtained after plasma polymerizing tetrafluoroethylene

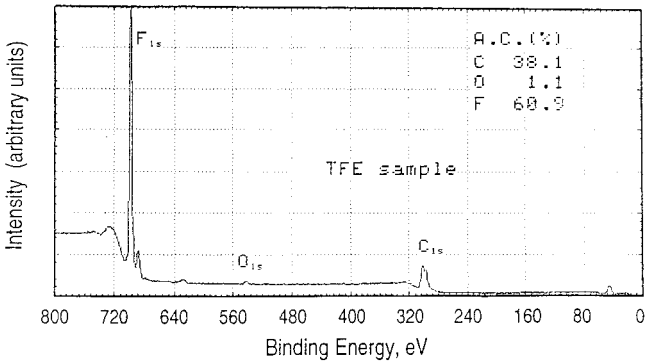

Figure 3. ESCA spectrum of TFE−plasma-treated PET.

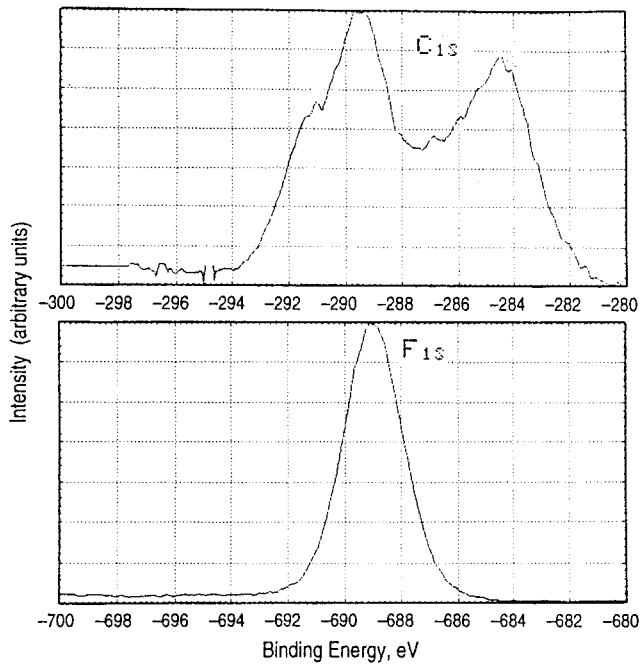

Figure 4. ESCA spectrum of TFE−plasma-treated PET: upper, C 1s peak; lower, F 1s peak.

on the surface of the PET film, was one clearly dominated by fluorine atoms, as apparent from the spectra shown in Figures 3 and 4. The C 1s spectrum [see Figure 4(upper)] reveals high concentrations of CF_n moieties, mainly CF_2 and CF groups, as demonstrated by the large peaks centered at 291.1 and 289.5 eV, respectively. Its worth noting that the large CF peak is fully consistent with the highly cross-linked nature, characteristic of most plasma polymers. The peak at 285 eV was initially considered to be due to the C 1s carbons of PET, this implying a noncontinuous or a very thin (less than 50 Å) plasma polymer layer. Nevertheless, a more in-depth analysis of the data revealed that the extremely small oxygen content (1.1%) is inconsistent with this explanation. It is reasonable to conclude, therefore, that the 285 ev peak is not due to PET's C 1s carbons but is related to the plasma polymer. Also, it may be surmised that the minute amount of oxygen found on the surface originated from the reaction between free radicals trapped within the highly cross-linked plasma polymer and oxygen atoms, when exposing the plasma polymer to air. As it is apparent in the F 1s spectrum presented in Figure 4(lower), the fluorine atoms appear as a sharp peak centered at 689.1 eV. The 0.63 (C/F) ratio measured for the TFE plasma polymer is somewhat higher than the ratio calculated for the

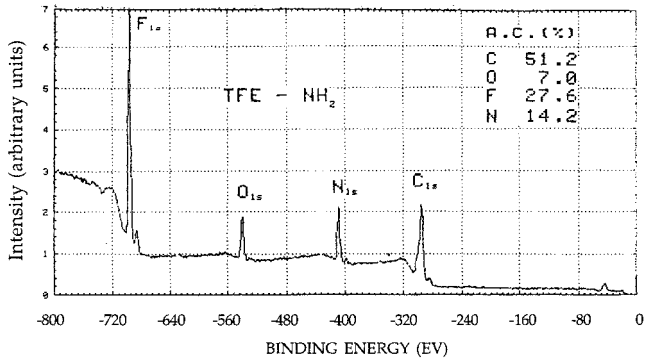

Figure 5. N 1s ESCA spectrum of the sample after being exposed to plasma of ammonia.

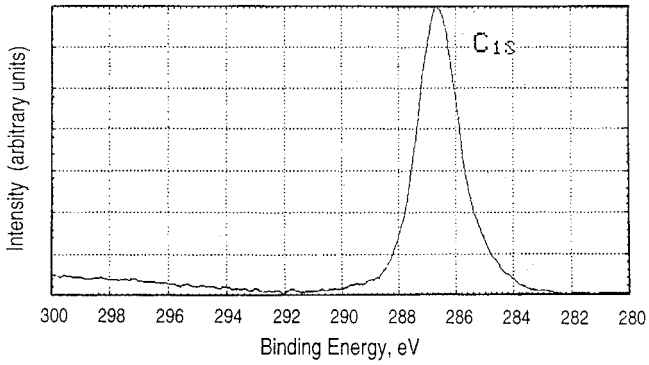

Figure 6. C 1s ESCA spectrum of the surface after grafting the PEG chains.

TFE molecule (0.50). This relative decrease in the fluorine content of the plasma polymer, when compared with that of TFE monomer, is fully consistent with the large CF peak seen in the spectrum shown in Figure 4(upper) and the high cross-link density of the plasma polymer.

Substantial amounts of nitrogen were found on the surface, after exposing the polymer to plasma of ammonia, as revealed by the large N 1s peak at 402.0 eV (see Figure 5). As expected, the low resolution ESCA spectrum of this new surface, showed also the C 1s and F 1s peaks due to the TFE plasma polymer. The somewhat higher oxygen and carbon contents may be attributed to the combined effect of two phenomena: a possible small extent of ablation of the TFE layer when exposed to the ammonia plasma, during which fluorine-rich volatile moieties are released, and the contribution of the underlaying PET substrate, now detectable by the ESCA analysis. The amine groups were then reacted with hexamethylene diisocyanate (HDI), as a result of which a urea bond was obtained, while the remaining free isocyanate group served as a reactive site for further derivatization. The last reaction of the surface modification scheme was the grafting of PEG chains (MW = 1000), by reacting their hydroxyl terminal group with the N═C═O functionality on the surface. The presence of the PEG chains was demonstrated by the C 1s spectrum which showed the sharp ether peak centered at 286.4 eV (see Figure 6). Furthermore, the appearance of the large C 1s ether peak was accompanied by a large increase in the O 1s peak due to the ether oxygen seen at 531.6 eV. Also, the (C/O) ratio measured at this stage was 1.82, quite close to the 2.00 theoretical value calculated for PEG.

FTIR Analysis. With the aim of gaining further insight into the nature of the surfaces generated, FTIR

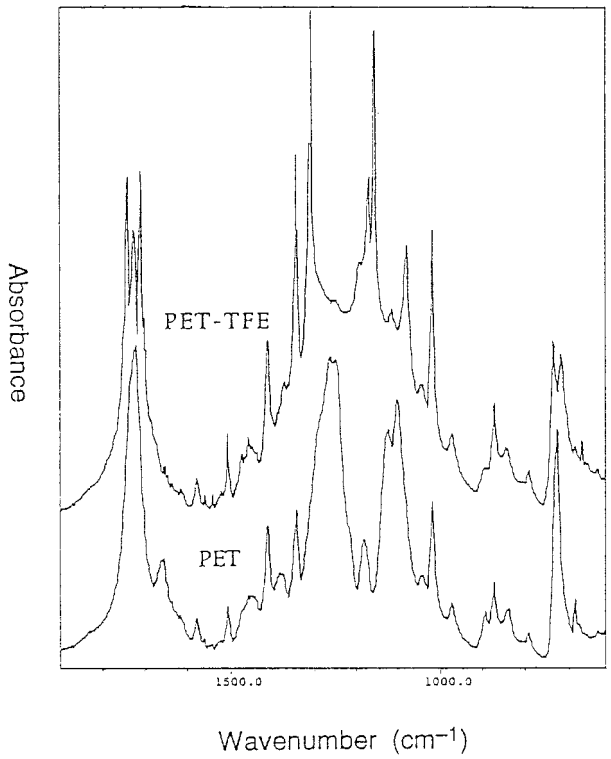

Figure 7. FTIR spectra of the original and TFE plasma-treated PET.

spectroscopy analyses were conducted at the different stages of the process. PET exhibited its characteristic bands at 1740 cm^{-1}, due to the stretching of the ester carbonyl group, and at 1100 $cm^{-1,}$ belonging to the stretching of the C−O−C bond. The TFE plasma-treated poly(ethylene terephthalate) film (Figure 7) showed the appearance of two strong main absorbance bands in the 1300 and 1150 cm^{-1} regions, due to the CF_2 and CF_3 bonds and the R_3CF bonds, respectively. Some changes in the carbonyl absorbance may be observed and are probably due to some chemical changes occurring at the substrate surface due to the bonding such as strongly electronegative, F-rich moieties, significantly affecting the carbonyl groups' molecular environment. The presence of the amine groups introduced by the ammonia plasma could not be detected directly due to the limited surface sensitivity of this technique, but their presence was demonstrated indirectly (see below).

Figure 8 presents the FTIR spectra of PET after being exposed to the two plasma treatments, TFE and ammonia [Figure 8(lower)], and, also, following the reaction with HDI, first, and finally after reacting with PEG. Given the conditions of the system, the reaction of the HDI molecules with the amine groups takes place through only one of its isocyanate groups, leaving the second one available for further derivatization. The FTIR spectrum of PET−TFE−NH_2, after reaction with HDI and thorough rinsing off of the unbound molecules, showed the characteristic peak of the free isocyanate group at 2272 cm^{-1}, indicating the presence of the HDI molecules. Furthermore, the sharp peak at 1640 cm^{-1} is attributed to the urea bond created by the reaction between the amine group and HDI.

The last stage of the derivatization process capitalized on the reaction of the free isocyanate groups with a hydroxy-terminated PEG. The characteristic peak of the isocyanate group at 2272 cm^{-1} disappeared, indicating

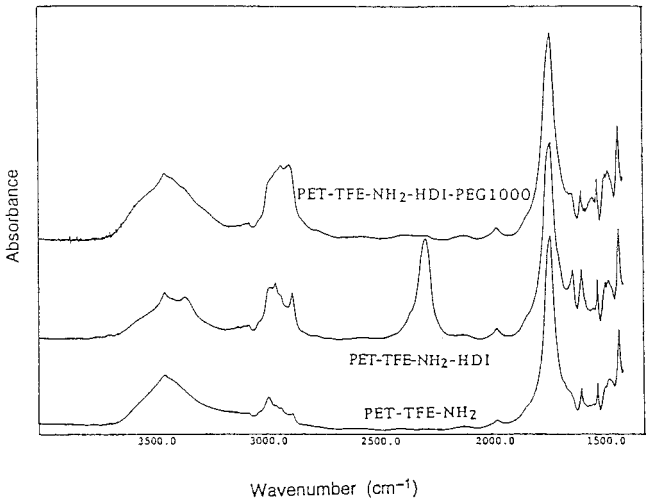

Figure 8. FTIR spectra of samples at different stages of the process: lower, after being exposed, sequentially, to TFE and ammonia plasma; medium, after reacting the amine groups with HDI; upper, after grafting the PEG chains.

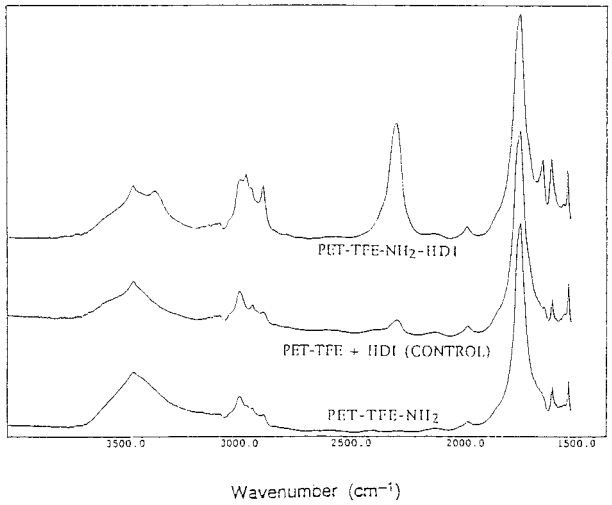

Figure 9. FTIR spectra: lower, after being exposed sequentially to TFE and ammonia plasma; medium, after reacting the TFE-treated surface with HDI, without previously exposing it to plasma of ammonia; upper, after reacting the amine groups with HDI.

that the isocyanate group reacted with the PEG molecules. The appearance of the urethane absorbance at 1720 cm^{-1}, seen here as a shoulder between the ester and urea absorbances at 1740 and 1640 cm^{-1}, respectively, is also indicative of the HDI−PEG reaction.

To conclusively demonstrate both the occurrence of the NH_2−HDI reaction and also, indirectly, the actual presence of the NH_2 groups at the surface prior to the reaction, a control experiment was conducted. Accordingly, when the TFE−plasma-treated surface was directly put in contact with HDI, without previously introducing amine groups into the surface, even a very mild rinsing procedure was successful in removing almost completely the adsorbed HDI molecules, as readily seen in Figure 9. Also, the urea linkage, absorbing at 1640 cm^{-1}, generated by the amine−isocyanate reaction, could not be found in the spectrum of the control sample. Fully consistent with the already described ESCA data, these findings provide supporting evidence, even though indirectly, proving the presence of amine groups on the surface, following its exposure to plasma of ammonia. In striking contrast to this

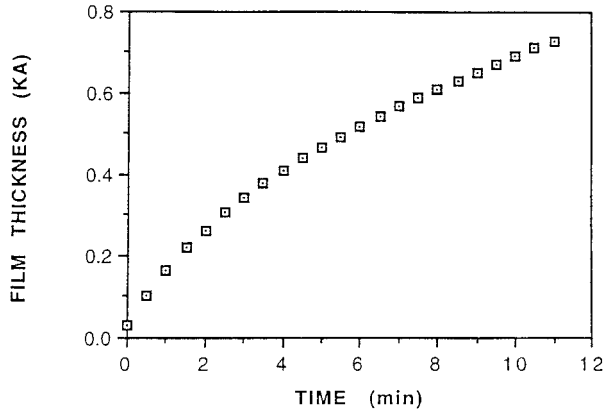

Figure 10. TFE−plasma polymer thickness as a function of reaction time.

behavior, the amine-containing surface readily reacted with HDI, the presence of the second N═C═O group being evident from the large peak centered at 2272 cm^{-1}. Also, the sharp urea band at 1640 cm^{-1} can now be readily seen.

The thickness of the TFE−plasma polymer layer was measured, its formation rate being followed during the plasma polymerization reaction. As shown in Figure 10, the thickness of the fluorinated layer was 230 Å already after 2 min, reaching 720 Å at the end of the treatment, after 10 min. Exposing the TFE first layer to plasma of ammonia did not result, as expected, in a measurable thickness change. Furthermore, within the time frame of these experiments (5−7 min), no reduction in the thickness of the plasma polymer due to ablation phenomena caused by the plasma of ammonia was measured.

The water contact angle of the untreated PET film was 76°, increasing drastically after the fluorinated layer was created (93°). As expected, the water contact angle decreases substantially after the incorporation of the amine groups into the surface, while an additional large decrease in the water contact angle (to less than 20°) was witnessed after grafting the highly hydrophilic PEG chains.

Summary

In the first step, tetrafluoroethylene was plasma polymerized, generating a highly cross-linked fluorinated surface layer. This extremely intractable and highly effective diffusion barrier was intended to affect both the chemistry as well as the transport properties of PET's surface layer, rendering it with superior stability. The next step introduced amine groups into the surface, by exposing the perfluoro plasma polymer to plasma of ammonia. The reactive amine moieties were then used as anchoring sites for further derivatization via a diisocyanate spacer. The ESCA and FTIR spectra obtained after each stage revealed the composition of the various surface layers. Additional supporting data were provided by water contact angle studies and by measuring the thickness of the plasma polymer layer.

The effects of this multistep modification of the surface of PET on its long-term stability and hemocompatibility are currently being investigated and will be reported separately, as well as the results of studies conducted on other polymers, most importantly polyether urethanes.

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