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Photocross-linking of dithiocarbamate-substituted PVC reduces plasticizer migration

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Medical grade poly(vinyl chloride) (PVC) sheets and tubes were surface modified by nucleophilic substitution of chlorine atoms of PVC by photoactive N,N-diethyl dithiocarbamate (DTC) in aqueous media in the presence of a suitable phase transfer catalyst (PTC) at 55°C. The modified surface was cross-linked by irradiation with u.v. light in an attempt to create a barrier for the diffusion of the plasticizer di-(2-ethylhexyl phthalate) (DEHP). Of the various PTCs examined for the reaction, tetrabutyl ammonium salts were found to be very effective, whereas crown ethers such as 18-crown-6 was least effective. The effect of concentration of PTC and DTC, time of reaction and irradiation dose on the extent of plasticizer migration was examined in petroleum ether for various periods of time at 30°C. The migration of DEHP from PVC modified under optimum conditions was less than 5% in 120 h, whereas the unmodified PVC lost virtually all its plasticizer (> 30%) during the same period. Determination of the stress–strain properties of modified PVC sheets showed a reduction of approximately 30%. However, the values were still within the range prescribed for vinyl chloride plastics used for medical applications. © 1997 Elsevier Science Ltd.

(Keywords: di-(2-ethylhexyl phthalate); plasticizer migration; poly(vinyl chloride))

INTRODUCTION

Plasticized PVC is one of the most widely used polymeric material in the medical field. Flexible PVC is used for the manufacture of blood bags, transfusion tubings, urine bags, etc. Flexible PVC is also extensively used for packaging food stuffs and pharmaceuticals. PVC as such is a rigid polymer, and additives such as plasticizers are required to increase its flexibility, distensibility and low temperature properties. PVC used in medical applications contains up to 40% by weight of the plasticizer, usually DEHP[1]. DEHP belongs to a class of agents described as hypolipidemic hepatocarcinogens. The toxicity of phthalate esters, particularly DEHP has been a matter of serious concern[2–4] and alarming reports questioning the safety of DEHP in PVC-based medical devices have been appearing in the literature since the 1980s[5–8]. DEHP is reported to be capable of producing adverse effects on pituitary gland tissues, cause liver abnormalities and testicular damage[9–14]. Metabolites of DEHP produced in contact with blood can act as a potential carcinogen[15,16].

Various attempts have been made to reduce plasticizer migration from flexible PVC. Methods employed include coating the PVC surface with various polymers such acrylates, polyesters and urethanes, cross-linking PVC during processing with peroxides, grafting hydrophilic monomers on to the surface of PVC by gamma-radiation and plasma treatment of PVC surface[17–20]. In recent communications from this laboratory, it was shown that coating the PVC surface with azidated PVC and photocross-linking the coatings by u.v. irradiation[21] or direct substitution of chlorine atoms of PVC with azide in aqueous media via phase transfer catalysis followed by photocross-linking[22] can reduce the plasticizer migration significantly from PVC sheets and tubes without adversely affecting their physical and mechanical properties.

Nucleophilic substitution of PVC with N,N-dialkyl dithiocarbamates is reported to proceed feasibly in dipolar aprotic solvents at temperatures between 50 and 60°C without additional dehydrochlorination[23]. The dithiocarbamate-substituted PVC is reported to cross-link on irradiation. If the nucleophilic substitution reaction is facile in aqueous media, then flexible PVC sheets and tubes could be surface cross-linked by the substitution of chlorine on their surface by a dithiocarbamate followed by photoirradiation. The diffusivity of plasticizer molecules such as DEHP through such a cross-linked network may then be considerably retarded. This study was therefore undertaken in order to examine the feasibility of preparing a dithiocarbamate-substituted PVC in aqueous media under phase-transfer conditions and to evaluate the migration characteristics of DEHP after photocross-linking the surface.

MATERIALS AND METHODS

Materials

Medical grade PVC tubes (Solmed, Denmark, o.d 9 mm) and sheets from Hindustan Latex, Ltd., Trivandrum, India were employed in the study. Sodium diethyl dithiocarbamate (DTC), and phase transfer catalysts (PTC) tetrabutyl ammonium hydrogen sulphate (TBAH), tetrabutyl ammonium bromide (TBAB) and tetrabutyl ammonium iodide (TBAI) were obtained from Spectrochem Ltd., Bombay, India. Cetyl pyridinium chloride (CPC) was from

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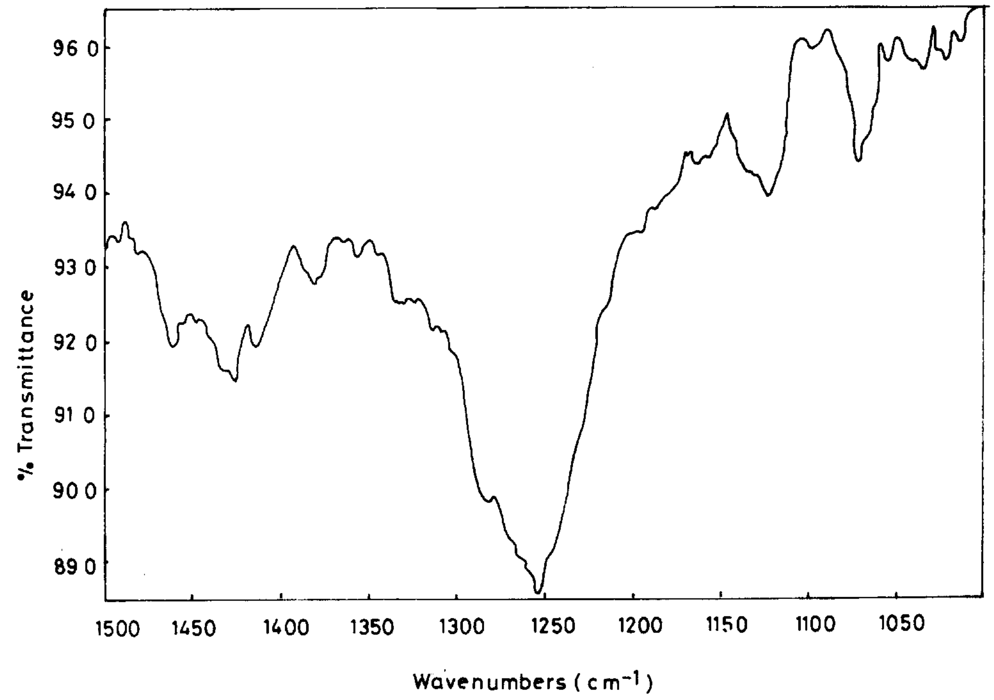


Figure 1 ATR-FTIR spectrum of plasticized PVC.

CDH Ltd., Bombay, India and 18-crown-6 was from Sigma Chemical Co., St Louis, MO, USA. All other reagents and solvents were of analytical or equivalent grade.

Methods

Surface modification of PVC. The nucleophilic substitution of chlorine of PVC by DTC was carried out as follows. PVC tubes (~1.5 cm long) were treated with DTC (0.05–0.80 mol dm^{-3}) in the presence of different PTCs (0.01–0.1 mol dm^{-3}) in 10 ml distilled water at 55°C for various time periods with occasional shaking. In the case of sheets, specimens (10 × 1 cm or 2.5 × 1.5 cm) having a thickness of approximately 0.4 mm were immersed in 30 ml of water containing different amounts of DTC and the catalyst at 55°C for 24 h with occasional shaking. After the reaction, the specimens were thoroughly washed with running tap water followed by distilled water, and subjected to mild sonication in a bath type sonicator for 1 min to remove any surface adhering reactants and dried in an air oven at 50°C to constant weight. Irradiation of the samples was carried out using a 125 W u.v. lamp (Philips HPL-N, India). The samples were hung in air at a distance of 15 cm from the centre of the lamp and irradiated for various periods of time.

Surface morphology. PVC sheets were examined before and after substitution and photocross-linking for change in surface morphology using scanning electron microscopy (SEM). Sheets were vacuum coated with gold and examined in the microscope (Hitachi, model S-2400, Japan).

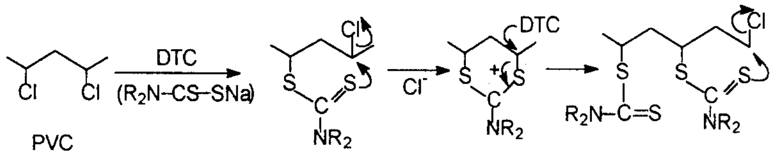
Infrared spectroscopy. Attenuated total reflection Fourier transform infrared spectra (ATR-FTIR) of unmodified and surface modified PVC sheets were taken in a Nicolet instrument (Model 410, USA) using baseline horizontal ATR accessory (Nicolet).

Gel content. Gel content due to surface cross-linking was determined by dissolving the modified and unmodified PVC tubes in 40 ml of tetrahydrofuran (THF) at room temperature (27°C). The undissolved fraction was separated, washed thoroughly with THF and dried *in vacuo* and weighed in an analytical balance. The gel content (%) was calculated based on the initial weight of the tubes.

Sulfur content. The percentage of sulfur present in control and modified PVC was quantitatively determined by the Parr–Bomb method[24]. PVC (0.5 g) was subjected to combustion in oxygen at atmospheric pressure. The combustion products were absorbed in alkaline hydrogen peroxide and the sulphate was determined as barium sulphate turbidometrically.

Plasticizer migration. The migration of DEHP from surface-modified and unmodified specimens was examined in petroleum ether at 30°C. Specimens were kept in 25 ml of extraction solvent in stoppered Erlenmeyer flasks and were shaken occasionally. Aliquots of 0.1 ml were withdrawn at various time intervals and the amount of DEHP migrated was assayed spectrophotometrically using a u.v.-Vis spectrophotometer (Milton Roy, Genesys 2, USA) at 275 nm. Values reported are the average of three determinations.

Mechanical properties. The stress–strain properties of the modified and control PVC sheets were measured using an Instron automated materials testing system 1.09 as per ASTM method D882 for thin plastic sheeting[25]. Exactly 10 × 1 cm strips were cut from the PVC sheets and their thickness was measured using a screw gauge. The sheets were pulled using a cross-head speed of 10 cm min^{-1}. At least six samples were tested in each case. Since medical uses of PVC bags are mainly for storing blood and its components at low temperatures, the stress–strain properties of the surface-modified PVC sheets were also measured after keeping the sheets at 4°C for 30 days in a refrigerator.



Scheme 1

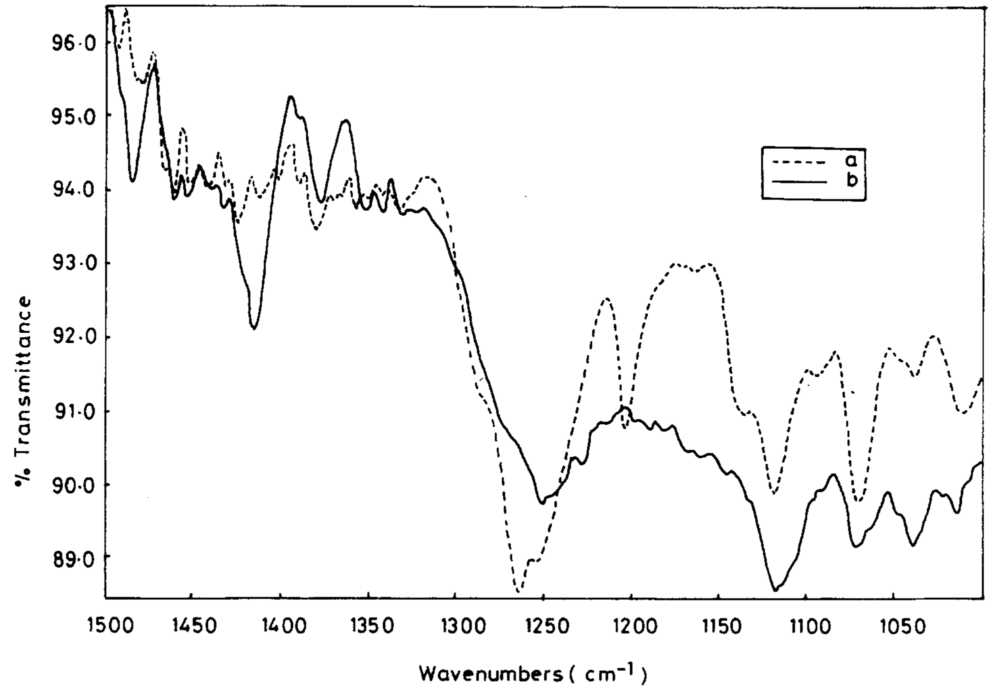
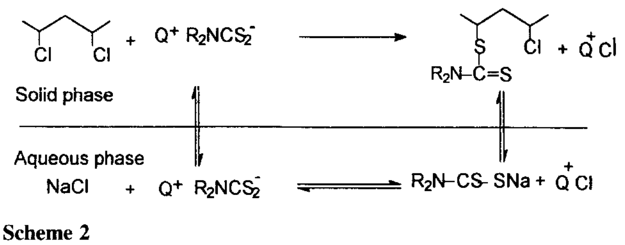


Figure 2 ATR-FTIR spectrum of DTC-substituted PVC showing the characteristic absorption due to C=S at 1202 cm^{-1} (a) and virtual disappearance of the peak on photocross-linking (b).

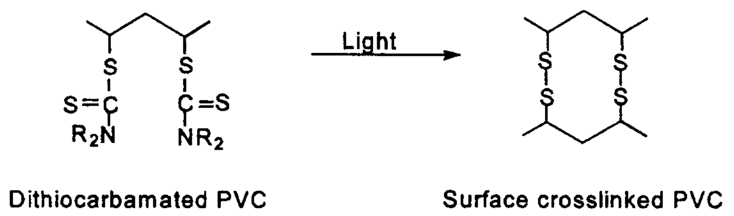


Scheme 2

RESULTS AND DISCUSSION

The nucleophilic substitution of PVC with DTC in dipolar aprotic solvents such as DMF takes place feasibly in the temperature range of 50–60°C via neighbouring group participation through the intermediary cyclic carbocation according to *Scheme 1*[23].

However, the substitution reaction is not known to take place in aqueous media. In our earlier work, we have shown that the azide anion could be transported from the aqueous phase to the organic solid phase of PVC in the presence of a suitable PTC to prepare azidated PVC[22]. In a similar fashion, if the soluble organic cation of the quaternay salt Q^+ transports the dithiocarbamate group from the aqueous phase to the organic solid phase of PVC, then nucleophilic substitution of PVC with DTC should take place predominantly on the surface of PVC. The reaction product



Scheme 3

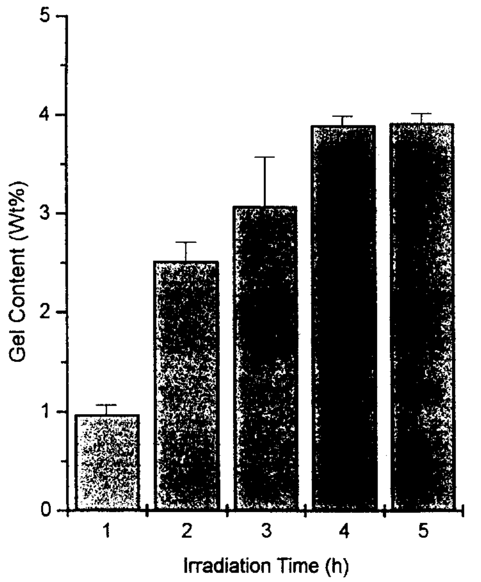


Figure 3 The amount of cross-linked gel formed on the surface of PVC on DTC substitution followed by photocross-linking as a function of iradiation time. [DTC] = 0.2 mol dm^{-3}, [TBAH] = 0.03 mol dm^{-3}, reaction time 24 h at 55°C.

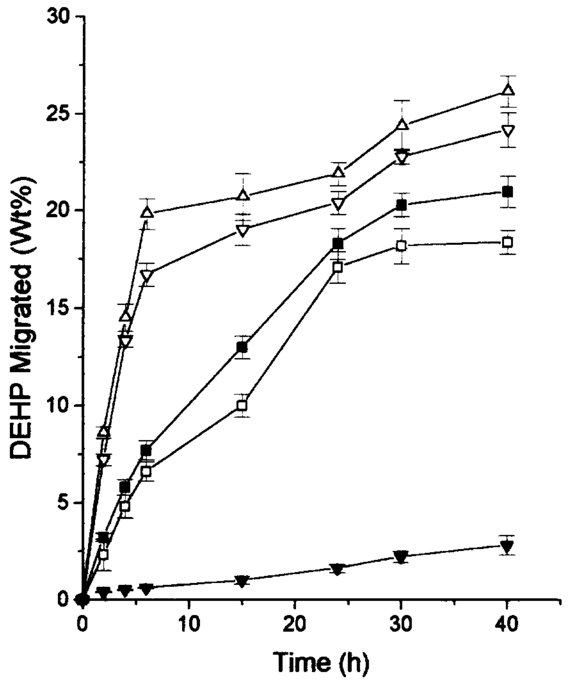


Figure 4 Kinetics of DEHP migration into petroleum ether at 30°C from PVC tubes modified at 55°C for various time periods and irradiated for 4 h. [DTC] = 0.2 mol dm^{-3}, [TBAH] = 0.03 mol dm^{-3}. Control (△), reacted for 2 h (▽), 4 h (■), 6 h (□) and 24 h (▼).

chloride ion will be transported back to the aqueous phase by the catalyst and repetition of this process should accelerate the reaction, as shown in *Scheme 2*. DTC is a photo-labile group. Upon photolysis, it undergoes homolytic bond fission, resulting in the formation of a thyl radical which in the absence of other photoactive group undergoes cross-linking. This results in the formation of a sulfur bridge as shown in *Scheme 3*. The sulfur bridges thus formed on the surface of flexible PVC are expected to act as a barrier to plasticizer migration.

Figure 1 shows the ATR-FTIR spectrum of plasticized PVC and *Figure 2*(a) shows the spectrum of DTC-substituted PVC having a strong characteristic absorption at 1202 cm^{-1} due to the C=S group. On photoirradiation, this peak completely disappeared indicating complete surface cross-linking [*Figure 2*(b)].

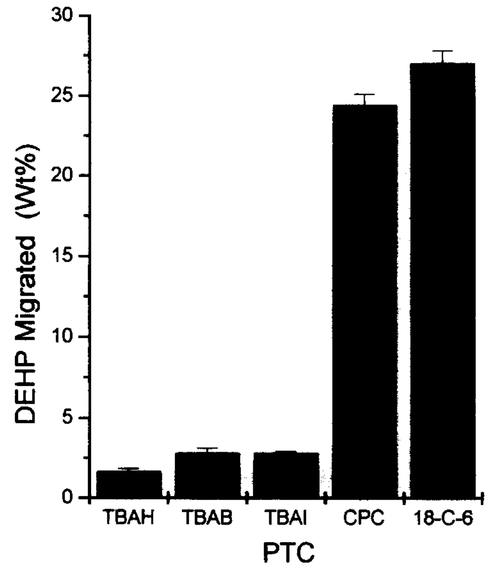


Figure 5 Amount of DEHP migrated into petroleum ether at 30°C in 24 h from PVC tubes modified at 55°C with different PTCs and irradiated for 4 h. [DTC] = 0.2 mol dm^{-3}, [PTCs] = 0.03 mol dm^{-3}.

The nucleophilic substitution of PVC by DTC was further confirmed by analysis of sulfur content in the modified specimen. The photocross-linked PVC was found to contain 1.5% by weight of sulfur, whereas in unmodified PVC there was no detectable sulfur present.

The cross-linked network formed on the surface of the modified PVC could be separated by treating the photo-irradiated PVC with THF at room temperature. Whereas the uncross-linked PVC and all the other additives in it undergo complete dissolution in THF, the cross-linked network does not dissolve and could be physically separated and subjected to gravimetric estimation. *Figure 3* shows the amount of cross-linked gel formed on the surface of modified PVC as a function of irradiation dose. The amount of gel formed increased with time of irradiation initially for the first 3 h and thereafter became constant. There was virtually no change in the weight of gel formed at 4 and 5 h irradiation. The maximum gel content was estimated to be less than 4% of the weight of plasticized PVC.

The migration of the plasticizer DEHP was examined from unmodified and modified PVC tubes in petroleum ether at 30°C. *Figure 4* shows the amount of plasticizer migrated from PVC tubes reacted at 55°C for various time periods and irradiated for 4 h. It can be seen that as the time of reaction is increased, there is a gradual decrease in the amount of DEHP migrated. Migration was found to be minimal from specimens reacted for 24 h and irradiated for 4 h. While the control PVC lost more than 25% of the plasticizer in 40 h, migration from specimens reacted for 24 h was less than 5%. The reduced migration from specimens reacted for prolonged periods is believed to be due to the higher degree of DTC substitution in them. This was further confirmed by examining the increase in weight of flexible PVC with respect to the reaction time. *Table 1* shows the percentage increase in the weight of PVC on reaction with DTC. The maximum weight increase was found for 24 h reaction. Therefore, all further surface

Table 1 Percentage increase in the weight of flexible PVC tubes on nucelophilic substitution of chlorine with DTC at a concentration of 0.2 mol dm^{-3} at 55°C for various reaction periods using TBAH as the catalyst at a concentration of 0.03 mol dm^{-3}

Time of reaction (h)	Increase in weight (%) ± SD[a]
2	0.91 ± 0.05
6	1.25 ± 0.03
15	1.84 ± 0.15
24	2.24 ± 0.03

[a]Average of three experiments.

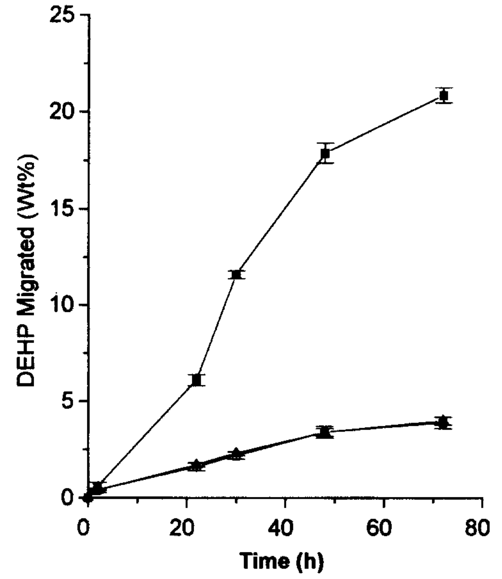


Figure 6 Kinetics of migration of DEHP into petroleum ether at 30°C from PVC tubes modified at 55°C for 24 h at different [TBAH] and irradiated for 4 h. [DTC] = 0.2 mol dm^{-3}. [TBAH] = 0.01 (■), 0.03 (□), and 0.1 mol dm^{-3} (▲).

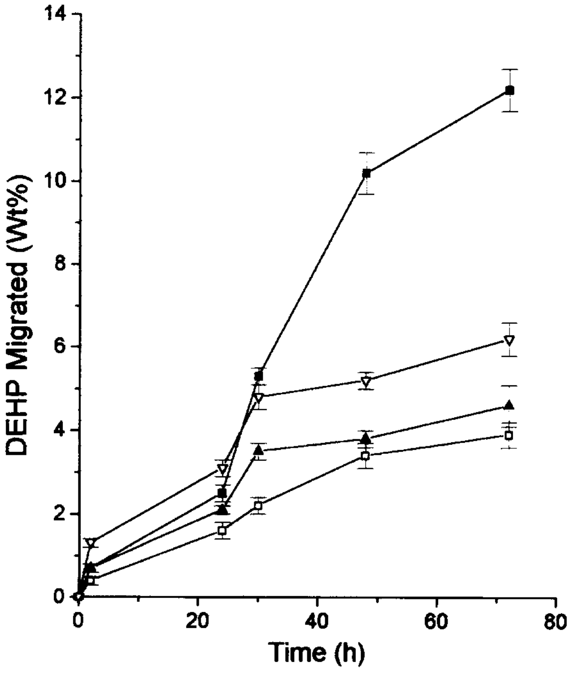


Figure 7 Kinetics of migration of DEHP into petroleum ether at 30°C from PVC tubes modified at 55°C for 24 h at various DTC concentrations using [TBAH] = 0.03 mol dm^{-3}. [DTC] = 0.05 (■), 0.2 (□), 0.4 (▲), and 0.8 mol dm^{-3} (▽).

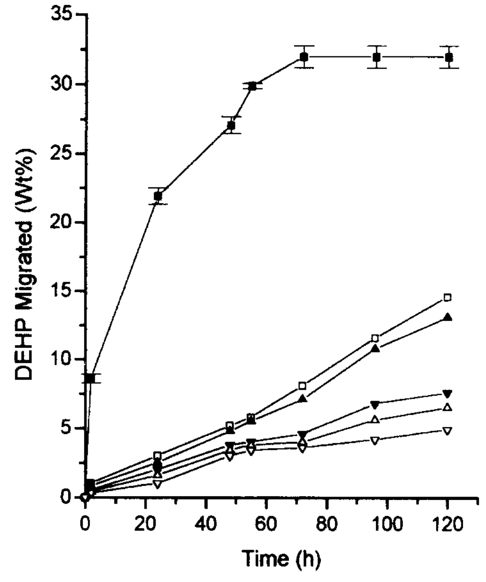


Figure 8 Effect of radiation dose on the extent of migration of DEHP from PVC tubes modified at 55°C for 24 h at [DTC] = 0.2 mol dm^{-3} and [TBAH] = 0.03 mol dm^{-3}. Control (■), 1 h (□), 2 h (▲), 3 h (▼), 4 h (△) and 5 h (▽).

modifications were carried out by reacting PVC with DTC for 24 h.

The effect of different PTCs on the extent of nucleophilic substitution of PVC as reflected by the migration of the plasticizer after photocross-linking was examined. PVC tubes were treated with DTC in the presence of various catalysts for 24 h at 55°C and subsequently photocross-linked for 4 h. Migration of DEHP from the modified tubes was examined in petroleum ether for 24 h. *Figure 5* shows the amount of DEHP migrated from tubes modified in the presence of different PTCs. Tetrabutyl ammonium salts were found to be highly efficient in affecting the nucleophilic substitution of PVC, while CPC and 18-crown 6 were found to be virtually ineffective. Similar observations have been noted in the transfer of azide anion from the aqueous phase to the solid PVC phase in our earlier work[22]. Of all the catalysts examined, TBAH was found to be the best for this reaction.

The effect of the catalyst TBAH and the nucleophile DTC on preventing the migration of DEHP was examined as a function of their concentration. *Figure 6* shows the kinetics of migration of DEHP from PVC specimens modified at different concentrations of TBAH at a constant concentration of the nucleophile. As can be seen, the catalyst concentration required for achieving effective substitution is very small. Beyond 0.01 mol dm^{-3}, the catalyst did not exert any effect on the extent of DEHP migration. This meant that the extent of nucleophilic substitution did not change beyond a certain catalyst concentration. The reason for this unusual kinetic behaviour is believed to be due to the aggregation of the quaternary salt-thiocarbamate on the polymer and the adsorbed salt reacts with PVC in a bimolecular process as observed in the case of azide transfer to solid PVC[22].

Figure 7 shows the kinetics of migration of DEHP from tubes modified at different nucleophile concentrations. The plasticizer migration was found to be minimum at a DTC concentration of 0.2 mol dm^{-3}. A further increase in the concentration of DTC resulted in increased migration. This phenomenon is presumably because of the high degree of association of the nucleophile with the quaternary salt at

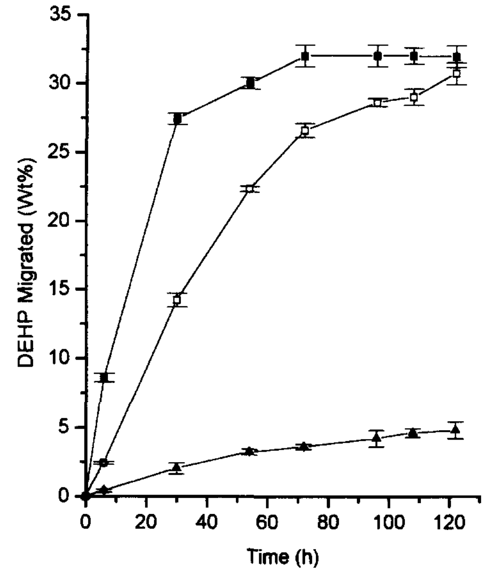


Figure 9 Kinetics of migration of DEHP from PVC tubes modified with [DTC] = 0.2 mol dm^{-3} and [TBAH] = 0.03 mol dm^{-3} at 55°C for 24 h. Control (■), DTC substituted PVC tubes unirradiated (□), DTC substituted PVC tubes irradiated for 5 h (▲).

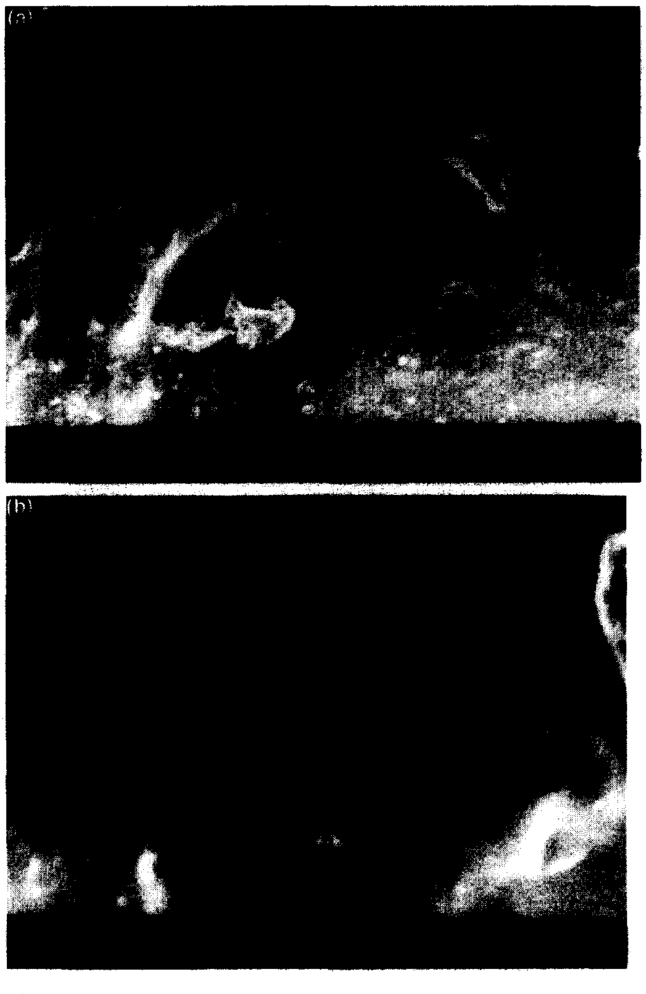


Figure 10 SEM of unmodified PVC sheet (a) and PVC sheet DTC substituted at 55°C for 24 h at [DTC] = 0.2 mol dm^{-3} and [TBAH] = 0.03 mol dm^{-3} and irradiated for 4 h (b).

Table 2 Stress–strain properties of PVC sheets before and after surface modification. Sheets were surface modified at a DTC concentration of 0.20 mol dm^{-3} and a TBAH concentration of 0.03 mol dm^{-3} at 55°C for 24 h and photocross-linked for 4 h

Sample	Ultimate stress MPa ± SD[a]	Ultimate strain % ± SD[a]
Control PVC sheet	19.38 ± 0.57	437.7 ± 26.3
DTC-substituted	15.35 ± 0.66	366.0 ± 22.7
DTC-photocross-linked	13.04 ± 0.35	288.7 ± 12.0
DTC-photocross-linked and kept at 4°C for 30 days	13.27 ± 0.29	307.7 ± 9.2

[a] Average of six determinations.

high concentrations, thereby precluding the chloride displacement reaction. Quaternary salts are known to associate strongly with large 'soft' anions rather than with small highly hydrated ions such as Cl$^-$ or CN$^-$[26].

Figure 8 shows the effect of irradiation time on plasticizer migration. As the time of irradiation increases the migration of the plasticizer decreases correspondingly. This is due to the increase in extent of cross-linking with irradiation. It has already been reported that u.v. irradiation alone without modification does not have any effect on the migration of the plasticizer[17].

Figure 9 shows the kinetics of plasticizer migration from control, DTC-substituted but unirradiated as well as DTC-substituted and irradiated PVC tubes. The unirradiated specimen showed slightly different kinetics of migration from the control, but on prolonged incubation in the extraction media, both the control and the unirradiated specimen lost almost similar amounts of DEHP. The slight retardation in migration from modified but unirradiated specimens seen in the early stages is possibly because of some cross-linking that occurred to the surface by daylight as well as heat during the course of reaction since thiocarbamates are known to be highly thermal and light sensitive. In comparison, the photocross-linked material lost only less than 5% of its plasticizer in 5 days.

Figure 10 shows the SEM of the unmodified PVC sheet and the photocross-linked sheet. There appeared to be no significant change in the surface morphology of the sheets before and after surface modification.

Table 2 shows the stress–strain properties of the control and surface modified PVC sheets. Substitution of chlorine on the surface of PVC by DTC resulted in a decrease in the stress and strain of the material. On cross-linking the surface, there was further decrease in the stress as well as strain. The stress as well as strain decreased by approximately 30%. The decrease in values was very similar to that observed in the case of PVC modified by azidation followed by photocross-linking[22]. The reduced stress–strain values are presumed to be due to the surface cross-linking of the sheets. However, the values were still well within the limits prescribed for vinyl chloride plastics used in medical applications.

CONCLUSION

The feasibility of chloride displacement reaction using a photoactive nucleophile such as DTC on plasticized PVC in a two-phase medium consisting of solid PVC and water is demonstrated by the use of a suitable PTC. Although the displacement reaction is known to occur in the presence of suitable PTCs in dipolar aprotic solvents in which PVC is soluble, such reaction is not known to take place in aqueous media. The method reported here is useful for the surface modification of flexible PVC sheets and tubes which find many medical applications. The technique results in the nucleophilic substitution of PVC by DTC predominantly on its surface which can be further cross-linked using u.v. radiation, thereby providing a barrier for the diffusion of the plasticizer DEHP from the matrix. Considerably reduced plasticizer migration from such modified specimens has been demonstrated. The substituted dithiocarbamate groups on the surface can also be used for photografting bioactive vinyl monomers on to the surface of PVC in order to increase its biocompatibility.

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REFERENCES

1. Ljunggren, J., *Artifical Organs*, 1984, **8**, 99.
2. Jaeger, R.J. and Rubin, R.J., *Science*, 1970, **170**, 460.
3. Thomas, J.A. and Thomas, M.J., *CRC Critical Review of Toxicology*, 1984, **13**, 283.
4. Rubin, R.J. and Ness, P.M., *Transfusion*, 1989, **29**, 358.
5. Sjoberg, P.O.J., Bondesson, U.G., Sedin, E.G. and Gustafsson, J.P., *Transfusion*, 1985, **25**, 424.
6. Myhre, B.M., *Annals of Clinical and Laboratory Science*, 1988, **18**, 131.
7. Schneider, B., Schena, J., Truog, R., Jacobson, M. and Kevy, S., *New England Journal of Medicine*, 1989, **320**, 1563.
8. Plonait, S.L., Nau, H., Maier, R.F., Wittfoht, W. and Obladen, M., *Transfusion*, 1993, **33**, 598.
9. Teirlynck, O., Kaufman, J.M., Bogaert, M.G. and Roels, H., *Toxicology Letters*, 1988, **40**, 85.
10. Agarwal, D.K., Lawrence, W.H., Turner, J.E. and Autian, J., *Journal of Toxicology and Environmental Health*, 1989, **26**, 39.
11. Dirven, H.A., van den Broek, P.H. and Jongeneelen, F.J., *Toxicology*, 1990, **65**, 199.
12. Oishi, S., *Archives of Toxicology*, 1990, **64**, 143.
13. Treinen, K.A. and Heindel, J.J., *Reproduction of Toxicology*, 1992, **6**, 143.
14. Grasso, P., Heindel, J.J., Powell, C.J. and Reichert, L.E., *Biological Reproduction*, 1993, **48**, 454.
15. Popp, J.A., Garvey, L.K. and Cattley, R.C., *Toxicology Industrial Health*, 1987, **3**, 151.
16. Tsutsui, T., Wantanabe, E. and Barrett, J.C., *Carcinogenisis*, 1993, **14**, 611.
17. Duvis, T., Karles, G. and Papaspyrides, C.D., *Journal of Applied Polymer Science*, 1991, **42**, 191.
18. Krishnan, V.K., Jayakrishnan, A. and Francis, J.D., *Journal of Material Science, Materials in Medicine*, 1990, **1**, 185.
19. Krishnan, V.K., Jayakrishnan, A. and Francis, J.D., *Biomaterials*, 1991, **12**, 489.
20. Iriyama, Y. and Yasuda, H., *Journal of Applied Polymer Science, Applied Polymer Symposium*, 1988, **42**, 97.
21. Jayakrishnan, A., Sunny, M. C. and Mini, N. Rajan, *Journal of Applied Polymer Science*, 1995, **56**, 1187.
22. Jayakrishnan, A. and Sunny, M.C., *Polymer*, 1996, **37**, 5213.
23. Okawara, M. and Ochiai, Y., in *Modification of Polymers*. Ed. C. E. Carraher and M. Tsuda, ACS Symposium Series 121, American Chemical Society, Washington, DC, 1980, pp. 45-46.
24. Haslam, J. and Squirrell, D.C.M., *Journal of Applied Chemistry, London*, 1961, **11**, 244.
25. *Annual Book of ASTM Standards*, ASTM, Philadelphia, PA, 1982, pp. 408-415.
26. Starks, C. M. and Liotta, C., *Phase Transfer Catalysis: Principles and Techniques*, Academic, NY, 1978, p. 6.