Investigation on Suitability of Poly(urethaneimides) as Biomaterials

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SYNOPSIS

The mechanical properties of poly(urethaneimides) (PUI) were compared with known biomedical polyurethanes. The resistance of PUI to extraction with hexane and water and to sterilization with ethylene oxide or water vapor was stated. Water sorption and the permeability of water vapor, oxygen, and carbon dioxide through PUI foils were investigated. In blood compatibility, the PUI foils were similar to cellulose material Cuprophane, used in dialysis. Preliminary *in vivo* testing of PUI implanted in rats indicated good biocompatibility of this polymer. © 1995 John Wiley & Sons, Inc.

INTRODUCTION

Among all polymer materials used in medicine for implants, polyurethanes (PU) were found to be the materials causing the coagulation of thrombocytes and formation of blood clots in the smallest degree. To improve their hemocompatibility, the surface of polyurethane products was modified by applying hydrophilic poly(ethyleneoxide), sometimes bound to heparin, a natural mucopolysaccharide, which is an agent counteracting coagulation of blood.[1] The biolization method was also used, based on seeding on the polyurethane surface a layer of antithrombogenic endothelium cells containing the hormone prostaglandin, which has an inhibiting effect on the process of thrombocyte aggregation. The prostaglandine BW 245C analog also exhibited such an effect.[2]

Another method of polymer hemotolerance improvement is the modification of their surface by introducing hydrophilic poly(N-vinylpyrolidone), used, e.g., in the case of polymethylmethacrylate[3] and polysiloxane implants.[4]

In view of the occurrence of the cyclic imide system in the hard segments of poly(urethaneimide) chains, it should be expected that such a structure of modification positively affect its suitability as a biomaterial.

As we stated before,[6] poly(urethaneimides), obtained from poly(oxytetramethyleneglycol) (PTMG), diphenylmethane 4,4′-diisocyanate (MDI), and pyromellitic acid dianhydride (PMDA), are characterized by the better phase separation of soft poly(etherurethane) segments and hard polyimide segments than it is in typical polyurethanes.[5,6] It was described earlier[7] that the good phase separation of the soft and hard segments and their hydrophobic–hydrophilic balance favor the hemocompatibility of polymers.

The use of polyimides themselves in medicine has been positively evaluated; e.g., polyimides have been used for the production of the cochlea implants and for dielectric layers of neuron microprobes.[8]

Poly(urethaneimides) differentiate themselves positively from polyimides by higher elasticity and stretchability and the possibility of alterating the hardness by a change of the content of both segments.[5,6] They are also characterized by good mechanical properties and resistance to hydrolysis in hot water.[9]

The preliminary hemotolerance tests of poly(urethaneimides) (PUI) obtained by us, carried out

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in the Drug Institute in Warsaw (analysis No. 937-940/920) have shown that their aqueous extracts are nontoxic for aquarium fish. Also, they do not cause erythrocyte hemolysis when testing by the intermediate method. In the direct contact of poly(urethaneimide) foils with erythrocytes, the hemolysis was of various kind for foils obtained from various substrates: 3.7–4% for PUI from PTMG, MDI, PMDA, and 20% when the tolylene diisocyanate was used in synthesis instead of MDI.

In view of the above properties, for further investigations we chose the poly(urethaneimides) based on PTMG with a M_n = 1000 and 2000 and MDI and PMDA.

In the presented work, the copolymers of this type have undergone physical and mechanical properties investigations, detailed hemotolerance investigations, and preliminary biocompatibility evaluations.

MATERIALS AND METHODS

Synthesis of Poly(urethaneimides) (PUI)

PUI were obtained in a two-stage synthesis in solution (in dimethylformamide, DMF) acc. to the method described by Masiulanis.[10] The substrates used were: poly(oxytetramethylene) glycols (PTMG), M_n 2000 (Quacker-Oats) and M_n 1000 (Du Pont); diphenylmethane 4,4′-diisocyanate (MDI), Suprasec MPR (ICI); dianhydride of 1,2,4,5-benzenetetracarboxylic acid (pyromellitic dianhydride) PMDA (Aldrich).

PTMG was purified prior to the synthesis by filtration of the melt and dehydrated under reduced pressure (1.35 hPa) at 90–95°C. MDI was purified by filtration of the melt at a temperature of 50°C. PMDA was used for synthesis as obtained. DMF was dried over P_2O_5 and distilled under reduced pressure.

The PUI foils were obtained by the pouring of the prepolymer into the centrifuge drum, gradual evaporation of the solvent at elevated temperatures (up to 60°C), and final heating in a vacuum dryer (1.35 hPa) at 150–160°C for 6 h.

Purification and Sterilization of PUI Foils

Before further tests, the PUI foil was washed in detergent containing water and next in distilled water in an ultrasonic washer. After cleaning, it was extracted with hexane in a Soxhlett apparatus for 5 h.

The foils were exposed to the action of (a) ethylene oxide (in mixture with CO_2) at 50°C, or (b) saturated water vapor in an autoclave at 121°C for 90 min in order to check the effect of sterilization on the foil strength properties. Before blood and biocompatibility tests, the rinsed PUI foils were sterilized with ethylene oxide in Medicor GST-21 apparatus for 24 h at 50°C and a pressure of 0.3 MPa. After sterilization, the samples were degassed for 3 weeks.

Mechanical Tests

The stress–strain properties of the foil were tested with the help of tensile tester FPZ 100 (Rauenstein, Germany) using samples 5 × 1 × 0.01 cm in dimension, at 23°C, at the extension rate of 4.5 mm/s.

To determine the hysteresis during stretching, the foil samples were exposed to cyclic elongation up to 200%. The percent of the area limited by the hysteresis curve in relation to the whole area between the upper curve (stretching) and the elongation axis was calculated from the first stretching cycle and return.

Creeping tests were carried out by cyclic loading of samples in the force range from 0 to 20 N.

The hardness was determined with Shore's A apparatus on samples made up from several foil layers (approximate value).

The PUI resistance to multiple bending was tested at ambient temperature on a G-Flexometer 729-type Bally acc. to PN-71/D-22143 (Polish Standard).

The dynamic mechanical thermal analysis (DMTA) in the −100–300°C temperature range was carried out on Polymer Laboratory DMTA Mk III analyzer (England), at a heating rate of 2 deg/min and at 10 MHz frequency. Multilayer 1.0 mm thick samples of PUI foils were used.

Testing of Contact Angles with Water, Water Sorption, and Water Vapor Permeability

Sessile contact angles with water were measured using a goniometer.

Water sorption was determined with an accuracy of 0.0001 g at 38°C by measuring the increase of weight of dried PUI samples after keeping them in distilled water for 24 h; the samples were pressed between filter paper and immediately weighed in a vessel.

The water vapor permeability was tested by the Desiccant Method acc. to ASTM E-96, by measuring the weight increase of anhydrous calcium chloride (with an accuracy of 0.0001 g) after being kept in a

vessel closed by PUI foil in a chamber at 38°C at a relative humidity equal to 100%.

Permeability of Gases

The permeability of oxygen and carbon dioxide was investigated at 37°C with apparatus described by Marjański and Kwiatkowski,[11] at a 100 mmHg pressure drop.

Determination of Extractibles in Boiling Water and *n*-Hexane

This determination was conducted using the procedures outlined in the Code of Federal Regulation Title 21, Chapter 1, Subchapter B, part 177.2600.[12] The PUI foils were extracted with distilled water and *n*-hexane, respectively, at reflux temperature. The dry residues were determined from the extracts after 7 h and next 2 h refluxing.

Investigation of PUI Foils Influence on Blood Morphologic Elements

Investigation of PUI hemocompatibility was carried out with humane blood, in polyethylene tubes from the dropper used in the blood transfusion; Cuprophane foil was used as a reference.

Level of hemolysis was measured using physiological saline extract of PUI foils, obtained after 24 h at a temperature of 70°C. This extract was thermostated for 24 h at 37°C with suspensions of erythrocytes.

A calcium clotting time of citrated blood and citrated plasma was measured by adding a sample of PUI foil to blood (time 0) and using the blood previously incubated with foils for 2 h in 37°C.

The influence of PUI on blood at increasing incubation time was investigated during the keeping of PUI foils with citrated blood and citrated plasma at 22°C in a time up to 120 min. Before and after incubation with PUI changes in blood were determined by measuring: (a) leucocyte count; (b) platelet count; (c) plasma kephalin time (partial thromboplastin time) (PTT); (d) plasma kaolin kephalin time (activated partial thromboplastin time) (aPTT); (e) plasma prothrombin time, recalculated on prothrombin index (PT); and fibrinogen concentration.

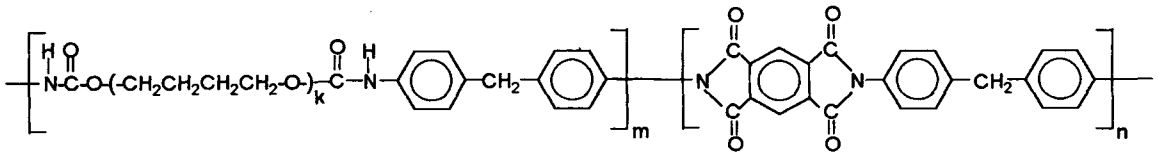
Preliminary *In Vivo* Testing

In vivo testing of PUI was carried out on 15 3-month-old white rats (Wistar breed), with a medium weight of 200 g. Two samples of foils of 1 cm diameter was implanted in subcutaneous tissue, one in the peritoneal cavity, and next two in the dorsal muscle.

After the operation, all rats were kept in standard laboratory breeding until planning autopsy 3, 7, and 14 days postimplantation. The microscopic study samples were taken from tissues adjoining the implant, together with capsule surrounding the foils. Samples were fixed in 8% formaldehyde and dehydrated in alcohol at 60°C. Histological specimens were prepared by cutting paraffin-embedded tissue on a microtome and staining with hematoxylin, eosin, or by the van Gieson method. Slides was observed in a biologic microscopy with an enlargement of 140×.[30]

RESULTS AND DISCUSSION

The chemical structure of the investigated PUI is shown below, and their characteristic are given in Table I.



Poly(etherurethane) soft segment

Polyimide hard segment

The Mechanical Properties of PUI

The mechanical measurements showed that obtained PUI exhibited similar strengths at 100% and 300% elongation, to appropriate properties of biomedical Pellethane 2363 (Table II).[13] The stress–strain properties of PUI (Fig. 1) and their elongation at break are in a range similar to that given in the literature for several biomedical polyurethanes (PU).[14] A modulus of elasticity at 10% elongation

Table I Characteristic of the Investigated Poly(urethaneimides)

PUI Designation	Substrates	Imide/Urethane Equivalent Ratio	Hard Segment Content[a] Mass %
I	PTMG (*Mw* 2200), MDI, PMDA	2	31.4
II	PTMG (*Mw* 2200), MDI, PMDA	3	38.7
III	PTMG (*Mw* 1000), MDI, PMDA	1	38.6

[a] Calculated as the ratio of the weight of PMDA + MDI to the total weight of the reagents; the evolution of CO_2 was taken into account.

significantly exceeds the "initial modulus" given for biomedical polyurethanes.[14] However, as we have determined from the graph described by Ward et al.,[15] the modulus of elasticity at a 10% elongation for the TLC-15 (Thoratec) polyurethaneurea, containing 30% of rigid segments, and obtained as the Biomer from PTMO, MDI, and ethylenediamine, is similar to the module of PUI (Table II).

Hysteresis and creeping tests of materials under cyclic loads are important in medical applications. As we stated, the area of the first hysteresis of PUI-I during elongation was similar to the hysteresis area of the biomedical Pellethane,[15] while in relation to the Biomer,[15] it was approximately two times greater (Fig. 2). For PUI-II, with a higher polyimide segment contents, the hysteresis area was higher than for PUI-I. It should be emphasised, however, that for all tested samples we observed a significant decrease of the hysteresis area during further load cycles (Fig. 3), resulting from the arrangement of the PUI segments. This indicates that it would probably be beneficial to use PUI foil after preliminary orientation by elongation.

As a result from the change of the PUI sample tension set from the number of load cycles (0–20 *N*) (polymer creeping) (Fig. 4), the polymer of this type departs to a degree from the ideal elastomer similarly to typical segmented polyurethanes.[16] The deviation from the theoretical straight line is a little higher for PUI-II, with greater content of rigid polyimide segments.

Preliminary investigations of PUI-II with a hardness of 91°Sh A, carried out on Bally apparatus, have shown that resistance to multiple bending is

Table II The Mechanical Properties of Commercial Biomedical Polyurethanes and Investigated Poly(urethaneimides) (PUI I–III)

Polymer	Hardness °Shore	Initial Modulus of Elasticity (MPa)	Stress at 100% of Elongation σ_{100} (MPa)	Stress at 300% of Elongation σ_{300} (MPa)	Tensile Strength σ_b[c] (MPa)	Elongation at Break ε_b (%)	Reference
Biomer Sol G	75A	2.8–5.5[a]	—	—	31–41	600–800	14
Biomer Ext G	—	—	—	—	28–35	—	14
Cardiothane 51	72A	—	—	—	43	580	14
Pellethane 2363	80A–75D	3.6–14[a]	—	—	35–48	350–600	13
80A	83A	—	5.86	10.0	41.4	550	13
90A	93A	—	10.55	21.4	46.5	500	13
55A	55D	—	17.25	31.0	44.8	430	13
Thoratec BPS-215	75A	10.3[a]	—	—	38	700	14
BPS-105	70A	4.1[a]	—	—	35	870	14
TLC-15	—	20.7[b]	—	5.5–12.4	31–49	800–900	15
Poly(urethaneimide) I	86A	20.4[b]	6.7	12.6	33.2	720	
Poly(urethaneimide) II	91A	49.3[b]	10.3	17.8	36.2	580	
Poly(urethaneimide) III	89A	84[b]	11.2	19	42.6	480	

[a] Acc. to [14] the "initial modulus."
[b] The modulus of elasticity $E = \sigma/\varepsilon$, calculated at a 10% elongation.
[c] σ_b—the tensile strength at break.

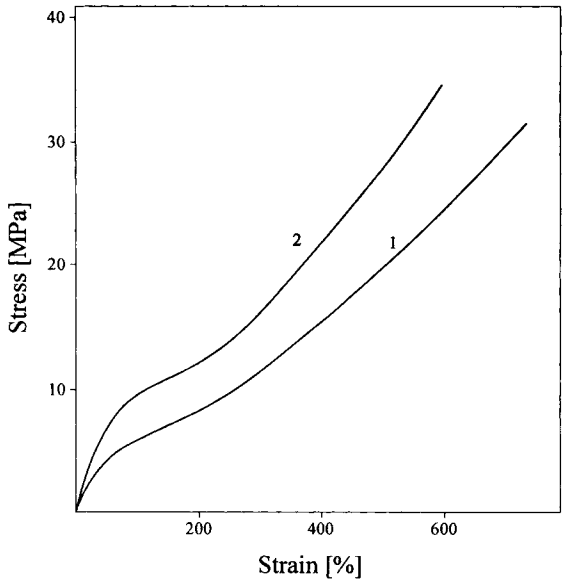


Figure 1 The stress-strain dependence for PUI-I (1) and PUI-II (2).

dependent on the foil thickness; the 0.07–0.13 mm foils used to stand over 2.5 mln flexures at ambient temperature.[9] In further studies, PUI-I foils of 0.1–0.14 mm in thickness, used to stand at room temperature 4.2–5.2 mln flexures, and the PUI-II foils 0.11–0.15 mm thick, 2.7–4.65 mln flexures. PUI exceed in the resistance to bending the biomedical PU of the Biomer Ext G (1.5 mln bends);[14] Pellethane 2363 and the Biomer Sol G are much more resistant to bending.[14]

Dynamic Mechanical Thermal Analysis of PUI

Investigations of PUI-I and PUI-II by the DMTA method showed separation of the hard and soft segments, indicated by the occurrence of several tan δ maxima, corresponding to their glass transition temperatures (T_g) [Fig. 5(A,B)]. For the PTMG containing soft segments T_g −64°C, −61°C, and for the hard polyimide segments T_g 160°C, 187°C were found for PUI-I and PUI-II, respectively. The magnitude and the temperature maxima of tan δ were dependent on the each segment content.

The intermediate maximum on tan δ curves at 32°C for PUI-I and 40°C for PUI-II is connected with initial organization of the hard segments, because its magnitude and temperature range increases with polyimide content. It is worth to noting that up to this transition an increase of bending storage

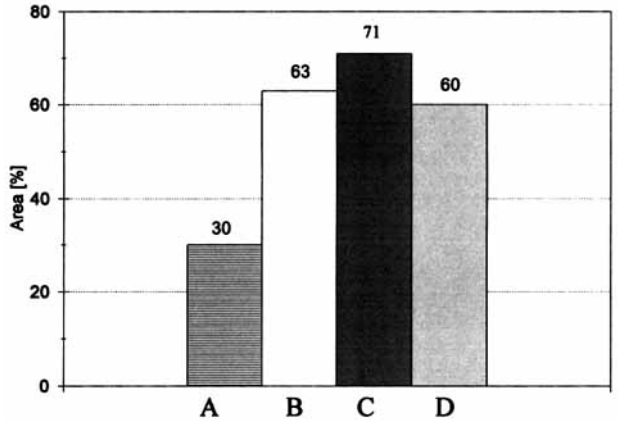


Figure 2 The area of the first cycle hysteresis curve for poly(urethaneimides) compared to biomedical polymers: (A) Biomer.[15] (B) Pellethane 80A.[15] (C) PUI-II. (D) PUI-I.

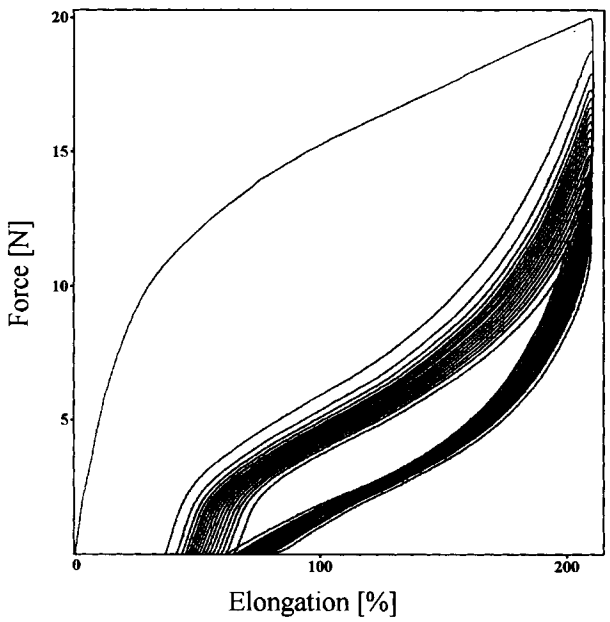


Figure 3 The PUI-I hysteresis curve in consecutive stretching cycles up to 200% of relative elongation.

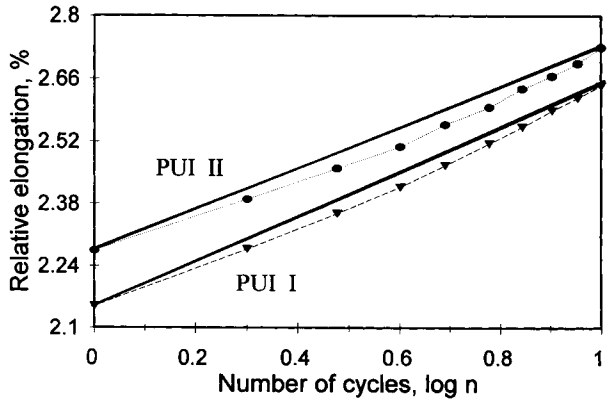


Figure 4 The dependence of the tension set of PUI-I and PUI-II from the number of stretching cycles.

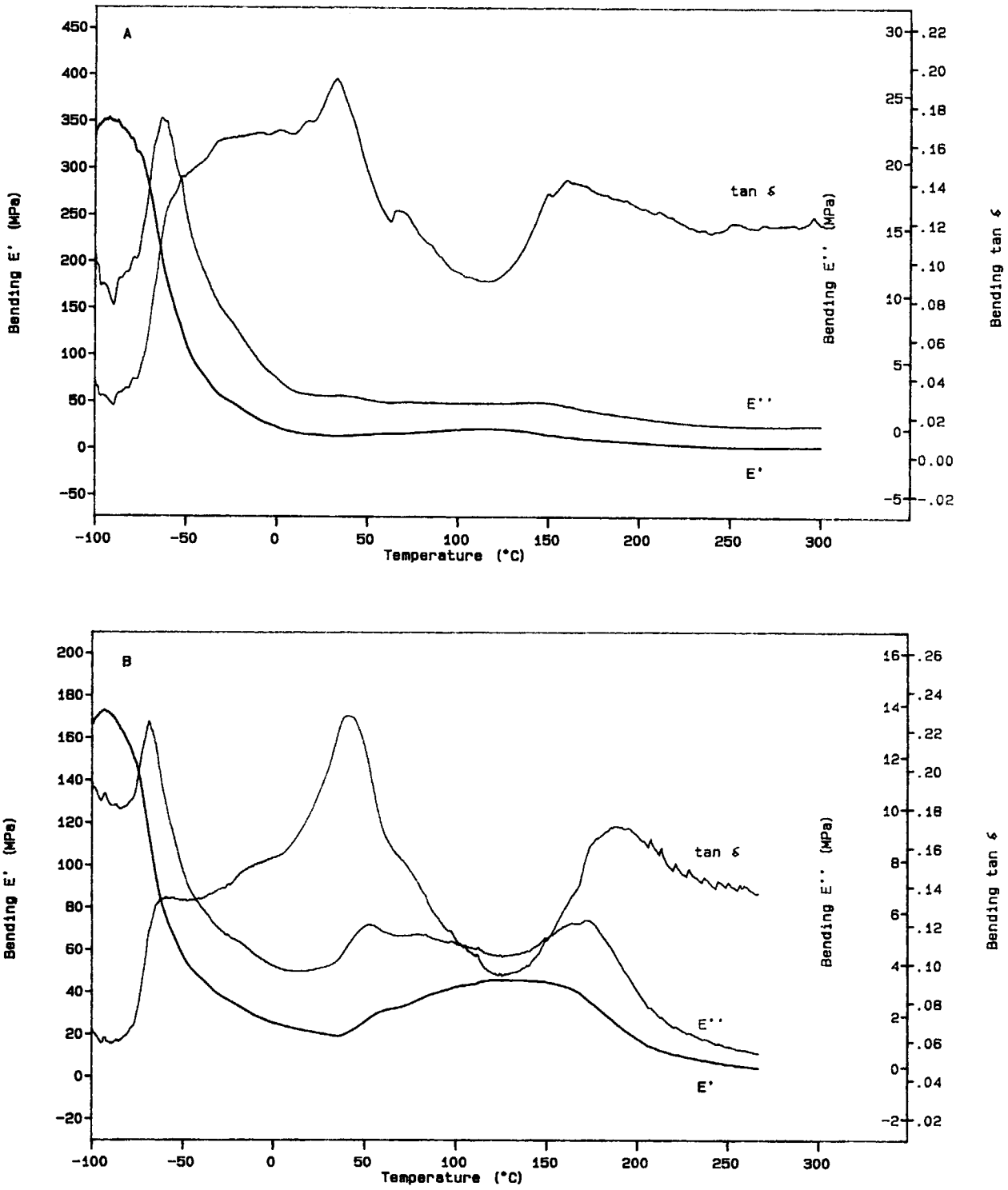


Figure 5 The temperature dependence of the dynamic storage modulus (E′,MPa), dynamic loss modulus (E″,MPa), and the tan δ of PUI-I (A) and PUI-II (B).

Table III The Effect of Sterilization in Ethylene Oxide[a] on the Strength Properties of PUI

	Strength Properties					
	Initial Samples		Samples after Sterilization		Samples after Hexane Extraction and Sterilization	
PUI	σ_b (MPa)	ε_b (%)	σ_b (MPa)	ε_b (%)	σ_b (MPa)	ε_b (%)
II	36.2	580	—	—	49.5	530
III	42.6	480	42	460	46	520

[a] Ethylene oxide + CO_2/50°C.

Table IV The Effect of Sterilization in Water Vapor[a] on the Strength Properties of PUI

	Strength Properties [Change Relative to Untreated, (%)]					
	Untreated		Samples after Sterilization		Samples after Hexane Extraction and Sterilization	
PUI	σ_b (MPa)	ε_b (%)	σ_b (MPa)	ε_b (%)	σ_b (MPa)	ε_b (%)
II	36.2	580	27 (−25.4)	560	23 (−36)	540
III	42.6	480	35 (−17.8)	490	34 (−20)	500

[a] 121°C/90 min.

Table V Solid Residue of the Water and *n*-Hexane Extracts (mg/inch^2)

	Water		*n*-Hexane	
	First 7 h	Next 2 h	First 7 h	Next 2 h
PUI I	0.058	0.007	0.029	0.007
Pellethane 2363 80 A	0.036	0.012	0.126	0.03
Max. allow. (12)	20	1	175	4

modulus and total modulus was seen (particularly in PUI-II) what indicated the increase of elasticity.

The stability of PUI to Sterilization Conditions and to Extraction with Water and Hexane

We stated that PUI are resistant to sterilization in ethylene oxide; this process does not cause a decrease of the stress–strain properties (Table III), while sterilization in an autoclave with water vapor causes a decrease of the PUI foil strength (Table IV).

After the extraction in water and hexane during 9 h at reflux temperatures, according to the Code of Federal Regulation,[12] we observed no or only very small changes in tensile strength properties of PUI; e.g., for PUI-I there was only a 2% decrease of the tension strength at break after such treating by water. The extractibles determined in mg/inch were very small, much lower than allowed. In Table V,

Table VI The Sorption of Water in Poly(urethaneimides) Foils at 38°C

PUI	Foil Thickness (mm)	Sorption of Water Δ m/m (%)
I	0.14–0.16	1
II	0.11–0.13	0.9

these are compared with extractibles from Pellethane 2363 80A found in ref. 12.

Physical Properties of PUI

The obtained PUI foils of thickness 0.8–0.16 mm were amber yellow in color and transparent.

The measured sessile contact angles with water 75 ± 1° for PUI-I and 68 ± 2° for PUI-II indicated that there is an increase a hydrophilic with greater content of cyclic imid linkages. These PUI contact angles were something lower then advancing contact angles found in ref. 17 for Biomer (83 ± 3°) and Pellethane 2363 80 AE (77 ± 3°).

The sorption of water by PUI-I and PUI-II foils at 38°C was found in the range of 0.9–1% (Table VI). For biomedical PU, e.g., for Biomer Sol G, Biomer Ext G, and Cardiothane 51, the sorption of water was equal to 1.2%, 0.18% and 1.6%, respectively.[14] For polyimides, the sorption of water was determined in the 1.3–7.4% range at 37°C.[18–20]

The water vapor permeability through PUI foils (Table VII) decreases with the increase of polyimide contents and is lower than that given in the literature for polyimides and for polyurethanes.[21,22]

The O_2 (7.7 barrer) and CO_2 (52 barrer) permeability of PUI-II measured at 37°C (Table VIII) is much higher than that reported for polyimides for which a 0.108 barrer/39°C O_2 permeability[23] and a 26 barrer/35°C CO_2 permeability[24] were found. In these properties, PUI are more similar to polyurethanes. For example, the O_2 permeability for polyurethane foils at 23°C was in the 1.5–4.8 barrer range,[25] and for a completely amorphous one, another PU was equal to a 6.28 barrer.[26] In comparison with permeability of other kinds of polymers reported by Rogers,[27] permeability of O_2 through PUI foils is approximate to permeability (at temp. 25–30°C) of polybutadiene–acrylonitryl copolymer, tetrafluoroethylene, cellulose acetobutyrate, and low

Table VIII The Permeability of Oxygen and Carbon Dioxide through PUI Foils

PUI		Permeability 10^{-10} · cm^3 (STP) $cm/cm^2 \cdot s \cdot cm$ Hg (barrer)	
		O_2	CO_2
I	0.82–0.90	8.85	68.43
II	0.92–1.02	7.77	52.05

Table IX Calcium Clotting Time in Hemocompatibility Investigations of PUI

	Calcium Clotting Time (s)			
	Whole Blood		Serum	
Time of Incubation (min)	0	120	0	120
In glass	490	530	125	195
Couprophane	470	508	380	360
PUI I	620	600	260	350
PUI II	615	610	300	270

Table VII The Water Vapor Permeability through Poly(urethaneimide) Foils

PUI	Foil Thickness (m)	Water Vapor Transmission, WVT $[g/m^2 \cdot h]$	Permeance $(g/Pa \cdot m^2 \cdot s)$	Permeability[b] $(g/Pa \cdot s \cdot m)$
I	1.1×10^{-4}	32.6	13.71×10^{-7}	1.514×10^{-10}
II	1.1×10^{-4}	29.35	12.33×10^{-7}	1.356×10^{-10}
	0.9×10^{-4}	35.85	15.06×10^{-7}	1.355×10^{-10}

[a] $P = WVT/S(R_1 - R_2)$, S—the vapor pressure at 38°C, 49.692 mmHg = 66.09 × 10^2Pa; $R_1 \sim 1$, the relative humidity in the measurement chamber, $R_2 \sim 0$, in the vessel with anhydrous $CaCl_2$.

[b] Permeance × thickness.

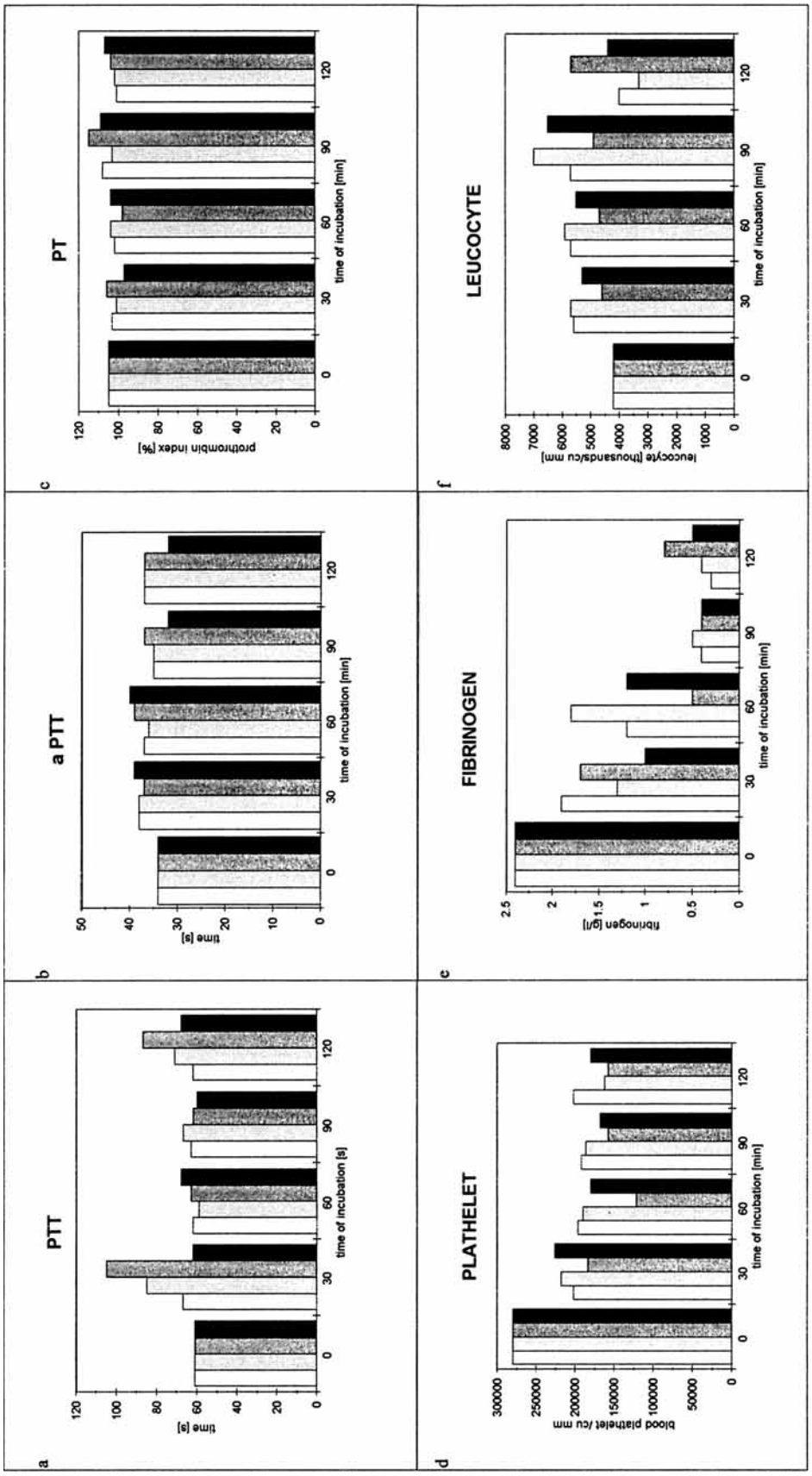


Figure 6 (a–f) Incubation time—variant changes of quantities of blood components with: clear column, PUI-I; lightly dotted column, PUI-II; heavily dotted column, Cuprophane; solid column, blood without foils.

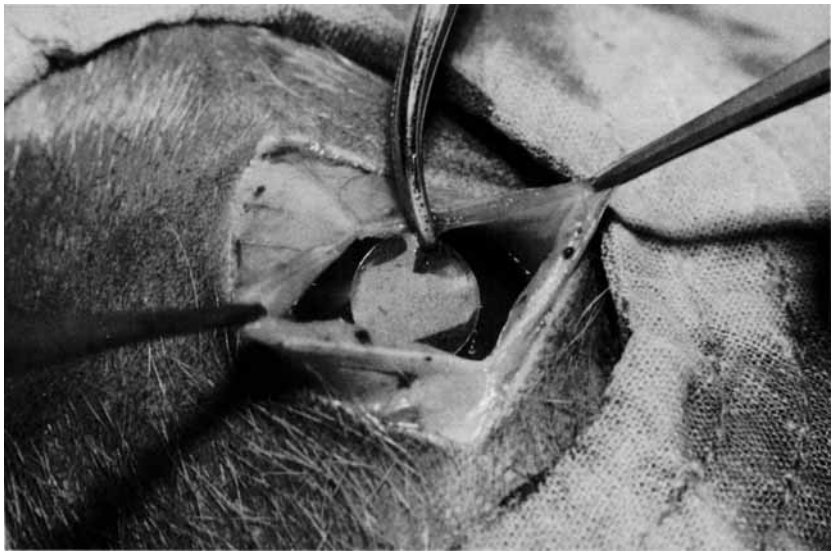


Figure 7 The implantation of a PUI-I sample into the peritoneal cavity of the rat's body.

density polyethylene; it is much higher then the O_2 permeability of polyamide (nylon 6—0.038 barrer) and polyester Mylar (0.03 barrer) but is much lower then the permeability of ethylcelulose (26.5 barrer) and silicone rubber (500 barrer).[27]

Investigation of Blood Compatibility of PUI[28]

The blood compatibility studies were carried out for PUI-I and PUI-II, for which saline extracts caused only 0 and 0.8% level of erythrocytes hemolysis, respectively.[28]

It was found that PUI foils like the Cuprophane foil do not activate the process of coagulation of the blood.

Calcium clotting time, presented in Table IX, was much higher for samples of blood with foils than for control blood in glass. In a whole blood, PUI foils caused longer clotting time then Cuprophane; in plasma, there was the opposite effect. Incubation of

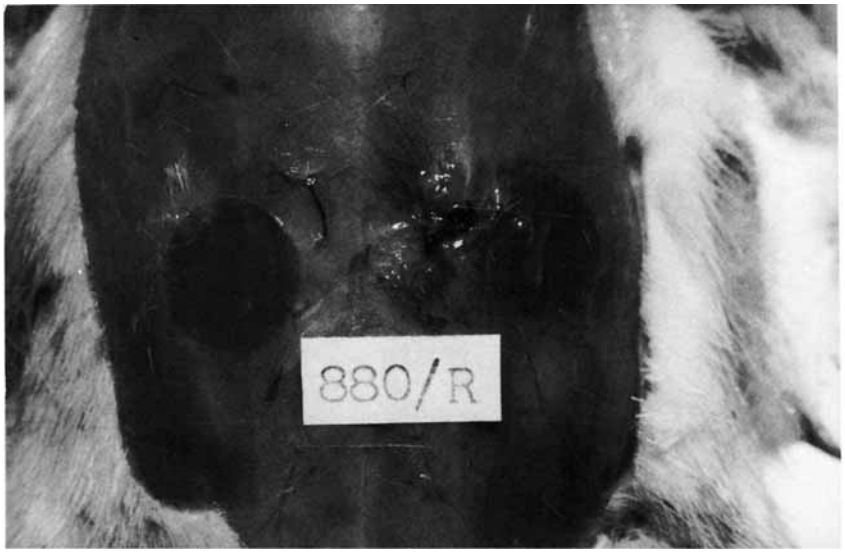


Figure 8 The macroscopic image of the PUI samples in abdominal integument of the rat after 3 days of implantation.

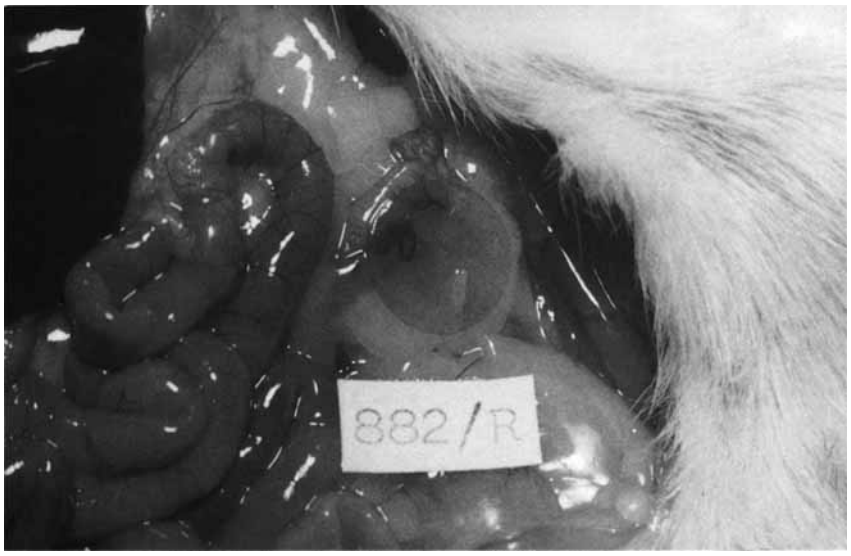


Figure 9 The macroscopic image of the PUI sample in the peritoneal cavity of the rat after 7 days of implantation.

plasma or blood with foils in time 120 min did not lead to greater changes of calcium clotting time.

The influence of PUI and Cuprophane on the blood elements and the measured indexes are shown in Figure 6(a–f). PTT, aPTT, and PT indexes [Fig, 6(a,b,c,)] fluctuated slightly on measuring during incubation of blood with PUI and Cuprophane foils, but were still approximate to the respective indexes of control blood in polyethylene tube. This means that PUI do not change the protrombin level.

A relatively less degree of platelet adsorption was observed in samples of blood with PUI foils than with Cuprophane [Fig. 6(d)]. After 120 min of incubation the platelet level failed down no more than 43%, both in control blood and in the samples with PUI. It is much better than was described for "thromboresistant polyurethane elastomers"[29] obtained with modification of typical PTMG based polyurethane by ethylene oxide-propylene oxide copolymer. With these polyurethanes, the platelet

Figure 10 The macroscopic image of the PUI samples in the abdominal integument of rat after 14 days of implantation.

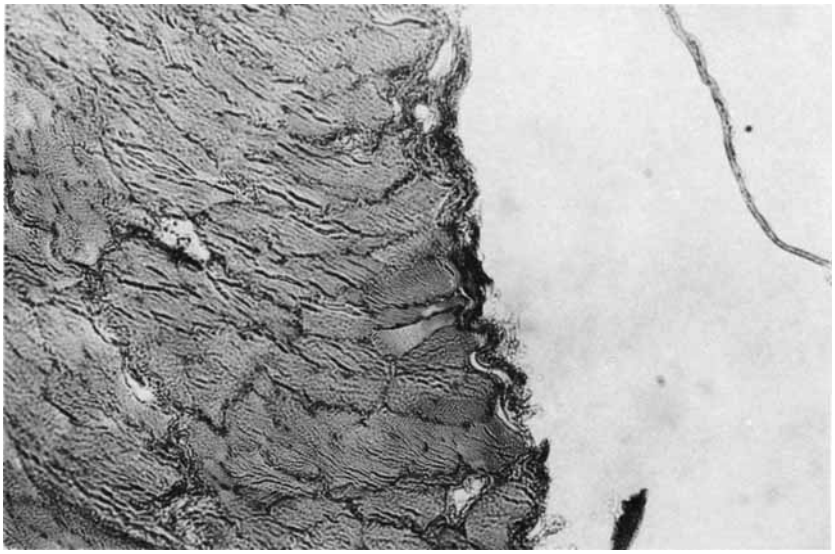


Figure 11 The microscopic image of the peritoneal cavity of the rat after 3 days of PUI implantation; on the right, the place after the removing of the PUI.

numbers level in blood failed down to 0% after 60 min of incubation.[29] Similarly, better results were also obtained with the fibrinogen level. It radically dropped, not after 60 min as it was in ref. 29, but after 120 min of incubation with PUI and Cuprophane foils, like in the control sample of blood [Fig. 6(e)].

The leucocytes number levels in the control blood and in blood with foils fluctuated considerably in measuring, but after 120 min of incubation were almost on the beginning level [Fig. 6(f)].

Investigations of PUI-I Biocompatibility[30]

The exemplary implantation of the PUI foil sample into the peritoneal cavity of the rat is shown in Figure 7.

After the implantation of all PUI samples, the proper healing of wounds was observed; just after 3 days the wounds were dry. Animals had a good appetite and thirst and a suitable increase of weight. All rats survived to the time of planned operations.

In macroscopic observations, after 3 days post-

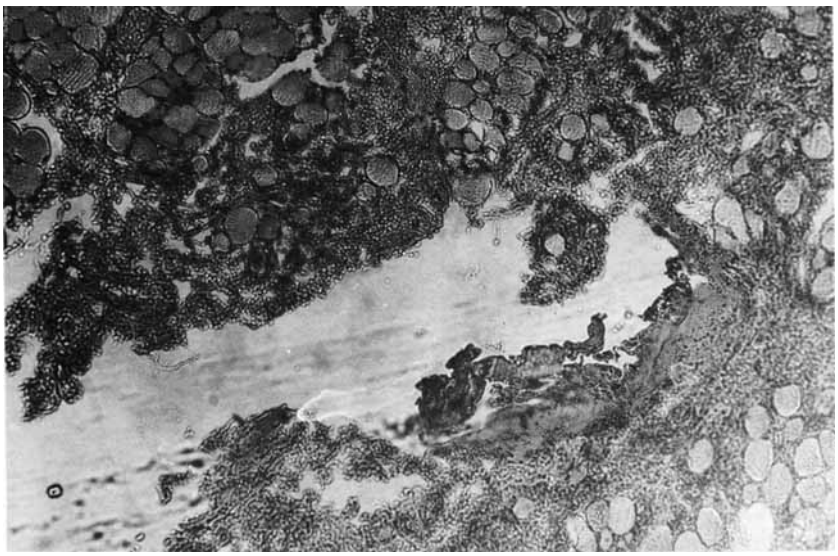


Figure 12 The microscopic image of the dorsal muscle of the rat after 3 days of PUI implantation; in the center, the place after removing of the PUI.

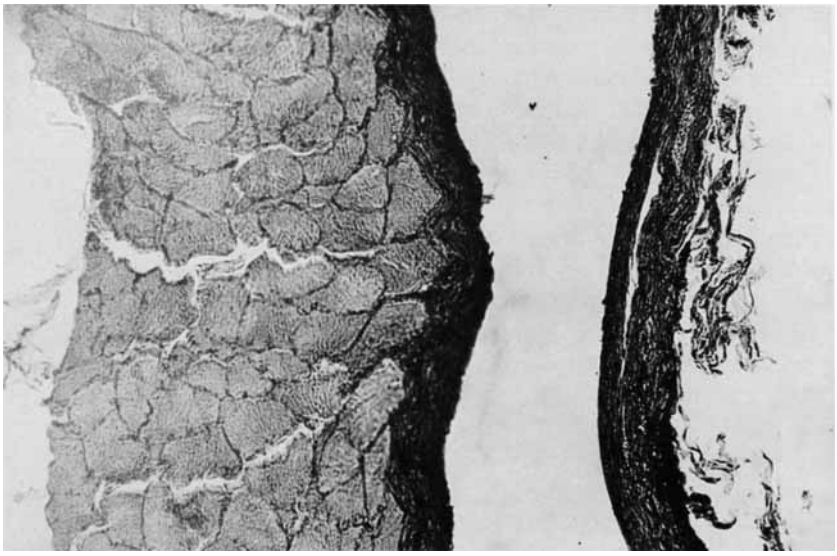


Figure 13 The microscopic image of the dorsal muscle of the rat after 14 days of PUI implantation; in the center, the place after removing of the PUI around by the band of fibrous tissue.

implantation in the abdominal integument and in the dorsal muscle the PUI samples were laying loose, and the surrounding tissues showed only a little congestion (Fig. 8). The organs in the peritoneal cavity did not show any changes.

After 7 and 14 days there were no observed pathologic changes in the tissues adjoining PUI implants (Fig. 9). In the last operation, it was visible that all implants laid loose and were enclosed in thin capsules (Fig. 10).

The microscopic study of the samples obtained after 3 days of implantation in the abdominal integument and in the dorsal muscle indicated the presence in some places of fibrinous exudate and extravasated erythrocytes; in some places there were visible foci of accumulated mononuclear lymphocyte type cells (Figs. 11 and 12).

In histological specimens obtained after 7 days postimplantation from the all tissues surrounding the PUI samples, the presence of thin band of con-

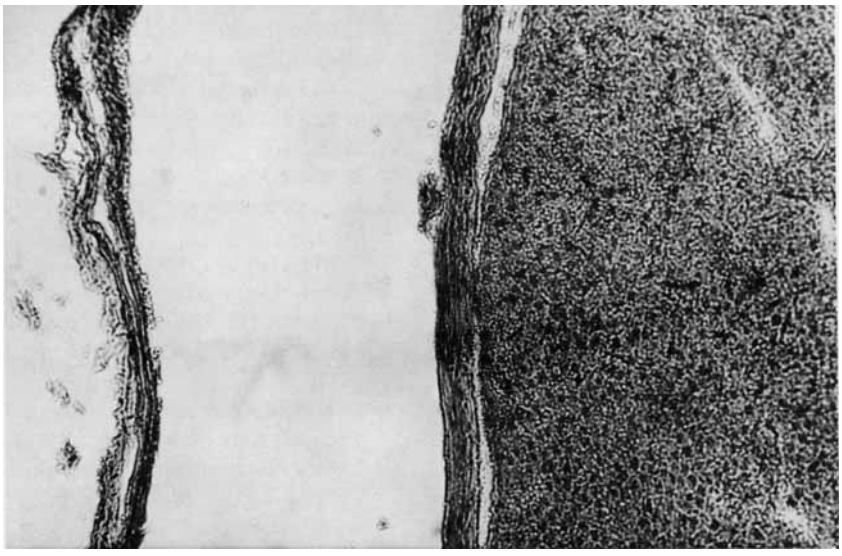


Figure 14 The microscopic image of the tissue from the peritoneal cavity of the rat after 14 days of PUI implantation; in the center, the place after the removing of the PUI, around by the band of fibrous tissue, sharply separated from the liver tissue.

nective tissue was observed. Past 14 days, the capsule generated around the implants took on the characteristics of fibrous tissue; it was separated from surrounding tissues and contained many fibrocytes, fewer fibroblasts and, in places, the limphocyte type cells (Figs. 13 and 14).

In the preparates stained by the van Gieson method, there were plentiful collagen's fibers.

On the basis of realized macro and microinvestigations it was stated[30] that PUI do not evoke systemic pathologic changes, and it may be evaluated as the material with good biocompatibility.

CONCLUSIONS

The investigations carried out indicate that PUI obtained from PTMG, MDI, and PMDA fulfill requirements for biomaterials in regard to stress–strain properties and resistance to sterilization in ethylene oxide. They are characterized by a water sorption and gas permeability similar to polyurethanes. In blood compatibility, the PUI foils were similar to Cuprophane foil, and through 14 days of implantation PUI did not cause pathologic changes in the rat's body. In continuation of this work we will change the parameters of the PUI synthesis to obtain polymers with better flex life. It is also necessary to investigate the biocompatibility and the stability of the PUI properties after a longer period of implantation in order to get an explicit answer if the PUI foil or coating may be used as biomaterial.

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