Effects of Gamma-Ray Irradiation on the Change of Characteristics of Polyurethane

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Synopsis

Investigations have been carried out on gamma-ray irradiated thermoplastic polyurethane (PU). The change of molecular weight as a result of irradiation and the change of absorbance of samples eluted daily by methanol extraction were determined. GPC patterns, tensile strength, and residual amount of radicals based on chemiluminescence were also measured. PU chain-extended with 1,4-butanediol (BU) showed degradation, while PU without chain-extended with BU (linear PU) showed mainly crosslinking by gamma-ray irradiation. G values were 1.1 (degradation) and 0.2 (crosslinking). A linear relationship between the irradiation dose and the residual radical amount was found. There was no significant difference in molecular weight as determined immediately following irradiation with analysis 6 months after irradiation. The influence of the amount of residual radical on the changes in the characteristics of PU was not significant. The elution of PU oligomers (n = 1~10) was confirmed from the GPC pattern of methanol extract. The changes in tensile strength correlated well with the changes in molecular weight. Sequential daily methanol extract analysis showed that elution occurred semilogarithmically. Methanol extract at an early stage is more toxic due to abundant elution of lower molecular weight compound.

INTRODUCTION

Polyurethane (PU) used in medical devices is synthesized by the reaction of 4,4′-diphenylmethane diisocyanate (MDI) and polytetramethyleneglycol (PTMG). 1,4-Butanediol (BU) is used as the chain-extending agent of PU. Polyurethane is widely used in health care applications, specifically in a large variety of medical devices such as potting material in artificial dialysis devices, plasma separators, intra-aortic balloons, ventricular assist devices, and vascular grafts because of its compatibility with blood.[1]

Gamma-ray irradiation, pressurized steam (autoclave), and chemical agents are used in sterilization practices. There have been reports of hazardous effects of sterilization on plastic materials. By gamma-ray irradiation and autoclave sterilization, high molecular weight materials may decompose, yielding toxic low molecular weight compounds. They are readily leached into body fluids, to which patients are commonly exposed. With the use of ethylene oxide for chemical sterilization, significant amounts may remain in PU.[2] Ethylene oxide has been reported to exhibit mutagenicity, carcinogenicity, and antigenicity.[3]

Characteristic changes in gamma-ray irradiated medical grade PU have not previously been examined by gel permeation chromatography (GPC). In the present studies, irradiation damage to PU was assessed in terms of molecular weight change. Such change can indicate degradation or the augmentation of

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crosslinking. Various parameters related to polymer chemistry were also evaluated.

Unirradiated PU and irradiated PU samples were extracted with methanol. Compounds extracted with organic solvent were analyzed by GPC and ultraviolet (UV) spectrophotometry. The time course of elution of degradated products was studied. The correlation of changes in peak top molecular weight (M_{GPC}) and the UV spectral characteristics with the irradiation dose was assessed.

The residual radical amount was supposed to remain in the irradiated PU. This may cause further deformation of PU after irradiation. Therefore, the residual radical amount, based on the chemiluminescence method, was determined after irradiation.

Additionally, tensile strength of PU samples prior and posterior to gamma-ray irradiation was also measured.

MATERIALS AND METHODS

Materials

Thermoplastic PU samples were synthesized by reaction of PTMG (M_w = 1000) with MDI in *N,N*-dimethylformamide (DMF). Polymerization was stopped by adding *n*-butanol after various reaction times: linear PU samples thus obtained had weight average molecular weights (M_w) of 220,000 (PU-1), 180,000 (PU-2), and 140,000 (PU-3). To provide chain-extended thermoplastic PUs, 1,4-butanediol (BU) was added to the reaction mixture before the addition of *n*-butanol. Thus, the thermoplastic PU samples having a M_w of 220,000 (PU-4), 180,000 (PU-5), and 140,000 (PU-6) were obtained. The chain-extended PU samples were similar to Pellethane® in structure. The structures of the PU samples are shown in Figure 1. These PU samples were dissolved in DMF to prepare 30% solutions. Fifteen-gram parts of each solution was placed into glass Petri dishes, 9 cm in inner diameter, to form a uniform layer. A PU film of a thickness of about 1 mm was obtained in the Petri dish after complete removal of DMF by evaporation at room temperature after 2 weeks, followed by vacuum evaporation for 2 days. The covered dishes were subjected to gamma-ray irradiation.

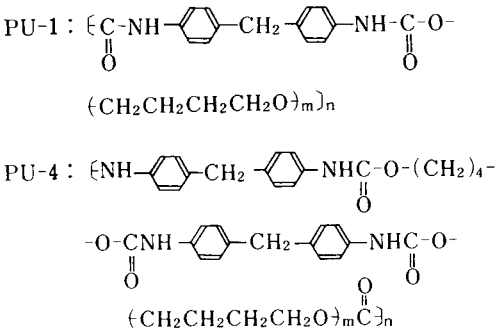

Fig. 1. Structure of polyurethane (PU).

Chromatographic grade DMF was used. The other reagents were special commercial grade.

Instrumentation

GPC analysis was performed on a Shimadzu LC-6A instrument. Other instruments used include a Shimadzu UV spectrophotometer SPD-2A, a Showa-denko SE-11 refractive index (RI) detector, a Yokogawa-dennki Type 3066 recorder, a SIC Chromatocorder 12, a Shimadzu C-R1A chromatopac data acquisition system, and a chemiluminescence photon counter. Equipment for tensile strength testing was a Shimadzu autograph AGS-50 for PU-1 through PU-3 and an Instron Model 1123 instrument for PU-4 through PU-6. A Danbel cutter was used for the preparation of the tensile strength test strip. A Shimadzu UV-210 spectrophotometer was used for UV detection.

Sterilization

Polyurethane samples were subjected to ^{60}Co gamma-ray irradiation doses at a rate of 2.5 Mrad/25 h from 0 to 10 Mrad at intervals of 2.5 Mrad.

Preparation of Samples

Polyurethane samples for GPC analysis were dissolved in GPC eluent and diluted to provide 0.05–0.1% solution. For methanol extraction, about 100-mg parts of PU samples were cut into pieces, 10 × 10 mm, and placed in glass-stoppered test tubes, 10 mm in inner diameter. To the test tube was added 10 mL methanol for extraction for 5 consecutive days. The methanol was replaced daily, and the recovered methanol was analyzed by UV spectrophotometry. The methanol extracts from these 5 days were combined and evaporated in a water bath kept at 40°C. The residue was dissolved in the GPC eluent to provide a 0.1–0.05% solution, which was applied to the GPC column.

Conditions of GPC Analysis

Columns: For GPC analyses of solutions of PU in DMF, a Toso-GPC column (7.8 × 300 mm) packed with TSK gel GMH (molecular weight exclusion limit 400,000,000) was used coupled with a TSK guard column HM (7.5 × 75 mm).

For GPC analyses of methanol extracts, Shodex GPC columns (8 × 250 × 2 mm) packed with AD-803/S (molecular weight exclusion limit 70,000) and AD-804/SS (molecular weight exclusion limit 400,000) coupled with an AD-800P precolumn (6 × 50 mm) were used. Columns of different molecular weight exclusion limits were required because molecular weights varied widely among the analytical samples.

Sample volumes of 200 μL were used. Elution was accomplished with 10 m*M* LiBr in DMF at 0.8 mL/min. The column temperature was kept at 50°C. The eluate was monitored optically at 290 nm with a RI detector. Weight average (M_w) and number average (M_n) molecular weights were computed by a resident program in the SIC chromatocorder 12. Polystyrene SM-105 supplied from Showa Denkou Co. Ltd. was used as a standard compound for GPC analysis.

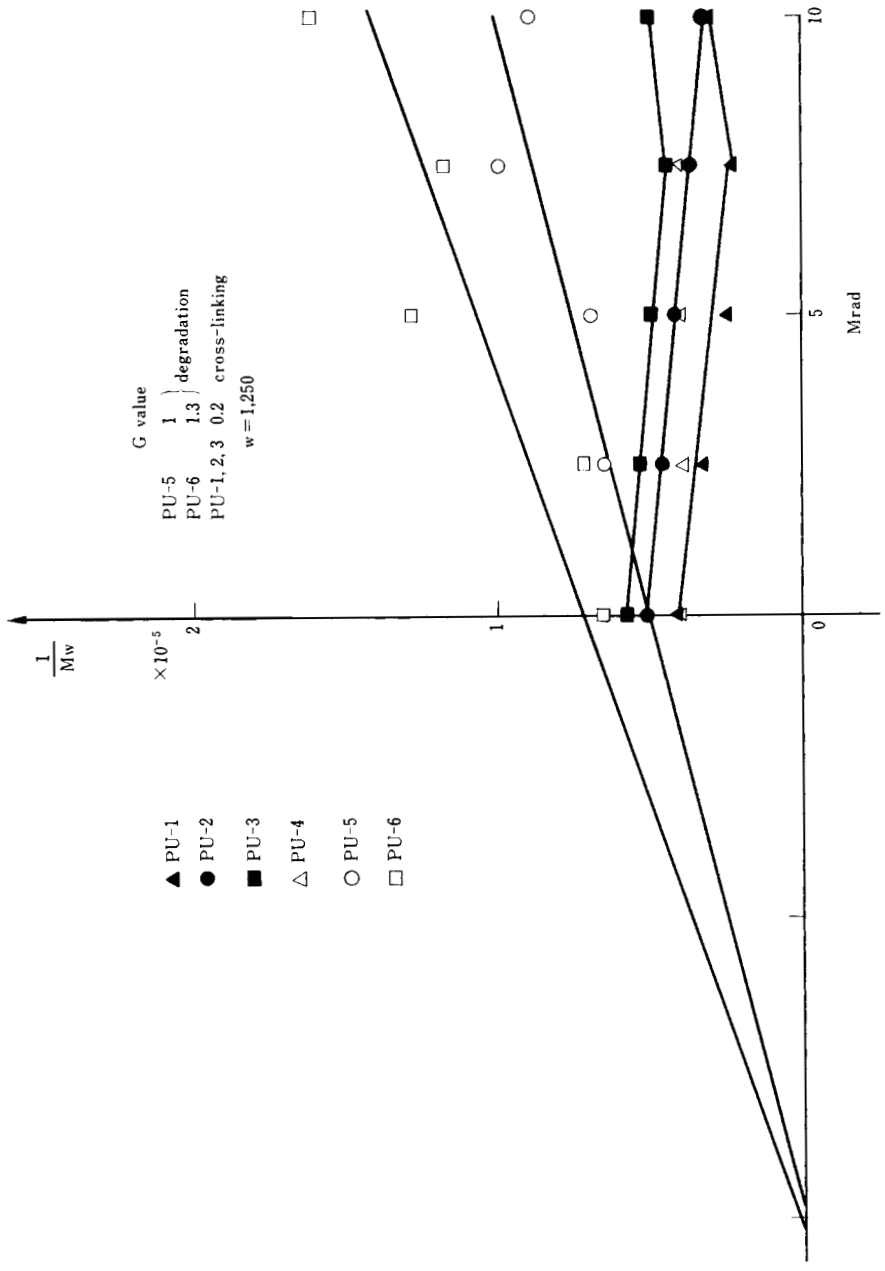

Fig. 2. Relationship between irradiation dose (Mrad) and $1/M_w$.

TABLE I
Molecular Weight (M_n, M_w) Change of Thermoplastic PU Sample by Gamma-Ray Irradiation[a]

Sample	Mrad	M_n	M_w	M_w/M_n
PU-1	0	38785	233447	6.02
	2.5	37785	299981	7.94
	5.0	33816	391755	11.58
	7.5	30010	423762	14.12
	10.0	34261	327554	9.56
PU-2	0	32773	191510	5.84
	2.5	30112	215012	7.14
	5.0	26996	239525	8.87
	7.5	25560	269538	10.55
	10.0	25903	340021	13.13
PU-3	0	24238	174586	7.20
	2.5	23461	185646	7.91
	5.0	21065	200147	9.50
	7.5	20043	222860	11.12
	10.0	19985	203454	10.18
PU-4	0	44983	254868	5.67
	2.5	40963	254348	6.21
	5.0	35202	254553	7.23
	7.5	31370	253198	8.07
	10.0	29451	318970	10.83
PU-5	0	26678	197545	7.40
	2.5	23674	150780	6.37
	5.0	20479	144073	7.04
	7.5	18119	101143	5.58
	10.0	17752	109313	6.16
PU-6	0	32304	152031	4.71
	2.5	27360	138655	5.07
	5.0	17659	76258	4.32
	7.5	17285	84248	4.87
	10.0	14398	61025	4.24

[a] Toso-GPC column was used for calculation of M_n and M_w.

Tensile Strength Testing

Sample PU strips were prepared by a Danbel cutter meeting JIS K-7113-2 specification. The test was carried out following JIS K 7113.[4]

Determination of Residual Radical Amount

Residual radicals were quantified by a chemiluminescence method. Irradiated and unirradiated PU samples of 3 × 3 cm were placed in a thermostated chamber maintained at 40°C. Light generated by radical recombination reactions was counted with a photon counter. This measurement was carried out 15 days after irradiation. The amount obtained using unirradiated PU was estimated as a blank value.

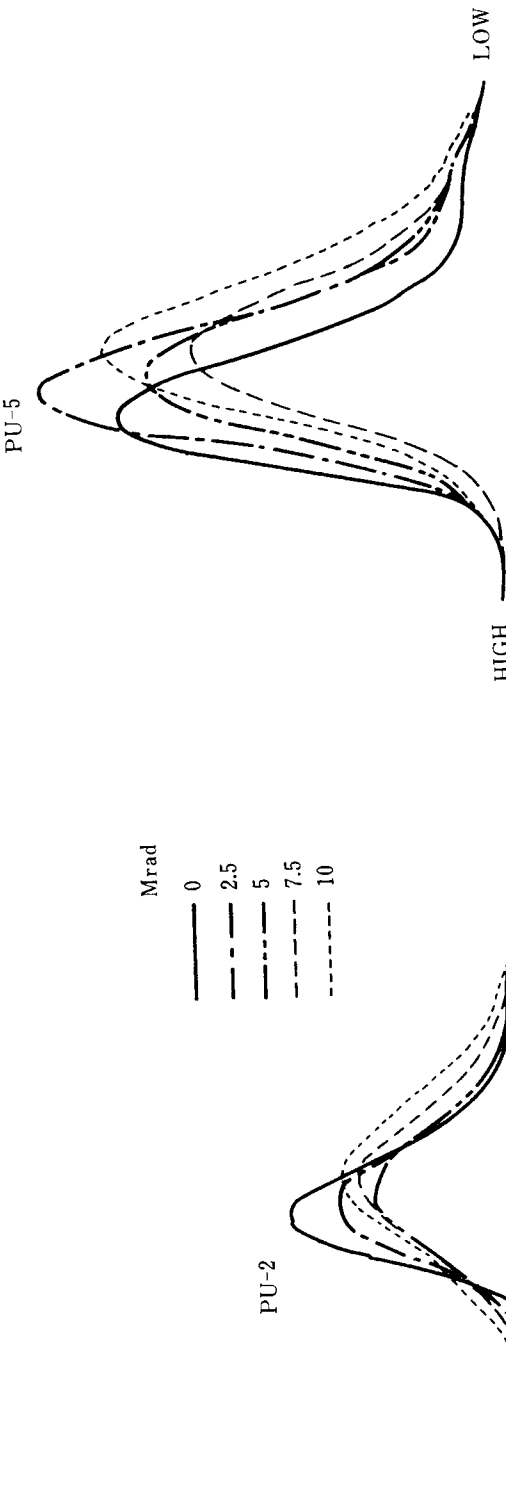

Fig. 3. GPC chromatogram of PU-2 (left) and PU-5 (right).

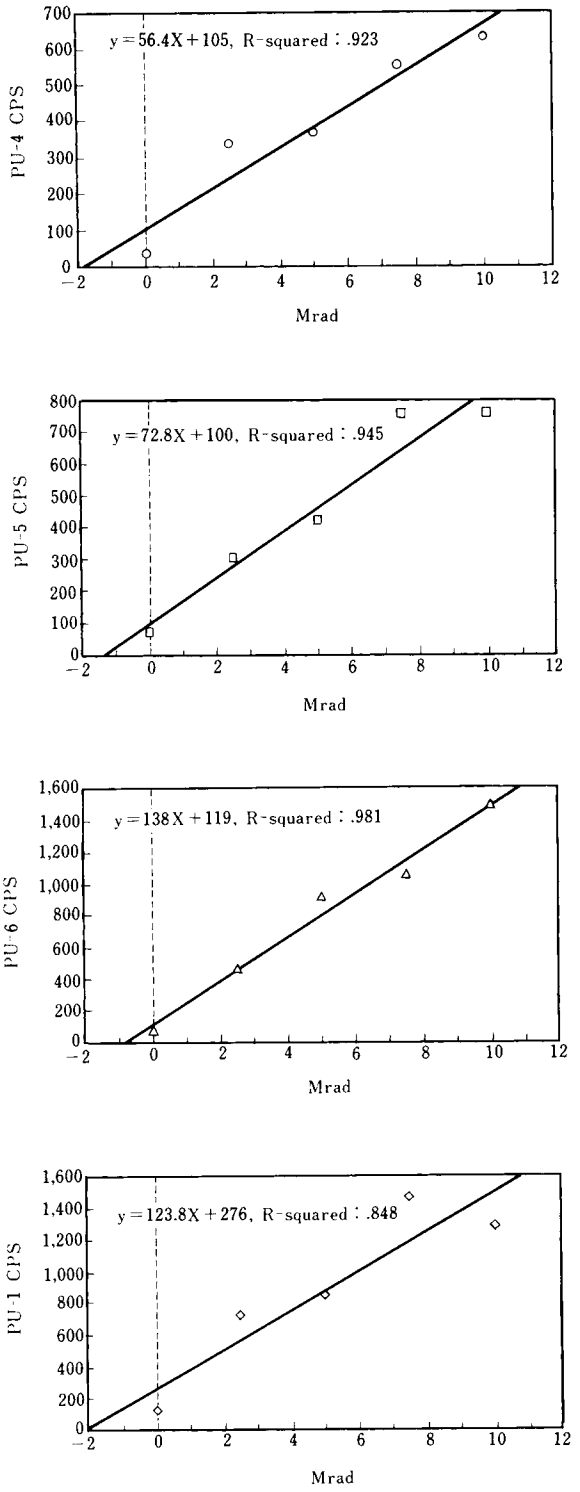

Fig. 4. Regression between irradiation dose (Mrad) and residual radical detected by chemiluminescence method (cps).

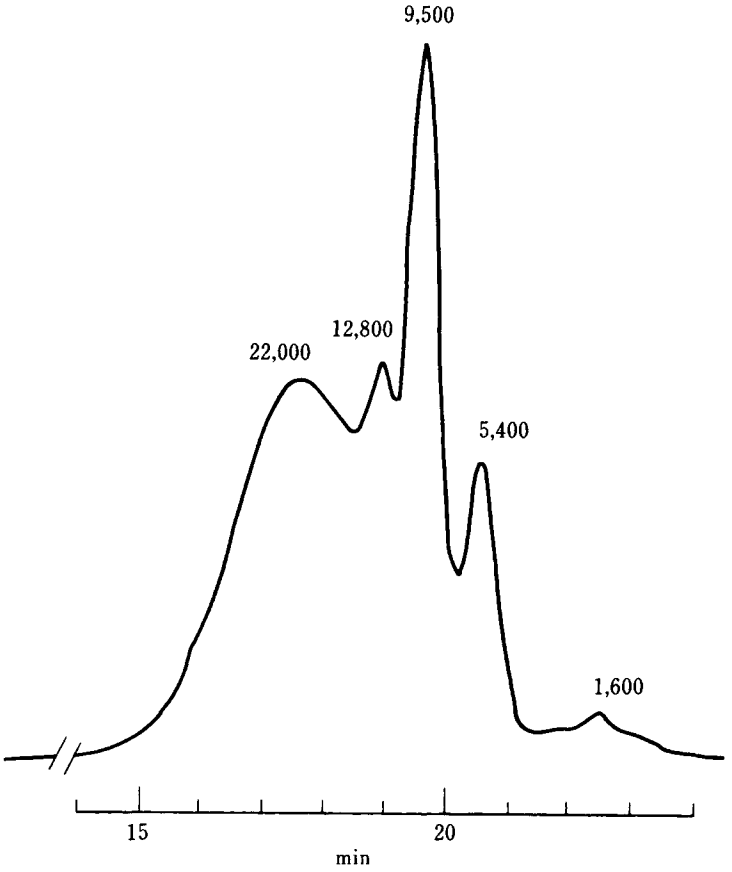

Fig. 5. GPC chromatogram of thermoplastic PU samples irradiated by gamma-rays. PU-4 irradiated at 5 Mrad gamma-ray was extracted with methanol. Detection was at 290 nm.

RESULTS AND DISCUSSION

Molecular Weight Change after Irradiation

Two weeks after being gamma-ray irradiated, PU samples were dissolved in DMF containing 10 mM LiBr (GPC eluent). The solutions were analyzed by GPC. G values (number of molecules increased or decreased when irradiated at 100 eV) were calculated with equations representing the relationship between doses of irradiation and $1/M_w$; their values are shown in Fig. 2.[5] For the calculation of G values, a monomer molecular weight of PU of 1250 was given.

In samples of PU-4 through PU-6, the M_w typically decreased with increasing irradiation dose as a result of degradation (Table I). In samples of PU-1 through PU-3, in contrast, M_w increased with increasing irradiation dose due presumably to increased crosslinking (Table I). G values for PU-1 through PU-3 and PU-4 through PU-6 were 0.2 (crosslinking) and 1.1 (degradation), respectively. These values agree well with those described in the literature.[5] In Figure 3, GPC chromatograms of samples exposed to different irradiation doses are superimposed. Figure 3 showed that irradiation simultaneously led to crosslinking

TABLE II
Relative Peak Height of M_{GPC} of Methanol Extract of Thermoplastic PU Sample[a]

Sample (Mrad)	Peak top molecular weight (M_{GPC})					
	22000	20000	12800	9500	5400	1600
PU-1 (0)		33.3	10.0	33.3	100.0	6.7
PU-1 (2.5)		46.9	9.4	31.3	100.0	9.4
PU-1 (5.0)		68.0	12.0	40.0	100.0	16.0
PU-1 (7.5)		64.0	12.0	36.0	100.0	16.0
PU-1 (10.0)		100.0	8.0	44.0	100.0	12.0
PU-2 (0)	17.4		6.6	32.8	100.0	4.6
PU-2 (2.5)	20.8		5.7	23.6	100.0	4.7
PU-2 (5.0)	41.2		7.9	29.4	100.0	4.4
PU-2 (7.5)	62.5		5.0	36.3	100.0	17.5
PU-2 (10.0)	112.6		11.5	43.7	100.0	4.6
PU-3 (0)		7.8	2.2	11.1	100.0	3.3
PU-3 (2.5)		9.6	1.1	10.6	100.0	2.1
PU-3 (5.0)		13.4	0.5	9.3	100.0	1.4
PU-3 (7.5)		20.5	1.2	8.3	100.0	3.1
PU-3 (10.0)		27.2	0.5	7.0	100.0	2.8
PU-4 (0)	31.4		57.1	200.0	100.0	22.9
PU-4 (2.5)	71.2		38.5	192.3	100.0	13.5
PU-4 (5.0)	140.9		27.3	193.2	100.0	6.8
PU-4 (7.5)	245.5		30.3	218.2	100.0	6.1
PU-4 (10.0)	278.9		36.8	221.1	100.0	7.9
PU-5 (0)		4.8	7.1	22.2	100.0	2.4
PU-5 (2.5)		14.7	5.3	20.0	100.0	2.7
PU-5 (5.0)		20.2	3.8	17.7	100.0	0.6
PU-5 (7.5)		41.4	6.0	13.8	100.0	1.7
PU-5 (10.0)		46.6	6.9	13.8	100.0	1.7
PU-6 (0)	72.1		54.4	205.9	100.0	20.6
PU-6 (2.5)	125.0		35.7	207.1	100.0	10.7
PU-6 (5.0)	324.1		41.4	248.3	100.0	12.1
PU-6 (7.5)	348.0		52.0	232.0	100.0	7.2
PU-6 (10.0)	465.9		63.6	281.8	100.0	13.6

[a] Shodex-GPC column was used for calculation of MGPC.

and degradation in PU-1 through PU-3. At higher doses, the starting time of GPC elution (elution of larger molecular weight components) decreased, while at the same time the completion time for GPC elution (elution of smaller molecular weight components) increased. In other words, the distribution of molecular weights increased with increasing irradiation dose. Furthermore, the retention time of the peak maximum increased. The peak top molecular weight (M_{GPC}) decreased with increasing irradiation doses.

In contrast, in the case of PU-4 through PU-6 as shown in Figure 3, the width of molecular weight distribution did not markedly change with an increase of irradiation. The retention time of the peak maximum increased with increasing irradiation dose, indicating degradation. There was no evidence indicating increase in molecular weight, which is expected to occur with increased

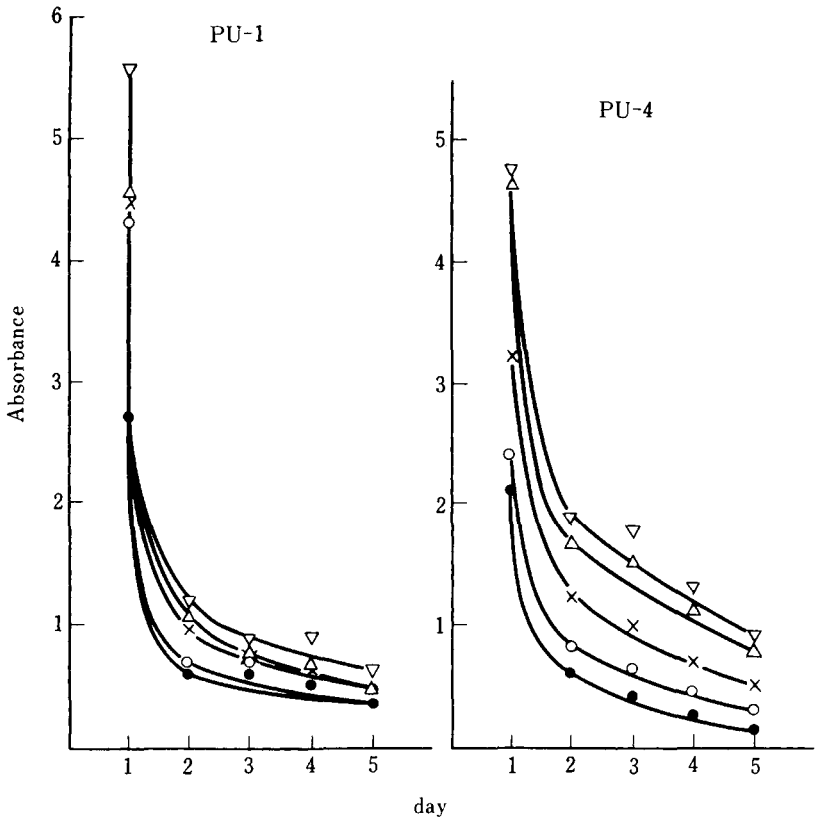

Fig. 6. Time course of absorbance detected at 245.5 nm for methanol extract of thermoplastic PU samples. Left and right are PU-1 and PU-4, respectively. ● 0; ○ 2.5; × 5.0; △ 7.5; ▽ 10.0 Mrad irradiation.

crosslinking. Therefore, irradiation only leads to the degradation of BU-chain-extended PU. It is interesting that PU samples synthesized with and without BU chain extending respond to irradiation in such a different manner.

The values for M_n and M_w as determined by GPC 6 months after irradiation were similar to those obtained 2 weeks after irradiation. There was no significant change of characteristics of PU during storage under air.

Determination of Residual Radical Amount

The quantity of residual radicals[6-8] increased linearly in proportion to the dose of irradiation (Fig. 4). The values for M_n and M_w as determined by GPC 6 months after irradiation were similar to those obtained immediately after irradiation, therefore residual radicals probably do not significantly influence the changes in characteristics of the PU samples with time. This was contrary to a study previously reported.[7]

Methanol Extracts of Irradiated Thermoplastic PUs

Methanol extracts of samples were analyzed by GPC using Shodex columns. The eluate was monitored by UV spectrophotometry at 290 nm (Fig. 5). Five

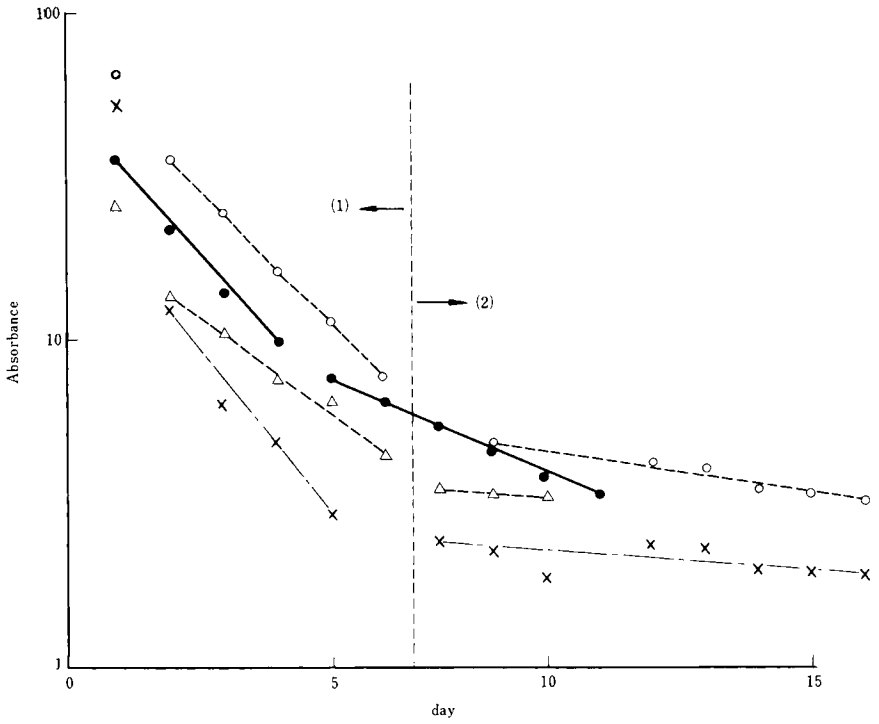

Fig. 7. Time course of absorbance detected at 245.5 nm for methanol extract of unirradiated thermoplastic PU samples. (1) and (2), respectively, designate the period from start to seventh day and from seventh to sixteenth day. ● — ● PU-1; △ - - - △ PU-4; × — - — × PU-6; ○ - - - ○ PU-8.

peaks appeared at molecular weights of 20,000–22,000, 12,800, 9500, 5400, and 1600 as M_{GPC}, corresponding to PU oligomers containing, per molecule, 13–14, 8, 6, and 3 urethane oligomers and monomer, respectively. Relative peak heights were calculated by taking the height of the peak of M_{GPC} 5400 as 100, and the resulting values (Table II) are a function of irradiation dose. As the irradiation dose increased, greater quantities of higher oligomers, i.e., those of M_{GPC} of 20,000–22,000 were formed. The oligomer of M_{GPC} 5400 was prominent in methanol extracts from irradiated samples of PU-1 through PU-3. In contrast, methanol extracts from PU-4 through PU-6 yielded the highest peak at M_{GPC}, 9500.

The time course of daily extraction of irradiated PU by methanol was followed by the characteristic absorption of PU at 245.5 nm and showed an exponential decline regardless of the irradiation doses (Fig. 6). Methanol extract of PU irradiated at higher dose indicated more absorbance. More absorbance was gained from a PU sample having lower molecular weight, e.g., in the order of absorbance of the methanol extract: PU-3 > PU-2 > PU-1 and PU-6 > PU-5 > PU-4 in the opposite order of the molecular weight of thermoplastic PU.

The time course of the extraction of unirradiated PU by methanol is plotted semilogarithmically in Figure 7. A 50-mL part of methanol was placed in a 9-cm Petri dish covering a 1-mm-thick film of PU. The methanol was replaced

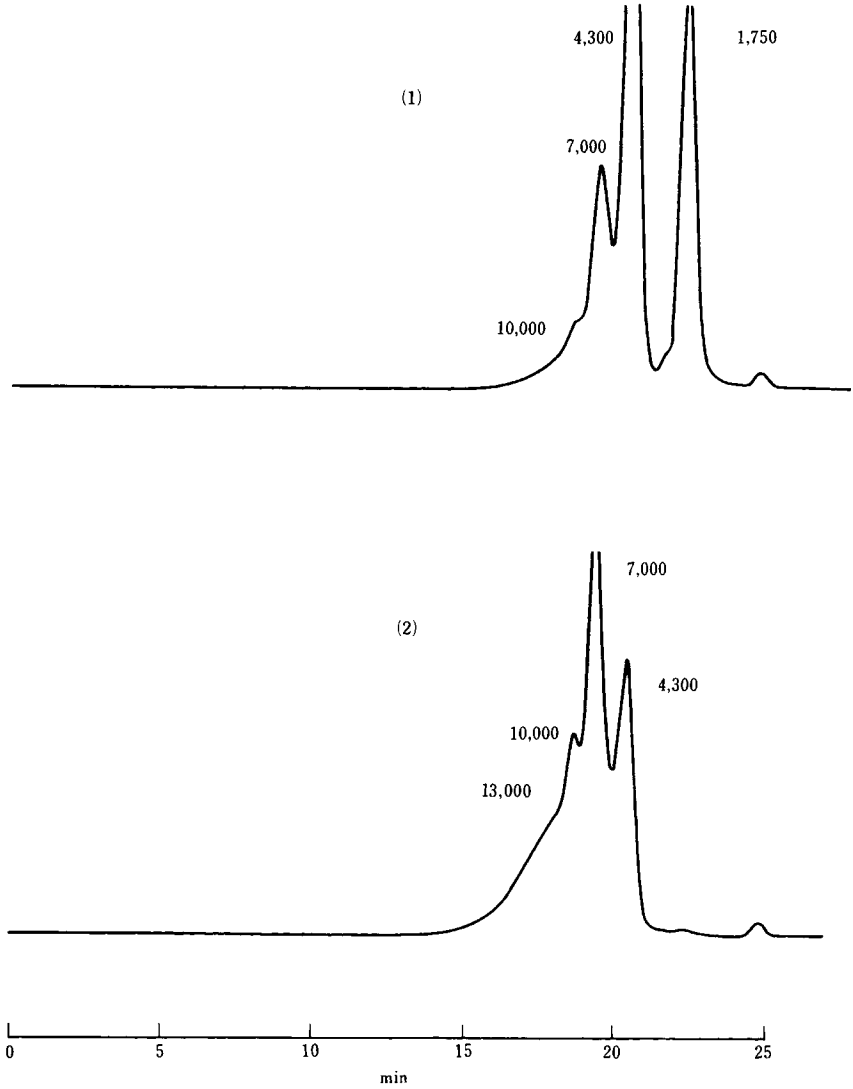

Fig. 8. GPC chromatogram of unirradiated thermoplastic PU sample. Methanol extract of sample was detected at 290 nm. (1) and (2) refer to Fig. 7. Upper and lower are (1) and (2), respectively.

every day, and the absorbance of methanol extract at 245.5 nm was determined (absorbance in sample 100 mg in 50 mL methanol). As shown in Figure 7, the exponential decrease was biphasic. Around day 7 of extraction, the slope of the elution line changed. Therefore, the methanol extracts from the start to the seventh day were combined and analyzed by GPC, separately from the extracts from the eighth day and thereafter. Extracts from the first week contained a monomer of molecular weight 1750, which was not detected in the other extract (Fig. 8). The ratio of the elution of smaller molecular weight components in the first week is greater than the components eluted from the second week. The first week extract containing the monomer was more cytotoxic than the

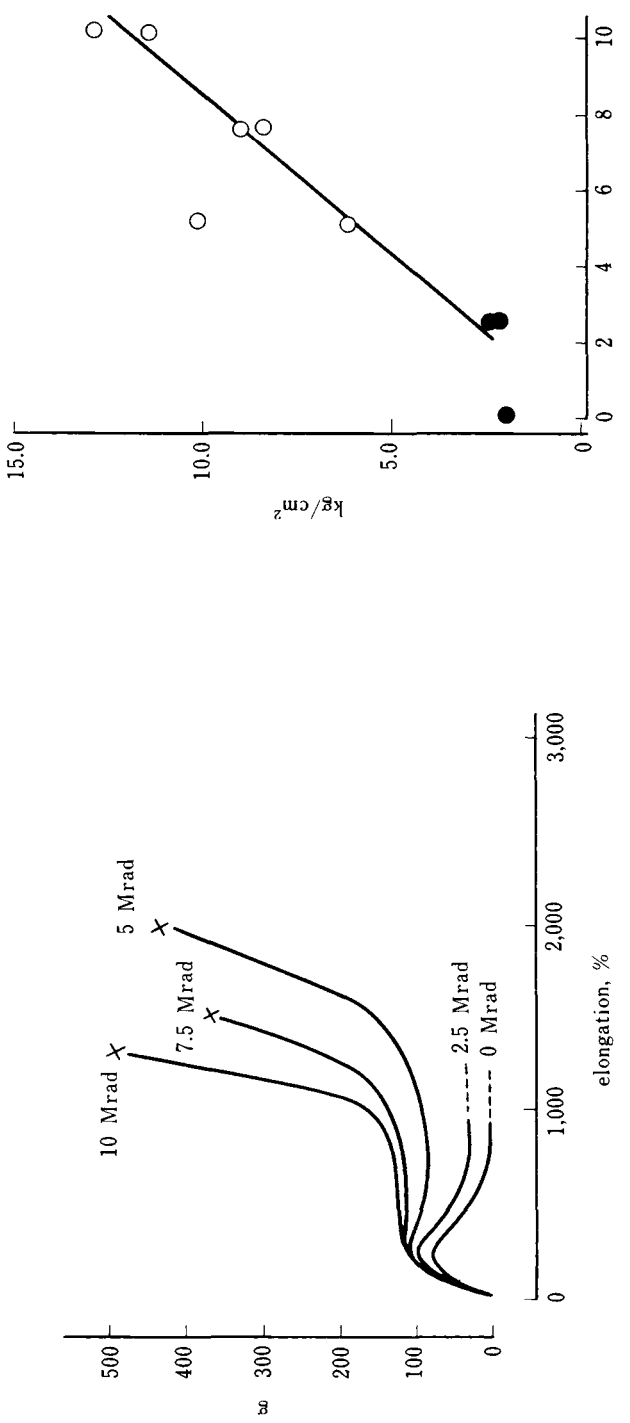

Fig. 9. Stress–strain relationship curve (left) and change of breaking and yield point stresses with irradiation dose (right). PU-1 at 0–10 Mrad irradiation for left: ○ breaking stress; ● yield point stress using PU-1.

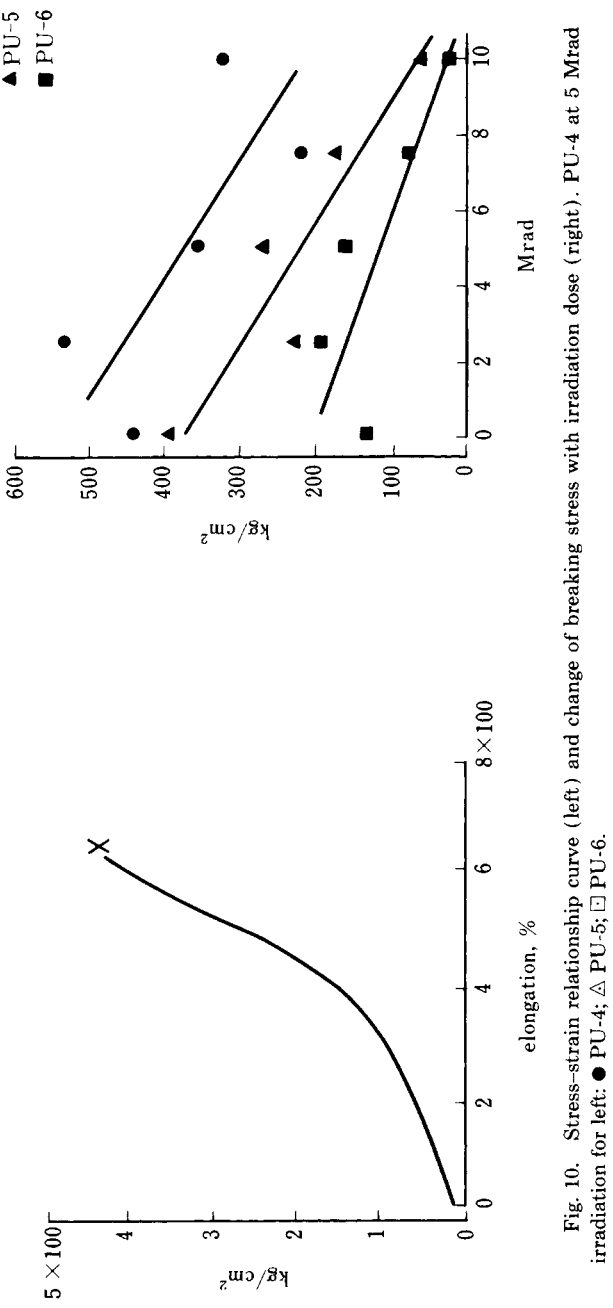

Fig. 10. Stress–strain relationship curve (left) and change of breaking stress with irradiation dose (right). PU-4 at 5 Mrad irradiation for left: ● PU-4; △ PU-5; □ PU-6.

extract from the second week as judged by its effect on fibroblasts of Chinese hamsters. Cytotoxicity of the former extract was about 6–10 times greater than that for the latter.[9] This result agrees well with the general view that the toxicity of lower PU oligomers are higher.

Tensile Strength Testing

The stress–strain (S–S) curves for unirradiated and irradiated linear PU sample, PU-1, showed a clear yield point and exhibited significant ductility (Fig. 9). In contrast, PU-4 through PU-6 did not show a clear yield point and was brittle rather than ductile (Fig. 10).

The S-S curve for PU-1 showed a significant change with the increasing irradiation dose (Fig. 9) due presumably to increased crosslinking and the degree of crystallinity in PU-1. The relationship between irradiation dose and the change of breaking stress for PU-1 is also shown in Figure 9; tensile strength increased with the increasing irradiation dose.

In contrast, breaking stress decreased with increasing irradiation dose with PU-4 through PU-6 (Fig. 10). This correlates with radiation-induced degradation and also suggests that the degree of crystallinity in PU-4 through PU-6 decreased with increasing irradiation dose.

The results of the tensile strength testing described here agree well with the results of M_w change as shown in Figure 2 and Table I.

We wish to thank Dr. H. Nakazawa for lending us his own constracted chemiluminescence photon counter.

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