

Photocrosslinking of Azidated Poly(vinyl chloride) Coated onto Plasticized PVC Surface: Route to Containing Plasticizer Migration

A. JAYAKRISHNAN,* M. C. SUNNY, and MINI N. RAJAN

Polymer Chemistry Division, Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Satelmond Palace Campus, Trivandrum 695 012, India

SYNOPSIS

The migration of phthalate esters which are commonly employed for plasticizing poly(vinyl chloride) (PVC) is a significant problem in PVC-based medical devices as well as in packaging used for food stuffs and pharmaceuticals. Medical-grade PVC resin was treated with sodium azide in dimethylformamide (DMF) to prepare the azide polymer. The polymeric azide was coated onto the surface of plasticized PVC sheets by dipping in a solution of the polymer in tetrahydrofuran (THF). Crosslinking of the azide polymer was accomplished by irradiating the surface using a 125 W UV lamp for various lengths of time. Migration of the plasticizer di-2-(ethylhexyl phthalate) (DEHP) from coated and uncoated samples was examined in *n*-hexane at 30°C. It was found that 50–80% reduction in migration of DEHP could be effected from plasticized PVC in comparison with the controls in 72 h by this technique depending on the concentration of the coating solution, coating thickness, azide concentration, and irradiation dose. © 1995 John Wiley & Sons, Inc.

INTRODUCTION

Plasticized poly(vinyl chloride) (PVC) finds a great number of applications in the medical field. It is the most widely used polymer for the manufacture of blood bags, transfusion tubings, urine bags, chest drainage systems, crystalloid sets, etc. Plasticized PVC is also widely employed for packaging food stuffs and pharmaceuticals. Being a rigid plastic, PVC is usually plasticized with a phthalate ester such as di-2-(ethylhexyl phthalate) (DEHP) to make it flexible. In general, plasticized PVC used in medical applications contains up to 40% by weight of this plasticizer.¹ The migration of DEHP from PVC-based devices into surrounding media such as blood, serum, and plasma is reported to result in toxic effects.^{2–4} In the absence of a cheap and viable alternative to DEHP, it continues to be used as a plasticizer in the manufacture of many PVC-based medical devices.

Several different approaches have been made to retard or prevent the migration of DEHP. These include, e.g., coating the PVC surface with polyurethane, polyacrylates, polyesters, or polyamides, crosslinking the PVC during processing using peroxides, irradiating the polymer in the presence of multifunctional monomers, and modification of the surface using glow discharge.⁵ We recently reported that grafting hydrophilic monomers such as 2-hydroxyethyl methacrylate and *N*-vinylpyrrolidone onto the surface of plasticized PVC using gamma radiation in aqueous media can reduce the migration of the plasticizer into organic extractants such as hexane.^{6–8} The method was found well suited for the modification of the inner surface of PVC tubings used in applications such as hemodialysis as it involved only filling the lumen of the tubes with the monomer solution, irradiating, and washing the residual monomer/polymer off using a continuous supply of water. Grafting PVC sheets on both sides led to stiffening of the sheets, and modification had to be restricted to only one surface to have acceptable physical and mechanical properties.

In the present work, a polymeric azide was pre-

* To whom correspondence should be addressed.

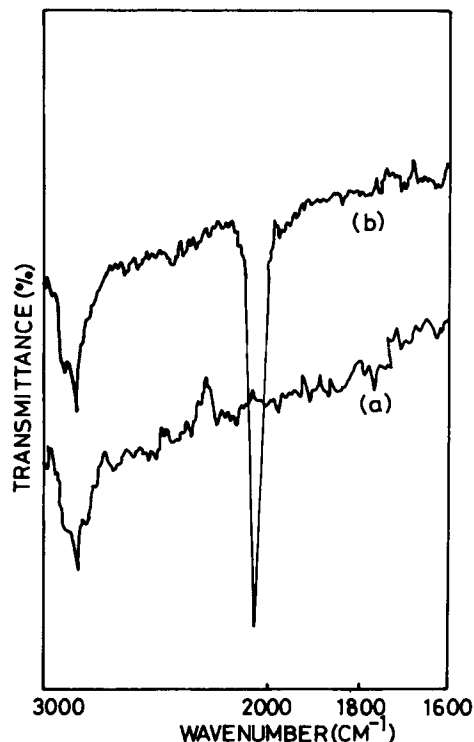


Figure 1 Infrared spectrum of (a) PVC resin and (b) the azide polymer, the latter showing the characteristic absorption due to the azide group at 2100 cm^{-1} .

pared from the PVC resin itself and was coated onto the surface of the plasticized PVC sheets from a solution of the azide polymer in tetrahydrofuran (THF). Photocrosslinking of the surface was accomplished by UV irradiation to generate a surface net to contain the migration of the plasticizer. Such modified PVC showed considerable reduction in the migration of the plasticizer into potential organic extractants such as hexane as opposed to controls.

EXPERIMENTAL

Materials

Medical-grade PVC resin having a k value of 70 was from Sriram Vinyl and Chemicals, Kota, India. Plasticized PVC sheets of medical grade having a thickness of 0.4 mm was a generous gift from Technoport Co., Japan. Sodium azide was from Sigma Chemical Co., USA, and solvents such as dimethylformamide (DMF), THF, and *n*-hexane were of analytical or equivalent grade from E. Merck India Ltd., Bombay, India. DMF and THF were used after distillation in the standard fashion.

Methods

Preparation of the Azide Polymer from PVC Resin

The azide polymer was prepared according to the method of Takeishi and Okawara.⁹ Briefly, to a solution of PVC resin (1 g, 16.0 mmol) in 50 mL DMF was added 1 g (15.5 mmol) sodium azide in a 100 mL round-bottomed flask fitted with a stainless-steel paddle stirrer. The suspension was stirred at 60°C for different period of times (1, 2, 3, 4, and 5 h) and the partially suspended material was poured into methanol to give a precipitation which after filtration was purified several times by dissolving in THF and reprecipitating in methanol. The IR spectrum of the polymer (films casted from THF solution) recorded in a Perkin-Elmer spectrophotometer (Model 597) showed a characteristic absorption band due to the azide group at 2100 cm^{-1} (Fig. 1). Conversion of chlorine into azide was quantitatively determined using IR spectrophotometry.

Coating of Polymeric Azide onto PVC

Different concentrations of polymeric azide were prepared in THF. PVC sheets ($20 \times 5\text{ mm}$) were

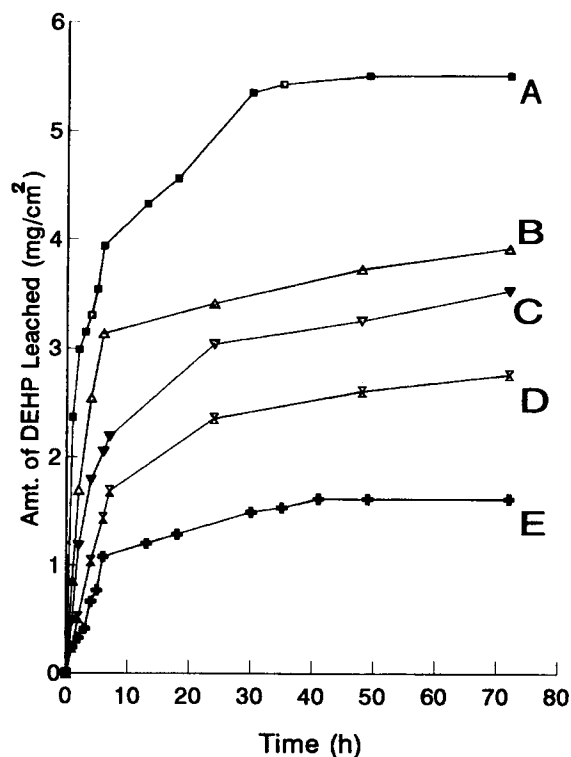


Figure 2 Migration of DEHP from PVC sheets coated twice with a 4% solution of azidated PVC having different azide contents and irradiated for 1 h into hexane at 30°C . (A) Unmodified, (B) coated with azidated PVC having 4, (C) 14, (D) 20, and (E) 27 mol % azidation.

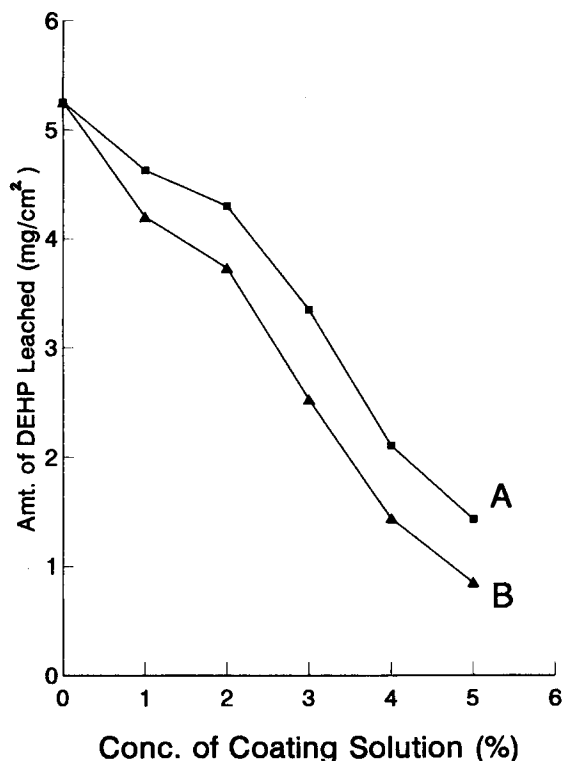


Figure 3 Plot showing the effect of concentration of the coating solution on the migration of DEHP from PVC sheets into hexane in 72 h. Specimens coated with azide polymer were irradiated for 1 h. (A) Sheets coated once; (B) sheets coated twice.

coated by dipping in the solution for about 30 s and drying them in an air oven at 60°C for 4 h. In the case of specimens coated twice, the second coating was applied after the first coating was allowed to dry in air for a few minutes.

Ultraviolet Irradiations

Samples were irradiated with UV light using a Philips HPL-N 125 W UV lamp placed at a distance of 15 cm from the specimen. After irradiation, samples were stored in the desiccator for migration studies.

Scanning Electron Microscopy

Scanning electron micrographs (SEM) of the bare PVC sheet and sheets coated with azide polymer were taken using a Hitachi (Model S 2400) instrument after vacuum coating with gold.

Migration Studies

Migration of the plasticizer from coated and uncoated sheets were carried out in *n*-hexane at 30 ± 1°C. Samples were weighed and kept in 50 mL of

hexane in stoppered Erlenmeyer flasks. The flasks were manually shaken occasionally. Aliquots of 1 mL were withdrawn at different intervals of time over a period of 72 h. An equal volume of the solvent was immediately added into the flask following the withdrawal. After dilution, the absorbance of the solution was measured in a UV-vis spectrophotometer (Hitachi 220, Japan) at 275 nm where DEHP has a characteristic absorption maximum. The amount of DEHP migrated into the medium was then calculated from a calibration curve of the plasticizer in *n*-hexane. Values reported are the average of three determinations with standard deviations less than 5%.

Thermal Analysis

A DuPont 990 thermal analyzer in conjunction with a standard DTA cell was used for the differential thermal analysis of PVC resin and the azide-substituted PVC resin in a dynamic atmosphere of nitrogen at a heating rate of 10°C per min. Weight loss of the samples was monitored in a DuPont Model 2000 thermogravimetric analyzer at a heating

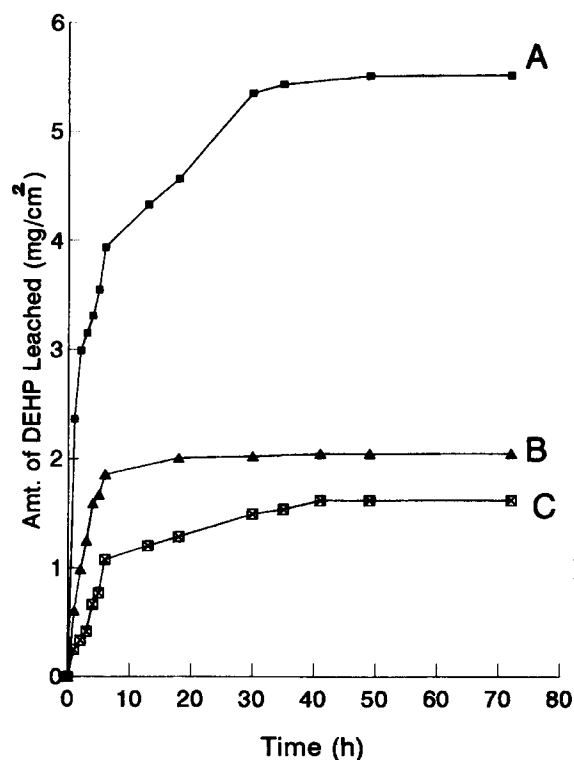


Figure 4 Amount of DEHP migrated into hexane as a function of time from PVC sheets coated using a 4% solution of the azide polymer and irradiated for 1 h. (A) Control sheet, (B) coated once and (C) coated twice.

rate of 10°C per min in an atmosphere of nitrogen. The particle size of the resin was 63–180 μm .

Platelet Adhesion onto Modified PVC Surface

Adhesion of platelets onto the surface of PVC and the azide polymer-coated PVC surface was examined using platelet-rich plasma (PRP) from calf blood. PVC resin and the azide-substituted polymer were coated onto microscopic coverglass slips from a 5% solution in THF. They were then dried in an air oven at 60°C. The polymer-coated coverslips were kept in small Petri dishes and 3 mL of PRP was carefully placed over them and allowed to remain there for 1 h. After 1 h, the samples were washed using phosphate-buffered saline (pH 7.4) by dipping the coverslips gently several times to remove the nonadhering platelets and was then fixed using 2% buffered formalin. After staining with Coomassie Blue, they were dried and mounted onto microscopic slides for examination.

RESULTS AND DISCUSSION

It has long been thought that the nucleophilic substitution of chlorine in PVC is rather difficult in contrast to elimination. But it was found that the azide anion, N_3^- , a rather weak nucleophile, could react with PVC in solvents such as DMF, dimethyl sulfoxide, or hexamethylphosphotriamide to give the azide derivative.¹⁰ This reaction offers an excellent opportunity for the preparation of a polymeric crosslinking agent as the azide group is capable of undergoing various chemical and photochemical reactions.^{11,12}

It is known that degradation effects occur simultaneously with crosslinking when PVC is irradiated with UV light.^{13,14} However, it is also reported that UV irradiation is rather ineffective when considering short-time data.⁵ Irradiation times of several days were required to observe any reduction in the migration of the plasticizer. When the polymeric azide is exposed to UV, photodecomposition of the azide into highly reactive nitrene takes place. The photogenerated nitrenes can react via several nonselective reactions including cycloaddition to the double bonds, insertion into C—H bonds, or hydrogen atom abstraction on the polymer, thereby crosslinking the polymer surface.

The amount of DEHP migrated into hexane for various periods of time from sheets coated twice from a 4% solution of azidated PVC in THF having different azide contents and irradiated for 1 h is shown

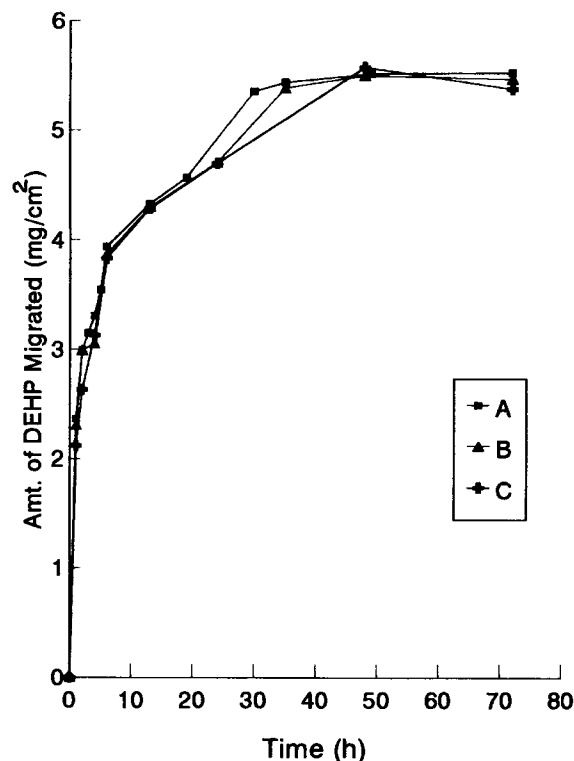


Figure 5 Amount of DEHP migrated into hexane as a function of time from (A) PVC sheets irradiated for 1 h, (B) sheets coated twice with a 4% solution of the azidated PVC but not irradiated, and (C) control sheet.

in Figure 2. The azide content of the polymer estimated using IR spectroscopy was found to be 4, 14, 20, and 27 (± 3 , $n = 3$) mol % for 1, 2, 3, and 4 h reactions. The resin reacted for 5 h with sodium azide was not found to be completely soluble in THF. As can be seen from Figure 2, increased azide content in the coating polymer leads to increased reduction in the migration of the plasticizer. Compared to unmodified PVC, coating with azidated PVC and irradiating the coating to form crosslinks results in reducing the migration of the plasticizer at all azide contents.

The increased crosslink density produced at higher azide contents could be attributed to the increased reduction of the plasticizer migration that is seen with increasing azide contents in the coating polymer. Since the 4 h reaction gave rise to an azidated polymer which was freely soluble in THF, whereas the 5 h reaction led to an incompletely soluble product, all further coatings were carried out using the PVC azidated for 4 h. With all azide coatings, an equilibrium appears to be attained in the migration phenomena after 30 h. Such equilibrium or the quasi-equilibrium nature of the migration was

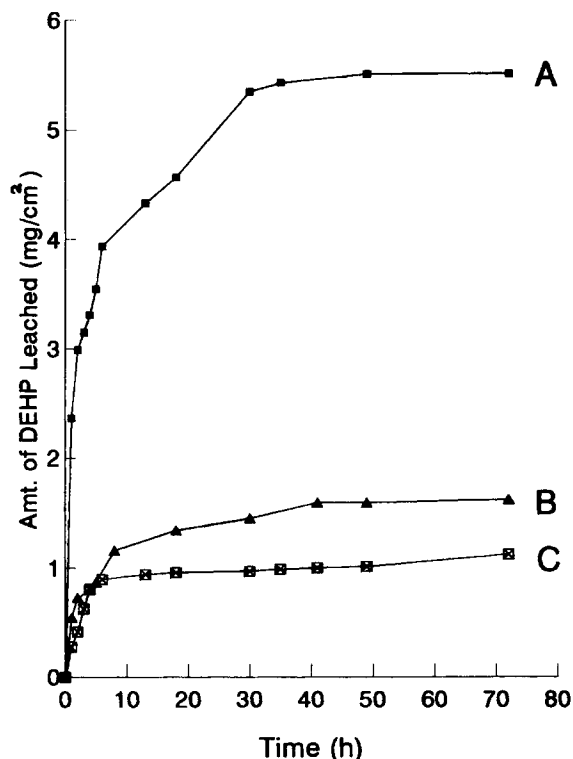


Figure 6 Amount of DEHP migrated into hexane as a function of time from PVC sheets coated using a 5% solution of the azide polymer and irradiated for 1 h. (A) Control sheet, (B) coated once and (C) coated twice.

observed by previous workers who examined the effect of prolonged UV radiation on PVC.⁵ Short-term UV irradiation has been, however, found to be ineffective in reducing plasticizer migration. Prolonged irradiation produces sufficient crosslink density on the surface of PVC to act as a barrier for diffusion to some degree. Together with the loss of the plasticizer, which leads the system to a nonrubbery or nearly nonrubbery behavior, an alteration of the polymer structure is expected to take place. Commercial PVC is a semicrystalline polymer and a rearrangement of the structure to a more ordered and compact one could be attributed to the equilibrium that is seen in the migration of the plasticizer.^{5,15}

The amount of DEHP migrated into hexane in 72 h as a function of the concentration of the coating solution is given in Figure 3. Sheets were coated once and twice using the solutions and the migration was examined. Sheets coated twice with the azide polymer showed less migration compared to sheets coated once. Also, it was seen that considerable reduction in migration was achieved when the concentration of the coating solution was 4% and above.

The amount of plasticizer leached into hexane as a function of time from sheets coated using a 4% solution of the azide polymer and irradiated for 1 h is shown in Figure 4. It was found that there is a decrease of 62% in the migration of DEHP from a single-coated sheet in 72 h in comparison with the controls. For samples coated twice, the percentage decrease in migration was calculated to be 70%. PVC sheets irradiated for 1 h and sheets coated with azide polymer but not irradiated also showed the same migration behavior as that of the control (Fig. 5). Although it is reported that UV irradiation of PVC leads to some crosslinking along with degradation of the polymer,^{13,14} these results demonstrate that short-time irradiation does not have any significant impact on the migration of the plasticizer.

The fact that there was virtually the same migration of the plasticizer from coated but unirradiated specimens also leads to the conclusion that coating the PVC surface with azidated PVC per se has no effect on DEHP migration. Migration experiments were carried out using 5% coating solution and irradiating the samples for 1 h. The results are depicted in Figure 6. The amount of DEHP migrated into hexane in 72 h from sheets coated once using

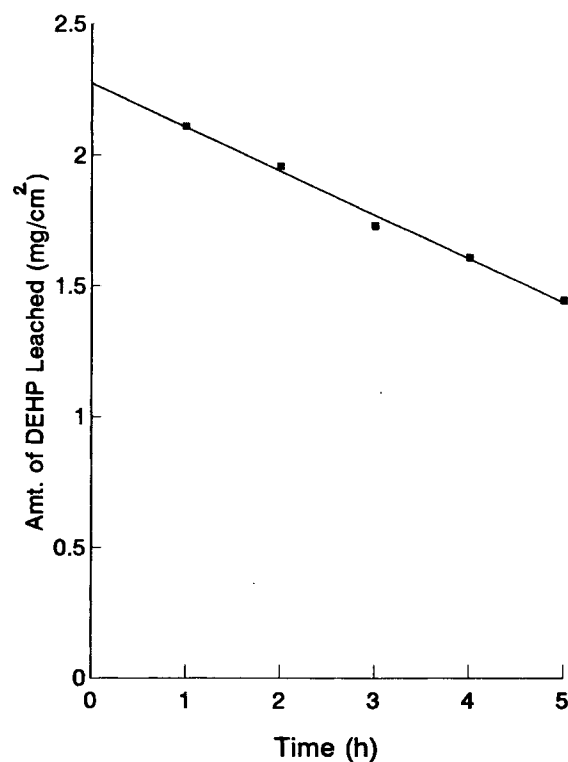


Figure 7 Effect of irradiation time on the migration of DEHP from PVC sheets coated once using 4% solution of the azide polymer.

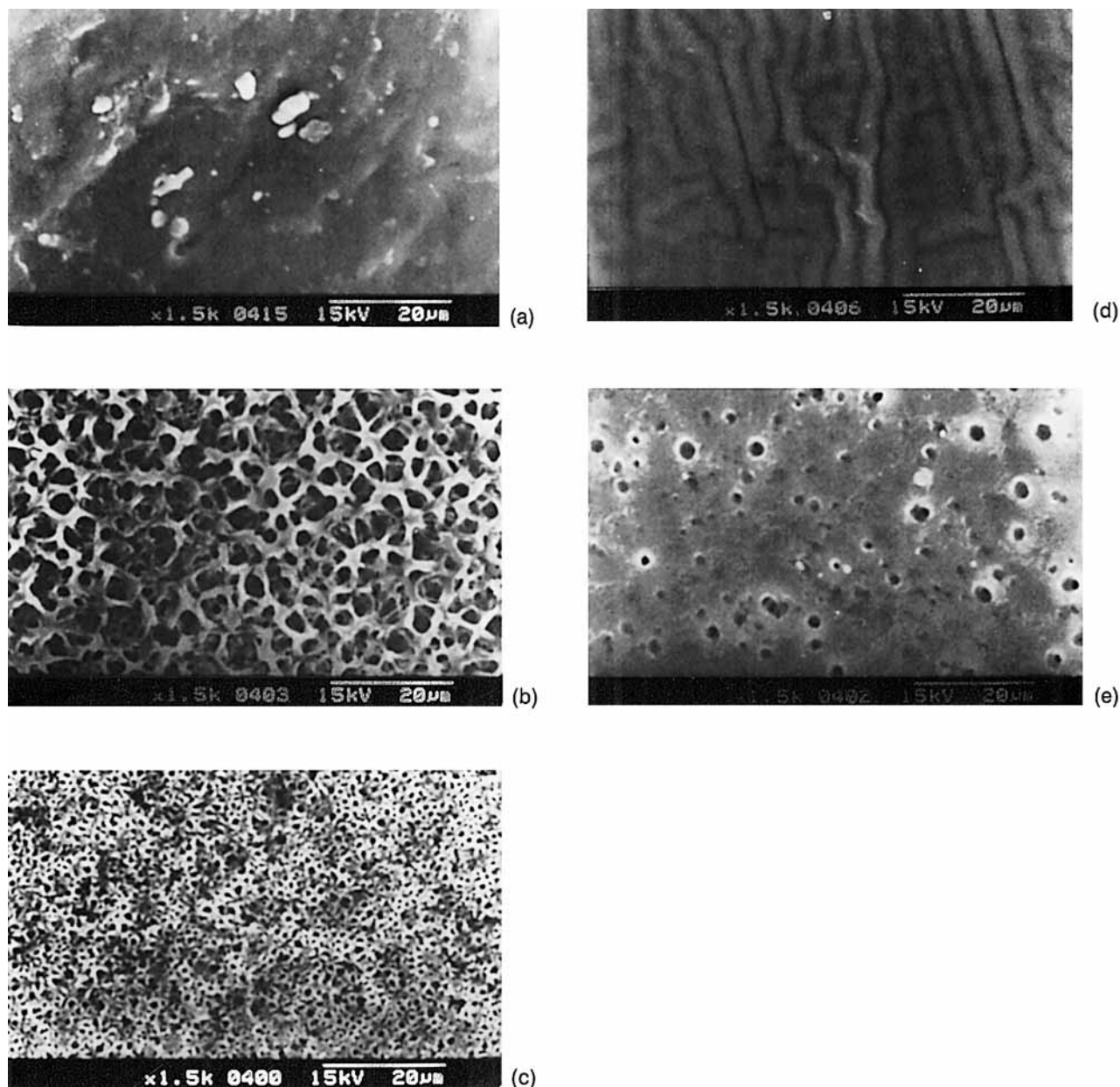


Figure 8 SEMs of the surface morphology of PVC sheets before and after coating with azidated PVC. (a) Unmodified, (b) coated once with 4% solution of azidated PVC and dried in air oven at 60°C, (c) coated twice with a 4% solution of azidated PVC and dried at 60°C, (d) coated twice and dried at ambient temperature by slow evaporation of the solvent, and (e) coated twice at 60°C and steam-sterilized.

5% azide polymer was found to be only 8%. For samples coated twice with the solution, there was only 5% migration. Thus, there was an 82% decrease in migration for sheets coated twice compared to controls. The data illustrate that increasing the azide concentration on the polymer surface results in increased reduction in DEHP migration. This is at-

tributed to the increased crosslinking of the coating on the surface on UV irradiation.

Increased irradiation time also was found to reduce the migration of DEHP. Samples were coated once using 4% solution of the azide polymer and subjected to irradiation for various lengths of time. Figure 7 illustrates the data. Increased radiation

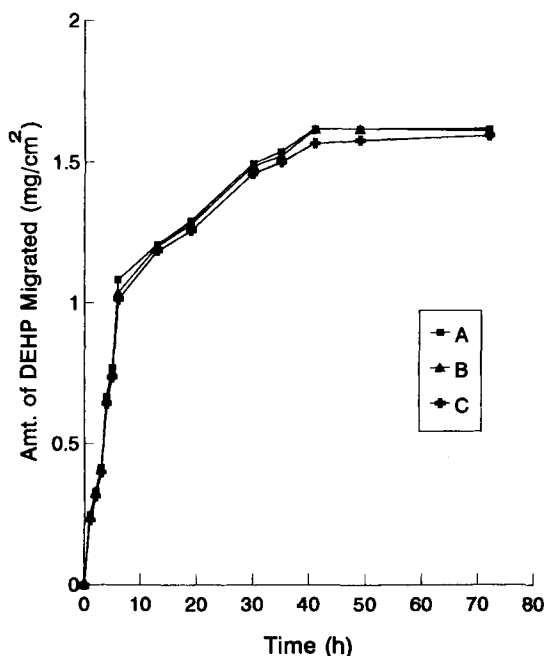


Figure 9 Migration of DEHP from PVC sheets coated twice using a 4% solution of azidated PVC and (A) dried at ambient temperature, (B) dried at 60°C, and (C) dried at 60°C and autoclaved, showing similar migration in all the three cases.

time resulted in a steady decrease in the migration of DEHP, though the differences were not highly pronounced. Prolonged radiation, however, induced pronounced color changes in the specimens, possibly due to formation of C=N and N=N bonds to a large extent.

SEM examination of the morphology of the coatings revealed interesting results. Figure 8(a) shows the surface of the unmodified PVC sheet. The surface has a nonuniform appearance. Coating with the azidated PVC once and evaporating the residual solvent (THF) at 60°C resulted in a perforated appearance on the surface [Fig. 8(b)]. Coating the surface twice with the azidated polymer reduces the surface imperfections, but a porelike structure is still seen on the surface [Fig. 8(c)]. Evaporation of the solvent was carried out in a slow manner by keeping the specimen in a beaker covered with a watch glass at room temperature. After allowing the solvent to evaporate, further drying was carried out in an air oven at 60°C as before. Figure 8(d) shows the surface morphology of such a coating devoid of any pores. The sample dried in the air oven [Fig. 8(c)] was further subjected to steam sterilization at 121°C at 15 psi ($138 \times 10^3 \text{ Nm}^{-2}$) for 20 min. Figure 8(e) shows the change in morphology of the surface after autoclaving. The pores on the surface have become

more or less closed and the surface appeared to have a less perforated appearance. Migration experiments were carried out using coated specimens prepared by the slow evaporation of the solvent as well as using the autoclaved specimens. There was hardly any difference in the kinetics of migration of DEHP from these specimens as compared to the specimens coated and dried in an air oven (Fig. 9). Thus, irrespective of the uniformity of the coating, the retardation of migration of the plasticizer is not different. This observation suggests that there could be some penetration of the coating solution into the matrix of the PVC, which upon irradiation and crosslinking forms a tight network of azidated PVC on the surface, which is responsible for the reduction in migration that is seen.

The DTA traces of the PVC resin and the azide polymer are shown in Figure 10. There is an endotherm at 285°C for the unmodified resin, while for the modified resin, it occurs at 220°C. Both are attributed to the decomposition of the polymer, which is further confirmed by TGA analysis (Fig. 11). Considerable weight loss is seen at both temperatures in the TG. With the virgin resin, the weight loss at ca. 285°C could be attributed to the dehydrochlorination of PVC, whereas for the azide polymer, the weight loss that begins at a lower temper-

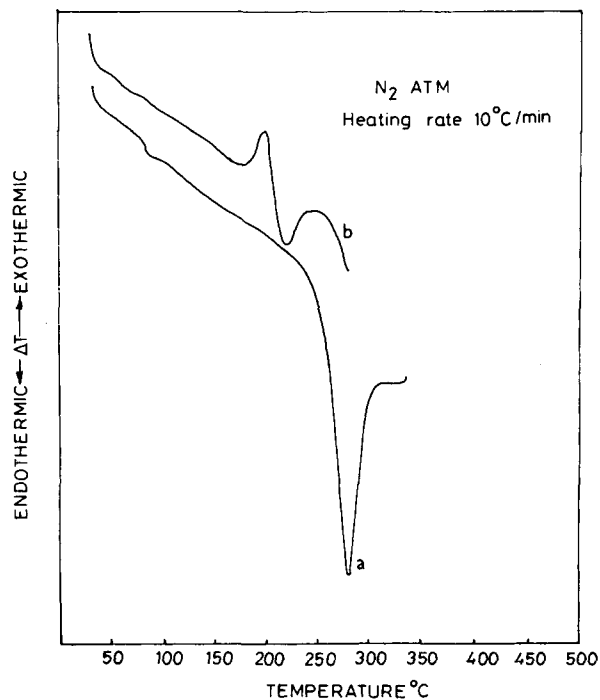


Figure 10 DTA traces of (a) PVC resin and (b) the azide-substituted resin showing endothermic peaks due to decomposition at 285 and 220°C, respectively.

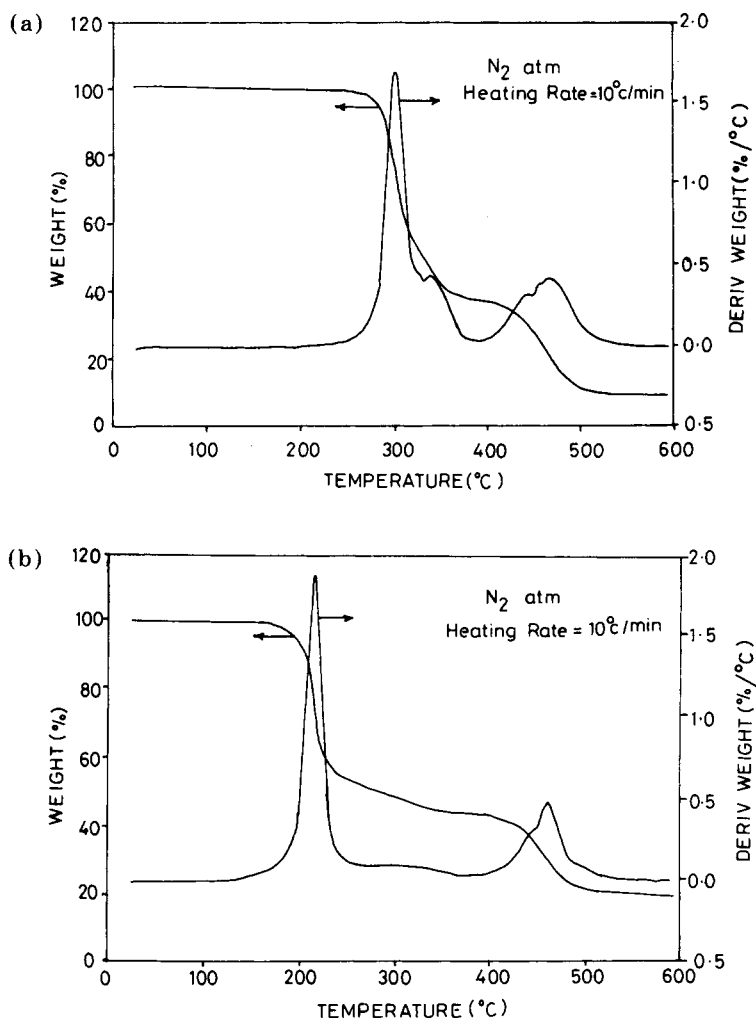


Figure 11 TGA of (a) PVC resin and (b) the azide-substituted resin, demonstrating weight loss due to decomposition at temperatures indicated by the endotherms in DTA.

ature could be ascribed to the decomposition of the azide. It is known that structural defects in the polymer chain are responsible for the initiation of thermal degradation in PVC. The steric order has also been known to influence the degradation process.¹⁶ Possible defects in the structure in PVC are branching, chloroallyl groups, end groups, oxygen-containing groups, and head-to-head structures. Introduction of azide groups induces alteration in the structural features of PVC, which is reflected in the reduced thermal stability. However, since there was no weight loss for the modified resin at or below 150°C, it would be safe to presume that devices having azide polymer on the surface would withstand steam autoclaving without undergoing degradation. This was further confirmed by examining whether there was any weight loss on the autoclaved spec-

imen of the azide-coated and irradiated PVC. No weight loss was observed.

Examination of the platelet adhesion phenomena on modified and unmodified PVC microscopically was not able to demonstrate any qualitative difference between the two surfaces. Both surfaces were found to promote platelet adhesion; it was hard to discern any difference in the adhesion characteristics on the two surfaces by this experiment. Possibly, the azide-containing surface may be advantageous in preventing the fungal growth occasionally seen in blood bags made of PVC. However, further work would be needed to confirm this hypothesis.

The authors thank Dr. C. K. S. Pillai of RRL, Trivandrum, for the TGA and Dr. K. Sreenivasan for the DTA analysis.

REFERENCES

1. L. Ljunggren, *Artif. Organs*, **8**, 99 (1984).
2. R. J. Jaeger and R. J. Rubin, *Science*, **170**, 460 (1970).
3. R. J. Jaeger and R. J. Rubin, *N. Engl. J. Med.*, **287**, 1114 (1972).
4. B. M. Myhre, *Ann. Clin. Lab. Sci.*, **18**, 131 (1988).
5. T. Duvis, G. Karles, and C. D. Papaspyrides, *J. Appl. Polym. Sci.*, **42**, 191 (1991), and references therein.
6. V. K. Krishnan, A. Jayakrishnan, and J. D. Francis, *J. Mater. Sci. Mater. Med.*, **1**, 185 (1990).
7. V. K. Krishnan, A. Jayakrishnan, and J. D. Francis, *J. Mater. Sci. Mater. Med.*, **2**, 56 (1991).
8. V. K. Krishnan, A. Jayakrishnan, and J. D. Francis, *Biomaterials*, **12**, 489 (1991).
9. M. Takeishi and M. Okawara, *J. Polym. Sci. Polym. Lett. Ed.*, **7**, 201 (1969).
10. M. Okawara and Y. Ochiai, in *Modification of Polymers*, C. E. Carraher, Jr. and M. Tsuda, Eds., ACS Symposium Series, American Chemical Society, Washington, DC, Chap. 4.
11. M. Takeshi and M. Okawara, *J. Polym. Sci. Polym. Lett. Ed.*, **8**, 829 (1970).
12. S. R. Turner and R. C. Daly, in *Comprehensive Polymer Science*, G. Allen and J. C. Bevington, Eds., Pergamon Press, New York, 1989, p. 198.
13. K. P. S. Kwei, *J. Polym. Sci. A-1*, 1075 (1969).
14. B. Ranby and J. F. Rabek, in *Photodegradation, Photooxidation and Photostabilization of Polymers*, Wiley-Interscience, New York, 1975.
15. C. D. Papaspyrides, *J. Appl. Polym. Sci.*, **38**, 1859 (1989).
16. D. Braun, in *Development in Polymer Degradation-3*, N. Grassie, Ed., Applied Science Publishers, London, 1981, p. 103.

Received April 12, 1993

Accepted August 24, 1994