Synthesis and derivatization of polybutadiene containing poly (ether urethane amide)s

D. Cohn, M. Aronhime, T. Stern*

Casali Institute of Applied Science, The Hebrew University of Jerusalem, 91904 Jerusalem, Israel

Abstract

A series of polybutadiene-containing poly(ether urethane amide)s was synthesized. The physical properties of the resulting polymers were observed to be significantly affected both by the polybutadiene content in the soft segment, as well as by the nature of dicarboxylic acid chain extender. Preliminary derivatization reactions of the polymers were performed via a free-radical reaction mechanism, using different acrylic monomers as a model, by which a range of polymer properties were obtained, including highly hydrophobic and hydrogel-like materials. © 2000 Published by Elsevier Science Ltd. All rights reserved.

Keywords: Polybutadiene; Poly(ether urethane amide); Free-radical mechanism

1. Introduction

Modifying the surface chemical and physical properties of biomedical polyurethanes has become an imperative issue regarding their long-term stability and biological performance. Despite their very good mechanical properties and other advantages, polyurethanes still require improvement in terms of long-term biostability and hemocompatibility.

Several reports have been published showing evidence of significant surface cracking and degradation of polyurethanes, both in vitro and in vivo [1–5]. The derivatization of polyurethanes, directed at the improvement of their hemocompatibility [6–16] and long-term stability [1–5,17–21], has been a subject of extensive research.

We have reported, in a previous study [22], the derivatization of a poly(ether urethane amide) via the Michael-like addition of Jeffamines to a double bond, which was introduced in the polymer hard segment, by chain-extending the initial prepolymer with an unsaturated dicarboxylic acid (e.g. fumaric acid). This modification led to significant changes, not only in the surface properties of the polymers, but also often in their mechanical properties, due to the interference of the Jeffamine molecules resulting in a less crystalline hard block.

This study focuses on the synthesis and characterization of a new poly(ether urethane amide) containing active derivatization sites in the polymer's soft segment. This was achieved by substituting the originally used poly(tetramethylene glycol) (PTMG) [22] with a hydroxy-terminated poly(butadiene), which has *cis*, *trans* and pendant vinyl double bonds along its chain. The derivatization of these double bonds can be carried out via several different mechanisms, using a wide variety of reagents. Although the main focus of this study is the introduction of a new group of polybutadiene (PBD)-containing polyurethanes, the possibility of derivatization via the most obvious mechanism, i.e. the free-radical reaction, is explored by using acrylic molecules as model reagents. Studies focusing entirely on the derivatization and tailoring of these polymers, including the electrophilic addition of isocyanate groups, are being published separately.

A number of studies dealing with PBD-containing polyurethanes have been published [23–26]. The soft segments of these polymers were composed entirely of PBD and most of them were crosslinked. Katano et al. [27], however, created a regulated drug release formulation using a PBD and poly(ethylene oxide)-containing polyurethane. The drug, crystal violet, was not chemically bonded to the polymer matrix. Mechanical properties were considerably poorer than those of the equivalent polyether or polyester urethanes. It was suggested that this phenomenon was due to poor adhesion between the PBD matrix and the dispersed hard segment. As a consequence, there was a void formation at the interface between the matrix and the dispersed phase, resulting in insufficient efficiency in stress transfer to the

* Corresponding author.
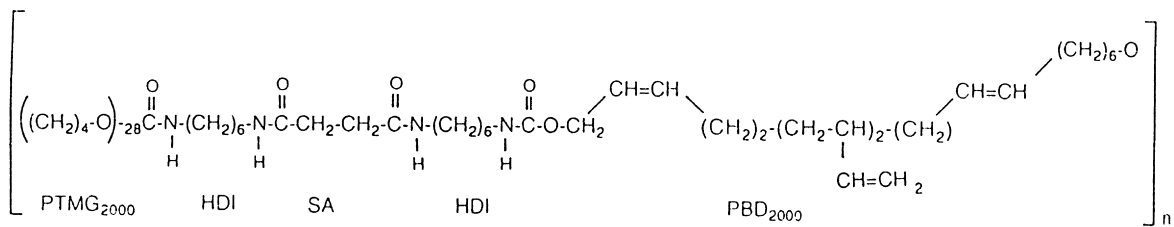
PEUSAB

Fig. 1. Schematic representation of the 50% PBD polymer, chain-extended with succinic acid.

polymer hard domain [28]. Serrano et al. [29] found incomplete phase separation in samples containing less than 33 wt% hard segment, by testing the transport–morphology relationship in segmented PBD polyurethanes.

In the present research, PTMG was introduced along with PBD in the polymer soft segment, at different ratios, aimed at enhancing the mechanical properties of the resulting elastomer, without the use of aromatic diisocyanates in the polymer hard segment. A preliminary derivatization trial of the polymers via the free-radical mechanism is discussed in this paper.

2. Experimental

Synthesis of PBD-containing polymers was carried out via a two-step solution polymerization in dimethyl acetamide (DMA) (Aldrich) at 67°C, in an inert atmosphere (N_2).

In the first stage, hexamethylene diisocyanate (Aldrich) was reacted with a mixture consisting of the appropriate molar ratio of hydroxy-terminated PBD (Polysciences) and PTMG (Polysciences), at a 2:1 molar ratio (the molecular weight of both PTMG and PBD was 2000). The polyether mixture was added to the hexamethylene diisocyanate dropwise, as a 12% DMA solution, over a period of 45 min, after which the reaction proceeded for an additional hour, under constant stirring.

Chain extension was performed with either succinic, fumaric or oxalic acid or with a mixture of two, which was added dropwise as a ~2% DMA solution, over a period of 45 min, at a dicarboxylic acid:prepolymer molar ratio of 1:1. The reaction proceeded for an additional hour. The
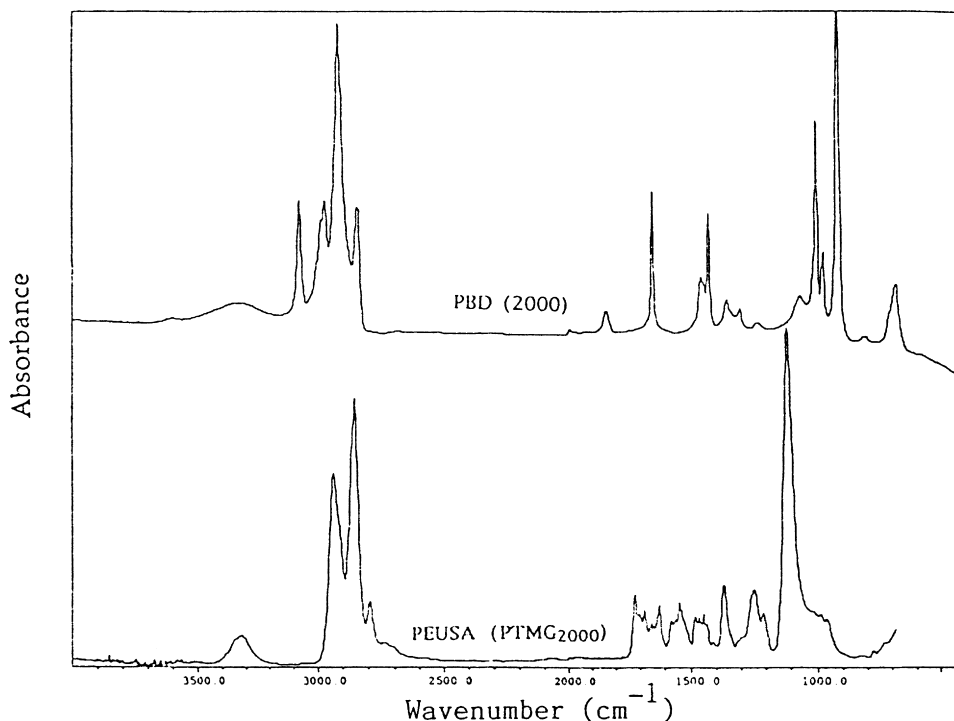

Fig. 2. FTIR spectra of polybutadiene and of a 100% polybutadiene-containing polymer.
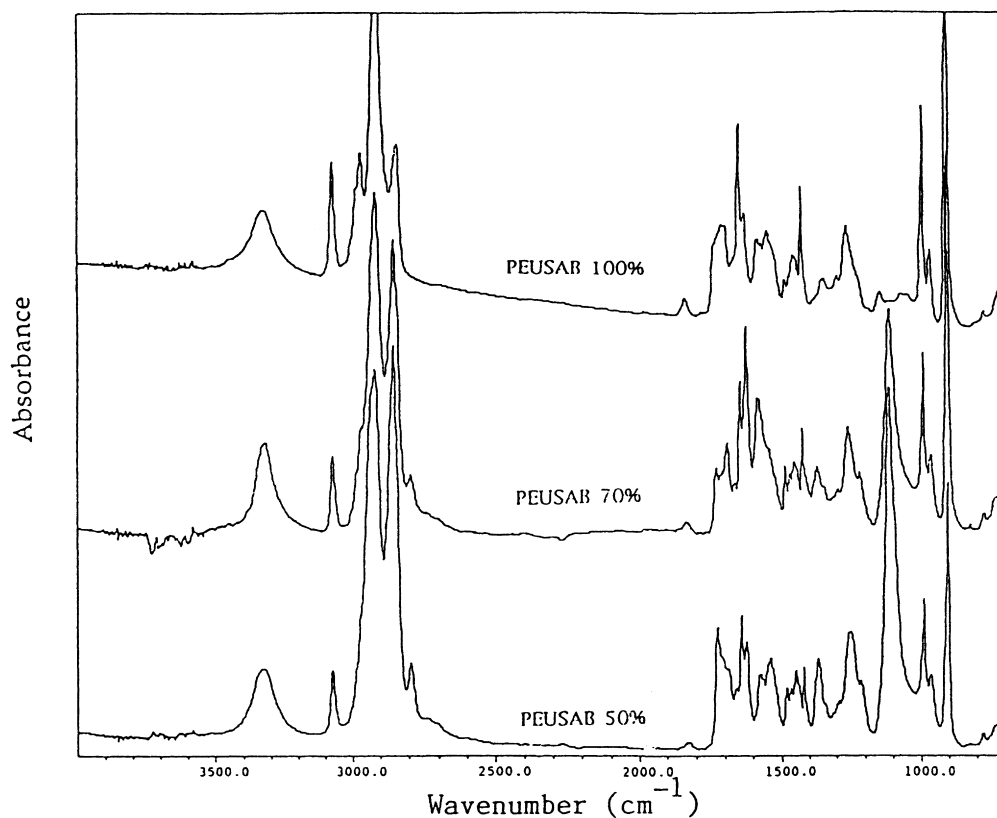
Fig. 3. FTIR spectra of the polymers containing 50, 70 and 100% polybutadiene.

resulting polymer was precipitated in deionized water, air-dried and dissolved in chloroform or in a mixture of chloroform and THF, at a concentration of 4%. 250 μm thick films were cast from the resulting solution, by evaporating the solvent at room temperature.

Grafting of acrylamide (AAm) on PBD-containing polymers was carried out on films, both in bulk and surface confined. In bulk, AAm (Aldrich) was grafted by immersing the polymer films in a dioxane solution of AAm of different concentrations at 60°C for a period of 90 min. Azobis iso-butironitrile (AIBN) was used as initiator at a concentration of 1%. After reaction, the films were thoroughly rinsed
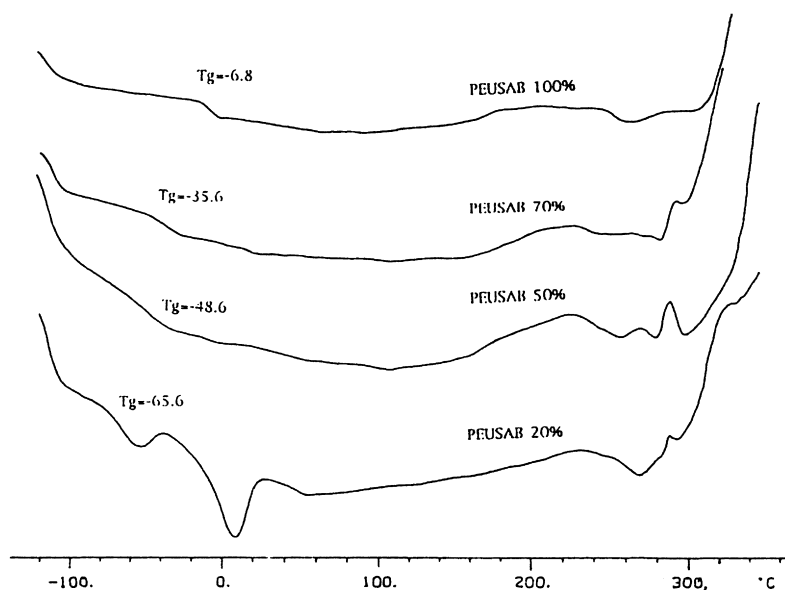
Fig. 4. DSC thermograms of the polymers containing 20, 50, 70 and 100% polybutadiene.
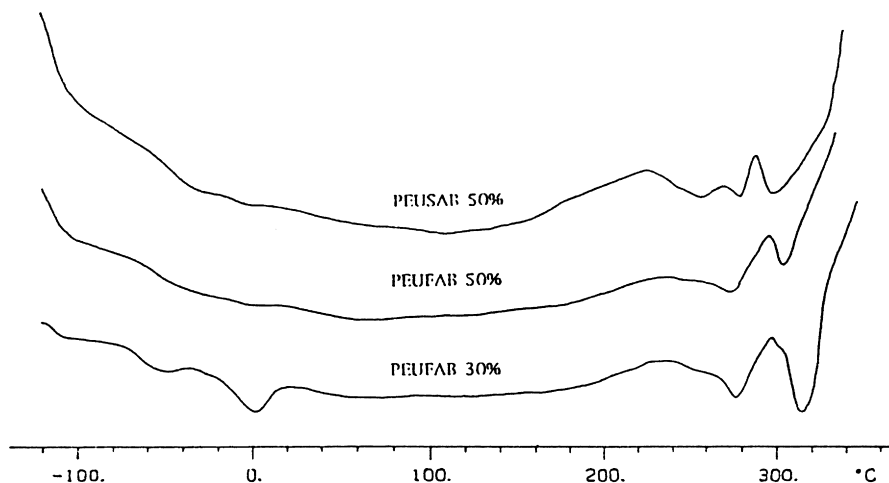
Fig. 5. Effect of chain extender on the thermal properties of the polybutadiene-containing polymers.

several times in deionized water and ethanol at 60°C. Grafting of polyethylene glycol methacrylate (PEGMA) was performed using a similar procedure.

Surface confined grafting of AAm was performed by pre-swelling the polymer films in a 0.05 M solution of AIBN in Dioxane at 37°C for 30 min, which were then immersed in a 3 M aqueous solution of AAm at 60°C for 90 min. The AIBN from the dioxane solution inside the film was able to diffuse into the outside solution, but the aqueous solution of AAm could not penetrate into the polymer film, the latter being relatively hydrophobic. Hence the reaction took place at the polymer surface.

All grafted samples were thoroughly washed with dioxane at 60°C, under magnetic stirring, three times for 3 h, in an attempt to remove the residual monomers and the initiator, after which the samples were dried in a vacuum

oven at 50°C, for 10 h. Surface-grafted, non-crosslinked samples were washed first with deionized water and then with acetone and methanol at 60°C, twice, for 3 h.

Fx-189, a perfluoroacrylate, was grafted in solution, the polymer being dissolved in DMF at a 4% concentration, at 60°C for 90 min. After reaction, the solvent was evaporated and the resulting film was rinsed three times in acetone and methanol at 60°C for 3 h and vacuum dried at 50°C.

A Ramé-Hart NRC C. A. goniometer (model 100-00-230) was used for contact angle measurements.

Water absorption of polymer films was determined by soaking the samples in deionized water at 60°C, until equilibrium values were obtained. The water content was expressed as the weight percentage of the dry polymer.
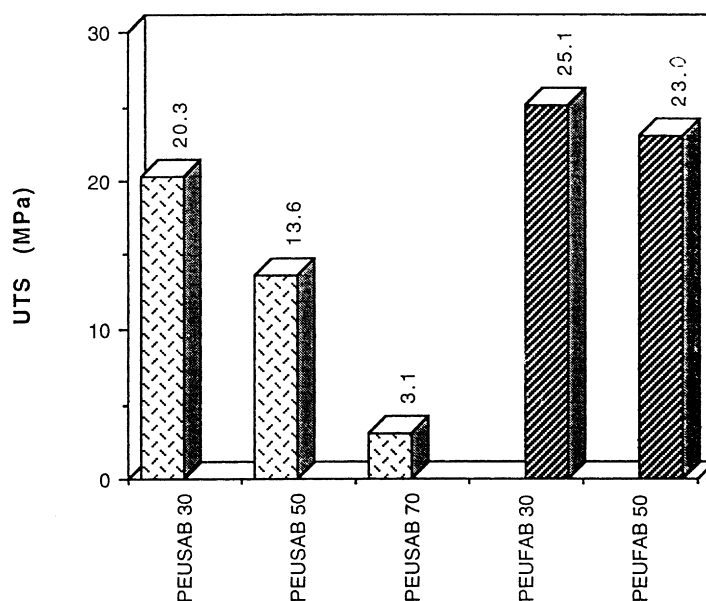

Fig. 6. Effect of chain extender and polybutadiene content on the ultimate tensile strength of the polymers.

$$(C_{7.5}F_{16})-SO_2-\underset{\underset{C_4H_9}{|}}{N}-CH_2-CH_2-O-\overset{\overset{O}{\|}}{C}-CH=CH_2$$

FX - 189

$$H_2C=CH-\overset{\overset{O}{\|}}{C}-NH_2 \qquad CH_2=\overset{\overset{CH_3}{|}}{C}\\ \qquad\qquad\qquad O=C-O(O-CH_2-CH_2)_nOH$$

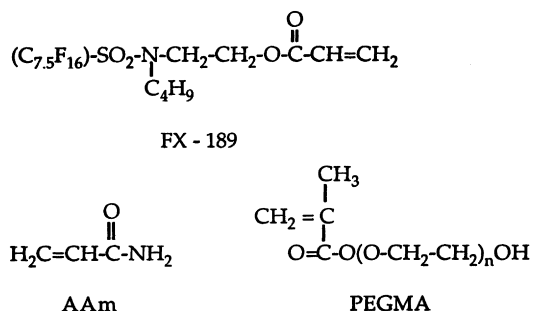AAm   PEGMA

Fig. 7. Schematic representation of the FX-189, acrylamide and PEGMA molecules.

Characterization of the mechanical properties was carried out on an Instron Universal Testing Machine (Model 1114). Crosshead and chart speeds of 50 cm/min were used.

Thermal analysis was performed using a Mettler TA 3000 DSC thermoanalyzer. The thermograms ranged between −100 and 350°C at a 10°C/min heating rate, under nitrogen atmosphere.

FTIR spectra were measured on a Nicolet 510 FTIR spectrometer. Samples were dissolved in chloroform and cast on a NaCl crystal.

3. Results and discussion

The polymerization reactions were carried out in solution, which was essential due to the fact that the presence of solvent (DMA) overcomes the otherwise distinct tendency of both reactants and products to macro-phase separate in the early stages of bulk polymerization [27]. A series of polymers was synthesized at different ratios of PBD and PTMG, ranging from 20 to 100% PBD in the soft segment. The resulting polymers have been notated as PEUSAB, PEUOXAB or PEUFAB when chain extended with succinic, oxalic or fumaric acid, respectively, followed by a number indicating the percentage of PBD in the polymers soft segment.

Fig. 1 illustrates the polymerization product, when the chain is extended with succinic acid. Here, the PBD and PTMG-containing soft segments of the polymer schematically appear in an alternating order, though it should be noted that the actual order of these two is probably random, influenced mostly by their initial ratio in the reaction mixture and the reactivity of the respective end groups and other kinetic aspects.

Table 1

	Contact angle	Water absorption %	% Reacted vinyl	Monomers per site (avg.)
PEUSAB 50	78°	2	–	–
PEUSAB 50-Fx 189	105°	∼0.5	91.9	∼1
PEUSAB 50-PEGMA	25°–30°	17	34.2	0.34
PEUSAB 50-AAm	∼15°	350	100	5.00

The chemical structure of the different PBD-containing polymers was verified by IR spectroscopy. Fig. 2 shows the FTIR spectrum of PEUSA, (containing 0% PBD–100% PTMG in the soft segment, chain extended with succinic acid) and the spectrum of PBD 2000. The main peaks belonging to the PBD may be seen, namely those belonging to the *cis*, *trans* and vinyl double bonds at 992, 967 and 908 cm^{-1}, respectively and also the peak at 3068 cm^{-1} belonging to the CH groups adjacent to the double bond.

One of the most prominent changes occurring with the increase in the amount of PBD (and the decrease of PTMG) in the polymer (Fig. 3) is the decrease of the peak at 1111 cm^{-1}, belonging to the ether groups of PTMG. This peak disappears altogether at 100% PBD. Simultaneously, there is a constant increase in the characteristic peaks of the PBD molecule, namely the peaks located at 992, 967, 908 and 3068 cm^{-1}, as the amount of PBD in the polymer increases.

The DSC thermograms of some of the polymers synthesized are shown in Fig. 4. The sharp endotherm of the 20% PBD containing polymer in the 10°C region, is related to the melting of PTMG. Increasing the PBD content to 50% led to the formation of an amorphous soft segment, which is most likely due to the inherent amorphous nature of PBD. The melting endotherm of the polymer's hard segment at approximately 275°C, decreases with the increase in the PBD content from 20 to 100%. This may be attributed to a lowering in both crystal strength and degree of crystallinity of hard domains. It is worth mentioning that according to the results obtained by FTIR spectroscopy (Fig. 3), there is a distinct increase of the H-bonded urethane at 1704 cm^{-1} in relation to the non-bonded urethane at 1721 cm^{-1}, as the amount of PBD in the polymer increases. Accordingly, at 30% PBD, the non-bonded urethane is much higher than the bonded one, as is usual in poly(ether urethanes); at 70% PBD, the two peaks are almost the same size; and finally at 100% PBD, the bonded urethane is significantly higher than the non-bonded one. Since at 100% PBD, hydrogen bonds can only occur within the hard segment phase, this suggests a much higher phase segregation with increasing amount of PBD in the polymer's soft segment. Hence, it may be concluded that although a higher phase segregation is obtained with increasing PBD content (due to the higher phase incompatibility), a population of weaker hard segment crystals is formed, possibly due to the influence of the amorphous PBD domains.

The use of fumaric acid instead of succinic acid as the chain extender, led to the formation of a sharper hard segment melting endotherm, as shown in Fig. 5, for the 50% PBD containing samples. This may be explained by the stiff and planar nature of the double bond, in conjunction with the adjacent amide groups, which consequently lead to an increased ability of the hard segment to crystallize. It should be mentioned that here too the endotherm sharpens as the PBD content decreases to 30%.
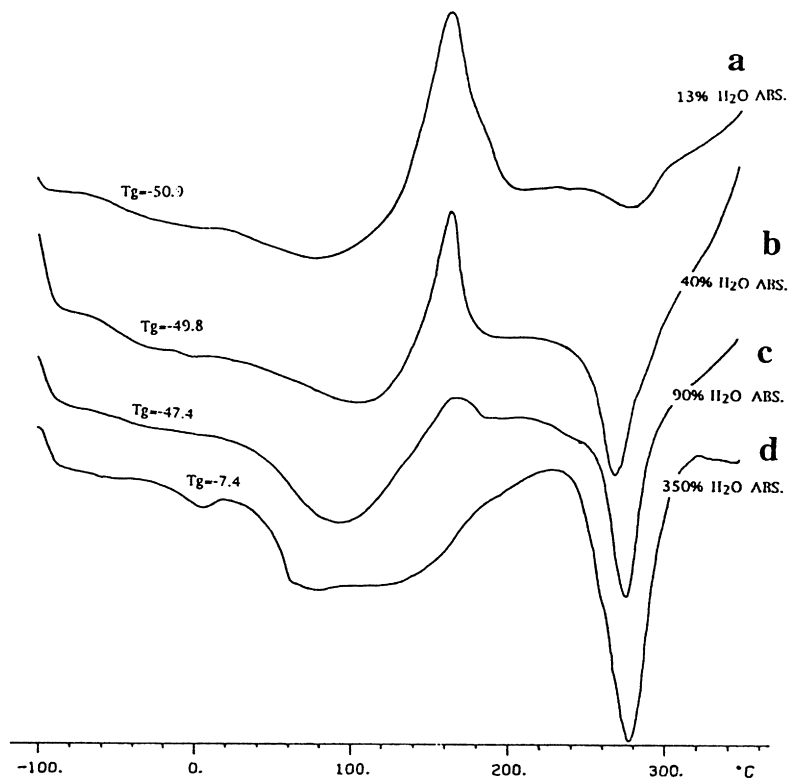
Fig. 8. (a) DSC thermograms of PEUSAB-50 at the polymer surface and grafted with: (b) 1; (c) 2; and (d) 5 average acrylamide units/site in bulk. Water absorption values are annotated.

The ultimate tensile strengths (UTS) of PBD-containing polymers are shown in Fig. 6. There is a gradual decrease in UTS, with increasing PBD content. The UTS values of the polymers chain-extended with fumaric acid are significantly higher than those of the polymers chain-extended with succinic acid. Also, the difference between the UTS values of the 50 and 30% PBD-containing samples, is much smaller in the fumaric acid chain-extended polymers.

3.1. Dertivatization reactions

Derivatization was accomplished via a free-radical reaction mechanism, using various vinyl monomers, exemplified in this paper by Fx-189, PEGMA-400 and AAm (Fig. 7). All reactions were performed on the 50% PBD-containing polymer PEUSAB 50.

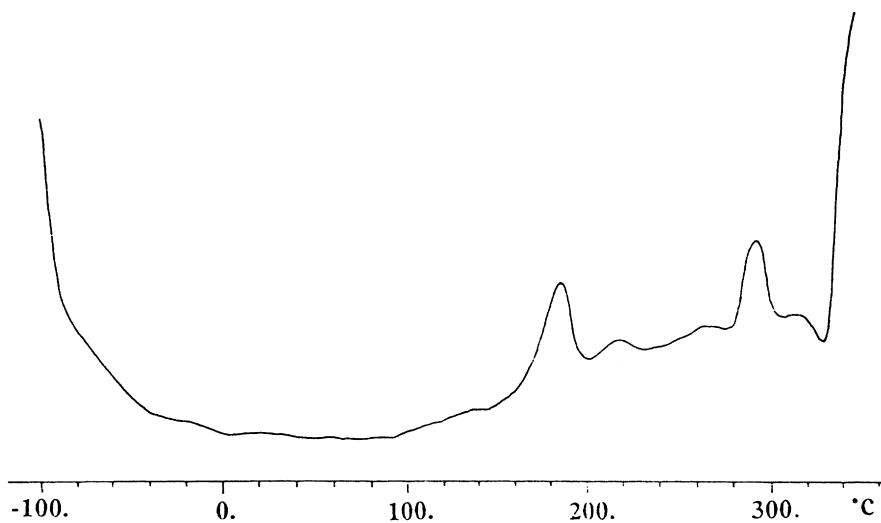Derivatization with Fx-189 led to significant hydrophobization of the polymer, increasing its contact

Fig. 9. DSC thermogram of an initiator (AIBN)-containing PEUSAB-50 film.

Table 2

AAm concentration (M)	Contact angle	Water absorption %	Monomers per site (avg.)
Surface grafted	30°–35°	13	–
1	25°	40	1.0
2	25°	90	2.1
4	15°	350	5.0

angle from 78 to 105°, while both PEGMA and AAm led to the hydrophilization of the grafted polymer. In all cases, the polymer was crosslinked as a consequence of the grafting reaction. Table 1 shows the maximum amounts of the monomers grafted, when using excess amounts of the monomers, under optimal conditions. The results are related to the amount of the vinyl double bonds, since these bonds are the most reactive in the free-radical reaction mechanism, although reaction of some of the two other types of double bonds should not be excluded. The results were obtained by means of elemental analysis and gravimetric measurements. Other analytical methods like FTIR and NMR were not possible since the grafted samples were crosslinked. Procedures that were intended to inhibit the crosslinking of the polymer, such as lowering the reactant concentration and the use of chain transfer-inducing solvents, e.g. $CHCl_3$, also inhibited the grafting reaction. Also, the possibility that not all the vinyl double bonds reacted and that of an unequal distribution of the monomers among the sites should be taken into consideration. The relatively smaller amount of grafted PEGMA, is probably due to the lower accessibility of the molecule to the active sites, due to its long hydrophilic PEG chain.

The DSC thermograms of PEUSAB 50 with increasing amounts of bulk-grafted AAm, are compared to the surface-grafted sample, in Fig. 8. The two characteristic endotherms of AAm, at approximately 100 and 280°C, grow with the increase in the amount of grafted monomer. The exotherm at approximately 150°C, on the other hand, decreases with the increase of AAm in the polymer, disappearing altogether in the sample containing the highest amount of AAm. When the grafting was performed only at the surface layers of the polymer, the two endotherms of AAm were very small with a very sharp exotherm between them. The occurrence of this exotherm may be explained by the reaction that is most probably taking place between the unreacted vinyl groups along the polymeric chain, initiated by trace amounts of AIBN, which may have remained in the sample, despite the thorough rinsing procedure which followed the reaction. To investigate this theory, a control experiment was carried out, in which a film of the same polymer was soaked in a AIBN/dioxane solution, rinsed and dried as described in Section 2, without the addition of AAm. The DSC thermogram of the AIBN-containing polymer is shown in Fig. 9. As expected, a similar exotherm is observed at approximately the same location, which supports the assumed

origin of the exotherm and the occurrence of the reaction mentioned above. Evidently, the exotherm does not occur in the polymer itself, as shown in Fig. 4. Furthermore, since the exotherm does not occur in the samples grafted with the highest amount of AAm, it may be concluded that most of the vinyl groups in the polymer actually reacted with the monomers.

A feature of special significance, is the increasing water absorption of the polymer with increasing amounts of grafted AAm. The amount of grafted AAm, (as measured by elemental analysis) as well as the water absorption and contact angles of the different samples are given in Table 2. It is worth noting the relatively low contact angle obtained even when grafting was performed only at the surface of the polymer, although there has probably been some extent of penetration of AAm into the polymer film, since there was a slight increase in the bulk water absorption of the surface grafted samples.

4. Conclusions

A series of PBD-containing poly(ether urethane amide)s was synthesized. A range of physical properties was achieved by varying the PBD/PTMG ratios and by using different dicarboxylic chain extenders. Increasing the PBD/PTMG ratio in the polymer soft segment led to a decrease in both crystal strength and degree of crystallinity of the hard domains, even though FTIR results suggest a significant increase in phase separation. Substitution of succinic acid with fumaric acid led to an enhanced crystallization ability of the hard domains and, as a consequence, to improved mechanical properties. Derivatizaion was performed on the PBD/PTMG = 1 polymers, this being the highest PBD content at which the polymer still retained the required mechanical properties. Significant hydrophobization was achieved following the reaction with Fx-189, while, hydrophilic polymers were obtained using PEGMA or AAm. The highest degree of derivatization was achieved with AAm, resulting in a polymer with hydrogel-like properties.

References

[1] Barbaro V, Bosi C, Chistolini P, Ialongo D, Rosa P. Biomaterials 1985;6:28–32.
[2] Marchant RE, Zhao Q, Anderson JM, Hiltner A. Polymer 1987;28:2032–9.
[3] Hergenrother RW, Cooper SL. Fourth World Biomaterials Congress, Berlin, Germany, 1992. p. 675 (24–28 April).
[4] Tyler JB, Ratner BD. Fourth World Biomaterials Congress, Berlin, Germany, 24–28. 1992. p. 677 (24–28 April).
[5] Pinchuk L. J Biomater Sci Polym Ed 1994:226–67.
[6] Chen JH, Wei J, Cheng CY, Laiw RF, Lee YD. J Biomed Mater Res 1998;41:633–48.
[7] Inoue H, Fujimoto K, Uyama Y, Ikada Y. J Biomed Mater Res 1997;35:225–64.
[8] Yuang L-YL, Cooper SL. Biomaterials 1998;19:31–40.

[9] Grasel TG, Pierce JA, Cooper SC. J Biomed Mater Res 1987;21:815–42.

[10] Liu LS, Ito Y, Imanishi Y. Biomaterials 1991;12:390–6.

[11] Llandor GR, Sefton MV. Biomaterials 1992;13:421–4.

[12] Tanzi MC, Barzaghi B, Amouchinsky R, Bilenkis S, Penhasi A, Cohn D. Biomaterials 1992;13:425–31.

[13] Mori Y, Nagaoka S, Takiuchi H, Kikuchi T, Noguchi N, Tanzawa H, Noishiki Y. Trans Am Soc Artificial Organs 1982;28:459–63.

[14] Nagaoka S, Mow Y, Takivchi H, Hokota K, Tanzawa H, Nishiumi S. Polym Prepr ACS 1983;24:67–8.

[15] Ito Y, Kashiwagi T, Liu SQ, Liu LS, Kawamura Y, Iguchi Y, Imanishi Y. In: Akutsu T, editor. Artificial hearts. Proceedings of the Second International Symposium on Artificial Heart and Assisting Devices, Tokyo, 1988. p. 35–53.

[16] Bamford CH, Al-Lamee KG. Clin Mater 1992;10:243–61.

[17] Tang YW, Santerre JP, Labow RS, Revenco I, Singh. Transactions of the Society for Biomaterials, 25th Annual Meeting, vol. 58. 1999. p. 22.

[18] Labow RS, Meck E, Santerre JP. Transactions of the Society for Biomaterials, 25th Annual Meeting, vol. 59. 1999. p. 22.

[19] Closckey CB, Santerre JP, Labow RS. Transactions of the Society for Biomaterials, 25th Annual Meeting, vol. 22. 1999. p. 193.

[20] Santerre JP, Labow RS. J Biomed Mater Res 1997;36:223–32.

[21] Tang YW, Santerre JP, Labow RS, Taylor DG. Biomaterials 1997;18:37–46.

[22] Stern T, Penhasi A, Cohn D. Derivatization of a new poly(ether urethane amide) containing chemically active sites. Biomaterials 1995;16:17–23.

[23] Lagasse RR. J Appl Polym Sci 1977;21:2489–503.

[24] Katsuhiro O, Hidetoshi S, Toshihide N, Shinzo Y, Hiroshi O, Yuji M. J Appl Polym Sci 1977;21:3223–35.

[25] Brunette CM, Hsu SL, MacKnight WS. Polym Engng Sci 1981;21:163–71.

[26] Brunette CM, Hsu SL, Rossman M, MacKnight WJ, Schneider NS. Polym Engng Sci 1981;21:669–74.

[27] Katono H, Maruyama A, Nadui K, Ogata N, Yui N, Kataoka K, Sakurai Y. The Third World Biomaterial Congress, Kyoto, Japan, 1988. p. 546.

[28] Schneider NS, Matton RW. Polym Engng Sci 1979;19:1122–9.

[29] Serrano M, MacKnight WJ, Thomas EL, Ottino JM. Polymer 1987;28:1667–73.