Modification of Natural Rubber Tubes for Biomaterials. II. Radiation-Induced Grafting of *N,N*-Dimethylaminoethylacrylate (DMAEA) onto Natural Rubber (NR) Tubes

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Synopsis

Radiation-induced simultaneous grafting of *N,N*-dimethylaminoethylacrylate (DMAEA) onto NR tubes has been studied to improve blood compatibility of NR tubes. In the grafting of DMAEA onto NR tubes, effect of grafting parameters such as solvent, monomer concentration, temperature, dose, and dose rate on the grafting yield was investigated. As the results, it was found that the grafting proceeds effectively in the presence of carbontetrachloride (CCl_4) as a solvent. The initial rate of grafting was found to be proportional to 0.70 power of dose rate and to 0.95 power of monomer concentration. The activation energy for this grafting system was calculated to be 6.78 kcal/mol. The evaluation of blood compatibility of NR-*g*-DMAEA was carried out by *ex vivo* test. Blood compatibility of those samples was found to be dependent on only grafting yield. When the degree of grafting is higher than 30 wt %, blood compatibility of NR tube could be improved by DMAEA grafting. This is the same tendency which that of previous grafting system of NR-*g*-DMAA.

INTRODUCTION

In a previous paper,[1] we have reported the kinetics of radiation-induced grafting of *N,N*-dimethylacrylamide (DMAA) onto natural rubber (NR) tubes and also the blood compatibility of the grafted NR tubes.

The blood compatibility of NR-*g*-DMAA was found to be significantly improved when it is more than 30 wt % of grafting. However, such amount of degree of grafting is only obtained when a special technique, so-called, two-step grafting, is employed. As a consequence of this, the grafting process is not economic due to loss of time as well as that of monomer.

Another hydrophilic monomer which is easily grafted onto NR tubes has been investigated. *N,N*-dimethylaminoethylacrylate was found to be one of the promising candidates as the hydrophilic monomer for such modification of NR tubes.

In the present article, the kinetics of radiation-induced grafting of *N,N*-dimethylaminoethylacrylamide onto NR tubes and their blood compatibility are presented.

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EXPERIMENTAL

Materials

Natural rubber (NR) tubes of 1 mm thick with inside diameter of 3.5 mm and outside diameter of 5.5 mm were purchased from Komine Rubber Mfg. Co. Samples were made by cutting the longer NR tubes into pieces of 35 mm length. The samples were washed thoroughly with tap water and subsequently washed with acetone and distilled water in an ultrasonic cleaner bath for 15 min. The NR tube samples were dried in vacuo and then weighed before use.

N,N-dimethylaminoethylacrylate (DMAEA) monomer, with chemical formula of $CH_2{=}CH_2{-}COOC_2H_4{-}N(CH_3)_2$, was supplied by Kohjin Co., and used as received. All other reagent grade chemicals were used directly without further purification.

Grafting Procedure

The simultaneous irradiation or direct method was used as the grafting technique. A piece of weighed NR tube sample of (35 mm length) was immersed into excess monomer solution in a specially designed glass ampoule.

The glass ampoule was degassed by five cycles of freezing and thawing technique, and closed when a vacuum degree of 10^{-4} torr was achieved. It was then warmed up to room temperature and irradiated by gamma rays from a Cobalt-60 source at a given dose rate. Dosimetry was performed by ferrosulfate (Fricke) dosimeter.

Following irradiation, the grafted NR tube was removed from the glass ampoule, washed thoroughly with tap water, and soaked overnight in distilled water. It was then boiled in distilled water for 5 h to extract the residual monomer and the homopolymer involved in the tubes. The tube was dried under vacuum at room temperature for 24 h, and weighed. The degree of grafting was determined by the percent increase in weight using the following formulae:

$$\text{degree of grafting (wt \%)} = \frac{(W_g - W_0)}{W_0} \times 100$$

where W_0 and W_g represent the weights of the initial and grafted NR tubes, respectively.

Infrared Measurements

Infrared spectrum was recorded on a JASCO IRA-2 spectrophotometer by attenuated total reflection (ATR-IR) technique. The test samples were mounted in an ATR-6 stainless steel holder with thin rubber pads (18 × 45 mm) placed between the holder and test sample to improve contact between the sample and the KRS-5 reflection element.

The ATR-IR spectras was taken at a 45° angle to the incident light.

Swelling Measurements

The clean and dried NR tube sample with known weight was immersed in a solvent (or in distilled water in the case of water uptake measurement) at 25°C until equilibrium was reached (24 h in most cases). The test sample was removed and the excess solvent or water deposited on the surface was quickly taken up with blotting paper and then weighed.

The degree of swelling was calculated by the following equation:

$$\text{degree of swelling (wt \%)} = \frac{(W_s - W_0)}{W_0} \times 100$$

where W_0 and W_s represent the weights of the dry and wet sample tests, respectively.

Blood Compatibility Assessments

The technique of blood compatibility assessment was the same as that described in a previous report.[1] Briefly, the NR tube samples were connected to each other by polytetrafluoroethylene (PTFE) tubes and by using a 19G Teflon sheated needle; blood from a femoral artery of a mongrel dog was introduced into the test samples. After the test samples were filled with the fresh blood, the PTFE tube connectors were clipped and then all the test samples were immersed in a water bath kept at 37°C for 15 min. The test samples were then removed from the water bath, put into 100 mL of distilled water in a beaker, and stirred gently. They were then removed from the beaker and dried.

The blood compatibility was then determined on the basis of visual observation of adhered blood clotting on the surface of the test samples. The decreased amount of blood clotting on the surfaces means the better the blood compatibility.

RESULTS AND DISCUSSION

Kinetics Study

The kinetics of radiation-induced grafting of DMAEA onto NR tubes have been studied, particularly to obtain an information on which grafting conditions were needed to produce a NR grafts DMAEA (NR-*g*-DMAEA). The effect of grafting conditions such as solvent, monomer concentration, irradiation temperature, irradiation dose, and dose rate on the grafting process was investigated.

Effect of Solvent

It is well known that solvent plays an important role to enhance graftability of a monomer onto a trunk polymer, particularly when the simultaneous irradiation grafting technique is employed.[2] In the present study, carbon tetrachloride (CCl_4) was used as a diluent (solvent) for DMAEA. Several trials to use other solvents such as ethanol, methanol, ethylacetate, and

TABLE I
Swelling Percentage of NR Tubes in Different Solvents and the Solubility Parameter Values of the Solvents

No.	Solvent	Swelling Percentage (wt %)	Solubility parameter $(cal/cm^3)^{1/2}$
1	Methanol	0.69	14.5
2	Ethanol	0.46	12.7
3	Acetone	18.88	9.9
4	Ethylacetate	84.02	9.1
5	Chloroform	702.15	9.3
6	Carbontetrachloride	793.05	8.6

acetone in this grafting system proved fruitless, since the grafting yield was very low compared to that obtained by using CCl_4.

A better swelling of NR tubes in CCl_4 and a miscibility property of DMAEA with CCl_4 may be one of the reasons that CCl_4 become a suitable solvent for grafting of DMAEA onto NR tubes. Table I shows the swelling behavior of NR tubes in different solvents and the solubility parameter value of each solvent was also listed. The solubility parameter of DMAEA was calculated by the substitution of the group molar attraction constant values of Hoy's[3] into the following equation:

$$\partial = d\frac{\sum G}{M}$$

where ∂ is the solubility parameter, ΣG is the sum for all the atoms and groupings in the molecule, d is the density, and M is the molecular weight.

The solubility parameter of DMAEA was found to be 7.79 $(cal/cm^3)^{1/2}$, which is approximately near to the solubility parameter values of CCl_4 (8.60) and natural rubber (8.35). Thus, it means that DMAEA is more miscible in CCl_4 and at the same time CCl_4 may be capable of bringing the monomer molecules as near as possible to the active centers (radicals) formed at the NR tube matrix. As a result of this, the higher degree of grafting is produced.

Effect of Monomer Concentration

Effect of monomer concentration on the grafting yield is shown in Figure 1. It can be seen that the degree of grafting increases with monomer concentration up to about 60 vol%, whereas, beyond this concentration, the degree of grafting decreases. The increase of grafting with an increase of monomer concentration may be attributed to an increase of monomer concentration at the reaction sites. However, at higher monomer concentration, reactions that are competitive to grafting may take place in the monomer solution, i.e., homopolymerization is more favored than grafting at higher monomer concentration.

Figure 2 shows logarithmic relationship between the rate of grafting and DMAEA concentration. From the slope of the curve, dependence of the

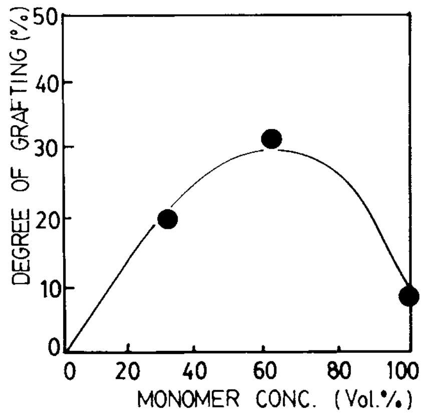

Fig. 1. Degree of grafting vs. DMAEA concentrations in carbontetrachloride. Dose rate 1.50 kGy/h, total dose 2.50 kGy, and irradiation temperature 27°C.

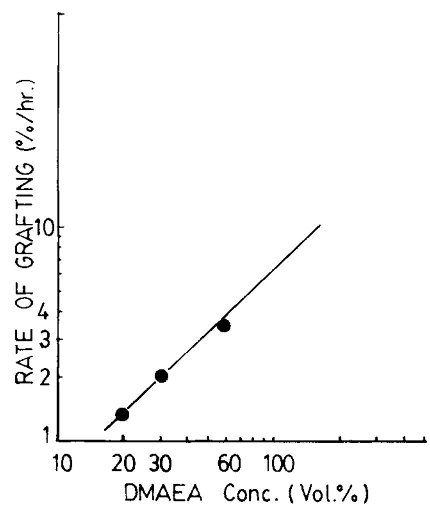

Fig. 2. Logarithmic plots of grafting rate vs. DMAEA concentration. Dose rate 1.50 kGy/h, irradiation temperature 27°C.

grafting rate on DMAEA concentration can be calculated. The rate of grafting was found to be proportional to 0.95 power of the DMAEA concentration.

This value suggests that the degree of grafting is much controlled by the amount of radicals formed.

Effect of Temperature

Figure 3 shows the relationship between the degree of grafting and irradiation time at various irradiation temperatures. It can be seen that the rate of grafting is higher at a higher temperature.

Generally, the increase in temperature facilitates the monomer diffusibility as well as the mobility of chain segment. Therefore, increasing monomer diffusibility causes the increase in initial grafting rate. However, the increase

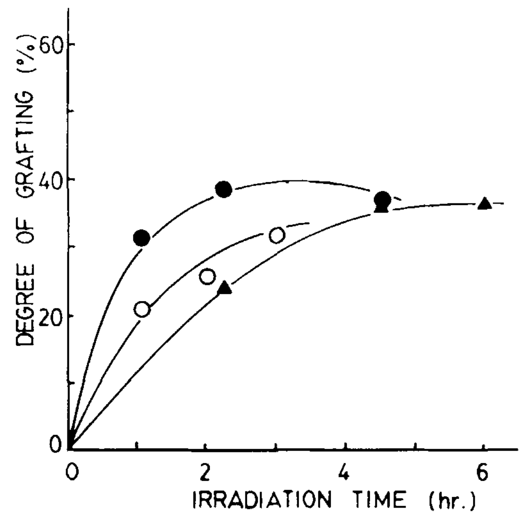

Fig. 3. Effect of temperature on radiation grafting of DMAEA onto NR tubes. Dose rate 1.50 kGy/h and DMAEA concentration in carbontetrachloride 60 vol %. (●) 50°C; (○) 27°C; (▲) 0°C.

in chain segment mobility favors the molecular termination. Therefore, the higher the temperature, the faster the grafting levels off.

Arrhenius plots for this grafting system are shown in Figure 4. The activation energy for the grafting process was calculated to be 6.78 kcal/mol. This value is a typical one for grafting initiated by ionizing radiation. Moreover, the value is lower than the activation energy of NR-*g*-DMAA[1]. It means that the grafting of DMAEA onto NR tubes is relatively less affected by the temperature changes.

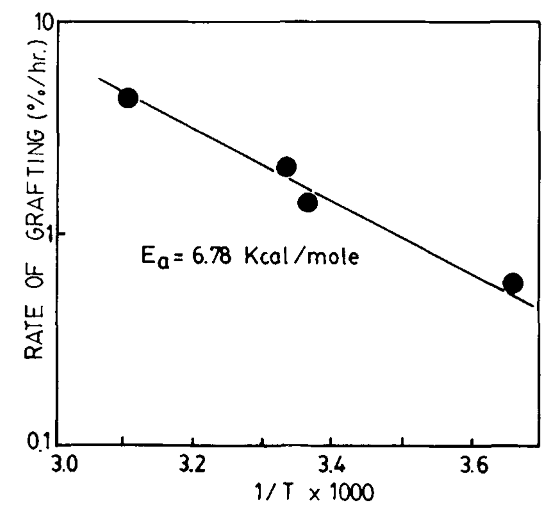

Fig. 4. Arrhenius plots of grafting rate. Grafting conditions are the same as in Figure 3.

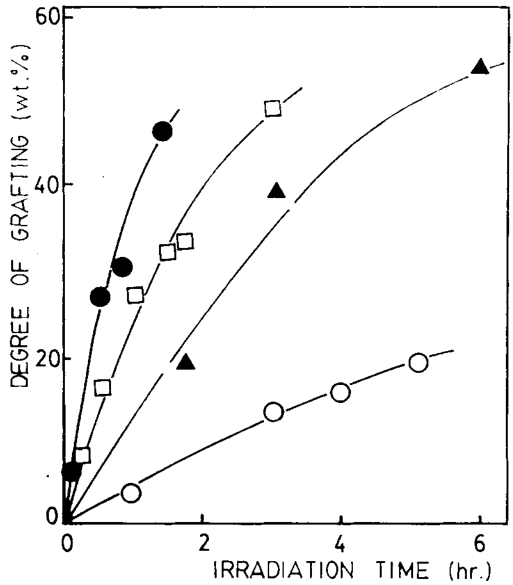

Fig. 5. Degree of grafting-irradiation time curves at various dose rates (kGy/h). Monomer concentration 60 vol % in CCl_4 and irradiation temperature 27°C: (○) 0.1 kGy/h; (▲) 0.33 kGy/h; (□) 1.5 kGy/h; (●) 3.26 kGy/h.

Effect of Dose and Dose Rate

Effect of dose and dose rate on the grafting yield is depicted in Figure 5. As can be seen, the degree of grafting is increased with an increase in irradiation time (dose) at a constant dose rate. Figure 5 also shows that the initial rate of grafting is increased with dose rate. These demonstrate that a high density radical formation is formed at a higher dose rate. Those radicals formed lead initiate grafting reactions and result something higher degree of grafting.

Dependency of the initial rate of grafting on dose rate is shown in Figure 6. From the slope of the curve, the dependency of the initial rate of grafting on dose rate can be calculated and it was found to be proportional to a 0.70 power of dose rate. The value indicates that the grafting was terminated by both unimolecule and biomolecule reactions.

From all the above results, it can be concluded that the grafting of DMAEA onto NR tubes should be proceeded by a free radical mechanism.

Considering the conventional steady state assumption[4] for radical, the rate of grafting, R_p, can be represented by the following equation:

$$R_p = k_p[M]^{0.95}(r_i/2k_t)^{0.7}$$

where $[M]$ is monomer concentration, r_i is the rate of initiation of polymer radicals, and k_p and k_t are propagation and termination rate constants, respectively.

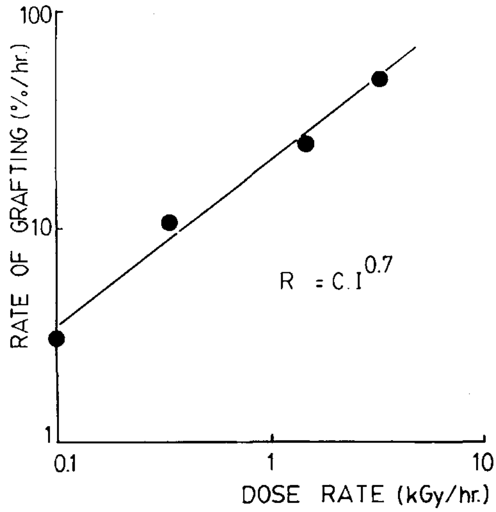

Fig. 6. Logarithmic plots of grafting rate vs. dose rate. Grafting conditions are the same as in Figure 5.

Infrared Measurements

Besides gravimetrically, the existence of DMAEA grafting onto NR tubes was confirmed by infrared spectrophotometrically. Figure 7 shows the spectra of grafted NR tube (NR-*g*-DMAEA) and original (ungrafted) NR tube. Comparison between the two spectra shows that a new absorption peak at 1720 cm,$^{-1}$ which corresponds to —C=C stretching vibrations in DMAEA

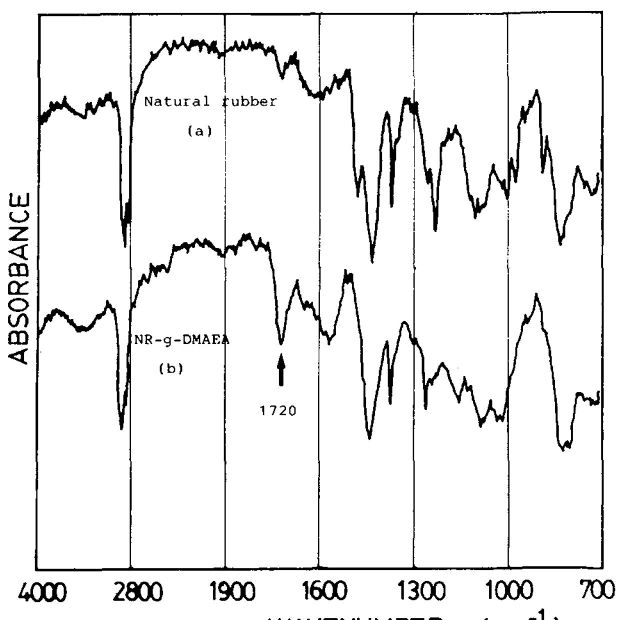

Fig. 7. Infrared spectra of (a) natural rubber and (b) natural rubber-DMAEA graft copolymer.

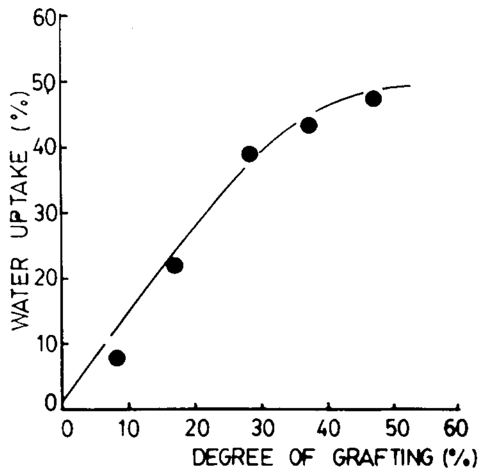

Fig. 8. Water uptake percent as a function of the degree of grafting at room temperature (25°C).

appeared in a grafted sample. Thus, this peak confirms that grafted chains exist in the NR tube matrix.

Swelling Behavior

The hydrophilicity of grafted NR tubes was characterized by the measurement of degree of swelling in water (water uptake measurements). Figure 8 shows the percent of water uptake as a function of degree of grafting of NR-*g*-DMAEA tubes. The water uptake percent increases linearly with degree of grafting and levels off at a certain degree of grafting. This suggests that the degree of swelling of NR-*g*-DMAEA depends mainly on the degree of grafting, i.e., on the amount of hydrophilic group in the NR tubes. The higher the degree of grafting, the higher the degree of swelling in water, but it will be saturated at a certain level.

Blood Compatibility Assessments

In the present study, the blood compatibility of grafted NR tubes having various degree of grafting were tested. As described in previous report, the testing method is in principal the same as that proposed by Ikada et. al.[5] with some modification in the way of observation. In this testing method, the blood compatibility is judged by the result of visual observation on the blood clot at the surface of the tested sample.

For convenience, the result of the blood compatibility test is grouped into three catagories, namely "poor," "fair," and "good." "Poor" is defined for the test sample which is a lot of blood clot occurred during the *ex vivo* test. "Fair" is given for the test sample where only a few clots are observed, and "good" is given for the test sample which is very clean or without any clot observed during the *ex vivo* test.

Table II shows the results of the *ex vivo* test for NR-*g*-DMAEA tubes. As can be seen clearly, all samples which contain less than 19.0 wt % degree of

TABLE II
Results of *Ex Vivo* Test of NR-*g*-DMAEA

Sample	Grafting conditions[a]			Grafting yield (wt %)	Visual appearance	Remarks
	DMEA concn in CCl_4 (vol %)	Dose rate (kGy/h)	Dose (kGy)			
GR 10-6	60	0.10	0.10	2.56	Clot	Poor
GR 10-1	60	3.30	0.55	7.01	Clot	Poor
GR 7-1	60	1.50	0.25	8.09	Clot	Poor
GR 10-7	60	0.10	0.30	13.31	Clot	Poor
GR 10-8	60	0.10	0.43	14.71	Clot	Poor
GR 7-11	30	0.33	1.48	17.92	Clot	Poor
GR 11-10	20	1.50	2.25	19.27	Few clots	Fair
GR 11-11	20	1.50	4.50	23.13	Few clots	Fair
GR 11-12	20	1.50	9.00	24.60	Few clots	Fair
GR 11-1	30	0.33	2.97	26.85	Few clots	Fair
GR 10-3	60	3.30	2.75	30.17	No clot	Good
GR 7-7	30	1.50	6.00	33.30	No clot	Good
GR 11-5	30	3.30	16.50	35.78	No clot	Good
GR 10-4	60	3.30	4.40	46.78	No clot	Good
GR 7-4	60	1.50	4.50	49.41	No clot	Good
GR 11-8	60	0.33	2.97	52.95	No clot	Good
GR 11-9	60	0.33	4.62	64.41	No clot	Good
NR tube original (control)					Clot	Poor

[a] Irradiation temperature = 27°C.

grafting including the virgin NR tubes (control) are poor in blood compatibility. The samples which contain degree of grafting from 19.0 to 27.0 wt % exhibit fair blood compatibility because only a few clots remain on the test samples. The samples which contain more than 30 wt %, on the other hand, exhibit good blood compatibility because no clot was observed on the test samples.

The grafting conditions are also described in the Table II, but, as can be evaluated, there is no significant effect of grafting conditions on the blood compatibility.

According to the results of the *ex vivo* test shown in Table II, the blood compatibility is predominantly controlled by the degree of grafting. The blood compatibility seems to be gradually improved by the increases of the degree of grafting. As a result, it was found that the degree of grafting of 30 wt % may be a boundary for improvement of blood compatibility of the NR tube.

Specifically, the blood compatibility of NR-*g*-DMAEA will be "good" when it contains at least 30 wt % or more degree of grafting. This same boundary was also shown by other grafting systems such as NR-*g*-DMAA[1] and SiR-*g*-NVP.[6]

At present, it is difficult to explain the reason for the existence of the boundary. But it may be speculated that, at the boundary, the balance between hydrophobic and hydrophilic groups may be achieved leading to creates a smooth interaction between blood and polymer surface. The importance of the hydrophobic–hydrophilic balance of polymeric biomaterial in exhibiting good blood compatibility has been postulated.[7]

In conclusion, the blood compatibility of NR tubes can be improved significantly by grafting DMAEA and at least a 30 wt % degree of grafting is needed to exhibit good blood compatibility. In addition, the one-step simultaneous irradiation grafting method is enough to obtain such an amount of degree of grafting. This is an advantage of the NR-*g*-DMAEA grafting system compared with the previous grafting system of NR-*g*-DMAA, which needs two-step simultaneous grafting to obtain grafting yield such as 30 wt %.[1]

References

1. Mirzan T. Razzak, Kazushige Otsuhata, Yoneho Tabata, F. Ohashi, A. Takeuchi, *J. Appl. Polym. Sci.*, to appear.

2. A. Chapiro, *Radiation Chemistry of Polymeric Systems*, *XV*, Wiley-Interscience, New York, 1962.

3. Hoy, in *Polymer Handbook*, J. Brandrup and E. H. Immergut, Eds., 2nd ed., Wiley, New York, 1975, p. IV-337.

4. H. A. J. Battaerd and G. W. Treage, *Graft Copolymers*, Wiley-Interscience, *New York*, 1967.

5. Y. Ikada, M. Suzuki, M. Taniguchi, H. Iwata, W. Taki, H. Miyake, Y. Yonekawa, and H. Honda, *Radiat. Phys. Chem.*, **18**, 1207 (1981).

6. A. Chapiro, *Eur. Polym. J.*, **19**, (10/11), 859–861 (1983).

7. A. S. Hoffman, Daniel Cohn, Stephen R. Hanson, Lawrence A. Hober, Thomas A. Hobert, Budhy D. Ratner, and Lamp D. Reynolds, *Radiat. Phys. Chem.*, **22** (1/2), 267 (1983).

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