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Radiation grafting of hydrophilic monomers on to plasticized poly(vinyl chloride) sheets

Part 1 *Surface characterization and plasticizer migration studies*

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Medical-grade plasticized poly(vinyl chloride) (PVC) sheets were surface modified using gamma-radiation grafting of a combination of hydrophilic monomers based on 2-hydroxyethyl methacrylate (HEMA) and N-vinyl pyrrolidone (NVP). The modified surfaces were evaluated for their surface properties using contact angle measurements, phase-contrast photomicroscopy and scanning electron microscopy. Surface energy calculations of the modified surfaces indicated that the surfaces became highly hydrophilic when grafted with even a 1% (v/v) solution of HEMA–NVP combination in the presence of 0.005 M $CuSO_4$. Migration of the plasticizer di(2-ethylhexyl phthalate) (DEHP) from the grafted sheets was examined in hydrocarbon solvents such as n-hexane, n-heptane and n-octane and in extractant media such as cotton seed oil and polyethylene glycol-400 (PEG-400). The migration from modified sheets was found to be <4% of the migration from unmodified control sheets in hydrocarbon solvents at 30° C over a period of 5 h. Accelerated leaching studies in cotton seed oil and PEG-400 demonstrated that virtually no plasticizer migrated out in the former over a period of 96 h whereas the rate of migration in the latter medium showed only a mild reduction. The migration behaviour was Fickian in nature for grafted sheets. The method described may be useful as a simple, versatile technique for preventing plasticizer migration from plasticized PVC for medical applications.

1. Introduction

The use of high-energy irradiation has been a popular synthetic approach to produce graft copolymers of poly(vinyl chloride) (PVC), especially due to the labile nature of the chlorine atoms in the polymer. Three techniques have mainly been employed [1]: (1) to irradiate the polymer alone at low temperature in the absence of oxygen, which is further reacted with a monomer to induce grafting; (2) to irradiate the polymer in the presence of air or oxygen to produce peroxy or hydroperoxy groups on the polymer matrix, which is further used in thermal or redox initiations for grafting; and (3) direct irradiation of the polymer in the presence of monomer(s) to effect grafting. Charlesby and Pinner [2] have reported that direct irradiation of polymer in the presence of monomers resulted in improved properties for the polymer. Although a considerable amount of work has been carried out on the grafting of a variety of hydrophobic monomers on to PVC by different groups [3–8], very little is reported on the grafting of hydrophilic monomers [9, 10] on to the polymer with a view to examining the properties of the grafted product. Hydrophilic polymers have been known to offer better blood-compatible surfaces [11, 12], and therefore surface modification by the grafting of hydrophilic monomers on to PVC may improve the blood compatibility of the polymer. Hence, we have attempted to study grafting of hydrophilic monomers such as 2-hydroxyethyl methacrylate (HEMA) and N-vinyl pyrrolidone (NVP) on to plasticized PVC sheets using gamma radiation from a cobalt-60 source and examined the surface properties of the grafted product and the migration behaviour of the plasticizer di(2-ethylhexyl) phthalate (DEHP) into organic solvents such as n-hexane, n-heptane and n-octane and simulated physiological extractant media such as cotton seed oil and polyethylene glycol (PEG-400).

The migration behaviour assumes greater importance due to the fact that the low molecular weight organic plasticizers introduced into PVC to impart flexibility and better low-temperature properties possess high mobility and migrate into their surrounding medium such as blood, plasma or food articles, resulting in toxic effects. Plasticizer migration from PVC has attracted the interest of numerous investigators [13–20]. Alarming reports questioning the safety of using DEHP as a plasticizer in medical PVC applications have been surfacing since the early 1980s [21–24]. Recent studies have indicated that an excess

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of DEHP is capable of producing adverse effects on pitutary gland tissues and causing liver abnormalities and testicular damage [25, 26]. A study report [27] made by the US Cancer Institute in 1981 has indicated the possibility of DEHP or its metabolite produced in contact with blood acting as a potential carcinogen. The carcinogenicity of DEHP in animals having been conclusively established [28, 29], a total ban on the use of this chemical in medical PVC applications through future legislation seems imminent from recent reports [30].

Various attempts have been made by different groups to find a better alternative to plasticized PVC or to use high molecular weight plasticizers such as tri(ethylhexyl) trimellitate to reduce the leaching characteristics of PVC [31]. Glow-discharge treatment of PVC sheets has been reported to retard migration to a certain extent [32]. However, all of these techniques have severe limitations. To the best of our knowledge no attempt has been made so far to study the surface modification of PVC by the grafting of hydrophilic monomers using gamma radiation with a view of evaluating the migration of DEHP from such modified surfaces. Compared with the glow-discharge technique, radiation grafting offers several advantages which include reproducibility, the simplicity of the procedure and its versatility.

2. Materials and methods

Calendered PVC sheets of medical grade having a thickness of 0.4 mm, a gift from M/s Technoport Co, Japan, were used in all of the experiments. Grafting experiments were conducted either on strips 100 mm × 10 mm or on bags 50 mm × 56 mm, especially fabricated for leaching studies in hydrocarbon solvents. PVC sheets were cleaned thoroughly by rinsing with a 0.5% non-toxic grade soap solution (Laxbro, India) for 3 min, then washed in running tap water for nearly 5 min and finally rinsed with distilled water for another 10 min. The sheets were then rinsed with Analar grade methanol (Glaxo, India) for 15 sec and dried in a vacuum oven for 30 min at 50 to 55° C. The monomers HEMA and NVP (BDH, UK) used in all of the experiments were distilled under vacuum before use. The purity of the monomers was checked using infrared spectroscopy (model 597, Perkin–Elmer) and high-performance liquid chromatography (Waters Associates, USA). No additional cross-linker was added during the experiments.

Preweighed specimens were then immersed in 20 ml monomer solutions of different concentrations containing 0.005 M copper sulphate (Analar grade; Glaxo, India) taken in test tubes and degassed with nitrogen for nearly 3 min. The samples were then irradiated using a cobalt-60 source for various doses. After irradiation, the samples were taken out, washed for 24 h with frequent changes of the deionized water, rinsed in methanol for 15 sec and dried in a vacuum oven and weighed. The percentage graft yield was then calculated using the expression

$$\text{Graft yield} = \frac{\text{Weight of grafted polymer} - \text{Weight of ungrafted polymer}}{\text{Weight of grafted polymer}} \times 100\%$$

A Perkin–Elmer infrared spectrophotometer with ATR accessory was used to record the spectrum of the grafted surface. The samples were placed on a KRS-5 crystal and the spectra were recorded with the incidence angle of the infrared beam at 45°. The morphology of the grafted and ungrafted surfaces were further examined under a scanning electron microscope (SEM; Cambridge, UK). Samples were sputter coated with silver and examined at an accelerating voltage of 20 kV. Phase-contrast optical microscopy (Nikon, Japan) was also used to study the surface morphological changes.

Captive air-in-water and octane-in-water techniques [33] were used to measure the contact angles to determine the polar and dispersion components of surface energy of the ungrafted and grafted surfaces. A Rame'Hart contact-angle goniometer was used for all contact angle measurements. All samples were equilibrated overnight in distilled water before they were subjected to measurements. The values reported are the average of six measurements on each sample. Surface energy parameters were calculated using the method of Andrade *et al.* [33].

Migration studies of DEHP in hydrocarbons such as n-hexane were carried out at 30° C using specially fabricated bags. The inner surface of the bag was grafted by filling the bag with the monomer solution containing 0.005 M Cu^{2+} and irradiating it at 0.5 Mrad. The bags were then washed free of the monomer, homopolymer, etc., as described above and the dried bag was filled with 20 ml migration medium for leaching experiments. Aliquots of 100 μl were withdrawn at intervals of 1, 2, 3, 4 and 5 h. An ungrafted bag filled with the same medium served as the control. The solvent was evaporated completely and the residue was dissolved in spectroscopic grade methanol, absorbance being measured at 274 nm using an ultraviolet–visible region spectrophotometer (Model 240; Shimadzu, Japan), where the plasticizer has a characteristic maximum (Fig. 1). The amounts of DEHP leached out into the medium at specific intervals were then calculated from a calibration curve for DEHP in methanol.

The amount of plasticizer migrated into cotton seed oil and PEG-400 was determined by calculating the percentage loss of weight after specific intervals. Strips of control (ungrafted) and grafted material were immersed in 20 ml medium at 70° C and the preweighed samples were removed at intervals of 24, 48, 72 and 96 h, washed with 0.5% soap solution for 5 min, rinsed with methanol and diethylether (Analar grade, Glaxo, India) for 15 sec each to remove the surface adhering oil, dried in a vacuum oven at 60° C for 60 min and weighed. Washing and drying were repeated until constant weight was achieved. The percentage loss of weight of plasticizer was then calculated.

Since the grafting medium contained Cu^{2+} at a concentration of 0.005 M, which was incorporated to

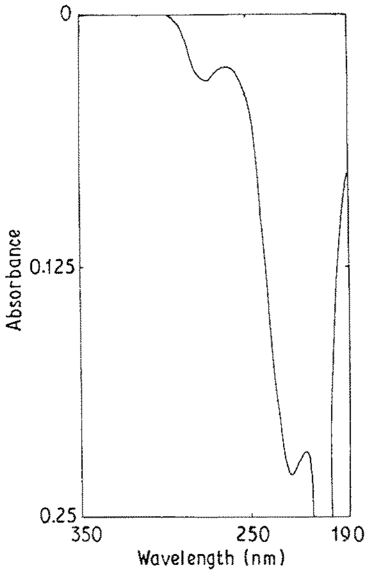


Figure 1 Characteristic ultraviolet absorption spectrum for DEHP in methanol. The absorption maximum at 274 nm was chosen for all DEHP estimations in migration studies.

prevent homopolymerization of the monomer, the residual copper content in the grafted polymer had to be determined in order to assess whether it was below toxic levels. This was carried out per the recommended procedure of Department of Health and Social Security, UK [34]. Grafted sheets of area 1250 cm^2 were autoclaved in doubly distilled water at 120 to 123° C at 14 to 15 p.s.i. (97 to 103 kPa) pressure for 20 min and the resultant extract was analysed for copper ions, using an atomic absorption spectrophotometer (Instrumentation Labs, USA; Model 551). The amount of copper ions estimated in parts per million (p.p.m.) was compared with the acceptable values reported.

3. Results and discussion

HEMA and NVP monomers were used in various proportions in the grafting experiments. The percentage graft yield value is found to increase proportionately with monomer concentration in all of the three different systems studied (NVP : HEMA = 25 : 75, 50 : 50 and 75 : 25 (all vol/vol %)). An increase in concentration of NVP in the monomer mixture, however, did not result in any significant change in the graft yield values over the concentrations examined. The results are shown in Fig. 2. No homopolymerization was observed in any of the systems studied, due to the presence of cupric ions in the reaction medium. Previous studies have indicated that cupric ions in the reaction medium completely inhibited homopolymerization in the grafting of hydrophilic monomers to various polymer substrates [35].

Increasing the radiation dose from 0.25 to 0.75 Mrad was also found to increase the graft yield substantially in a linear fashion for the N50–H50 system of all four concentrations studied (Fig. 3). With increasing graft yields, the sheets tend to become stiffer in the dry state and tend to curl up at concentrations above 5% (v/v) when irradiated at a dose of 0.5 Mrad or above. Another interesting observation was that optical clarity (transparency) increased with increasing NVP content, whereas a higher HEMA content in the system tended to make the sheets more opaque in all of the concentrations studied.

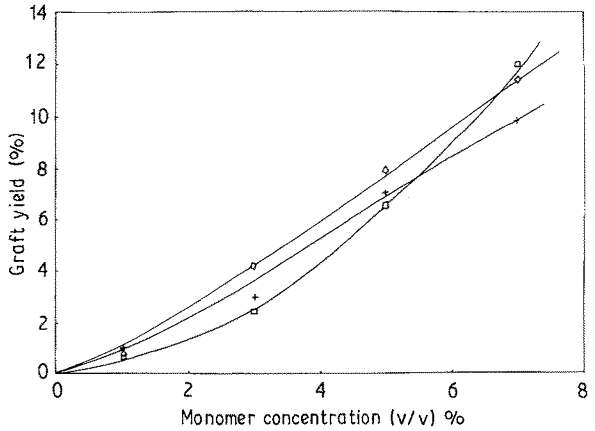


Figure 2 Increase in percentage graft yield on PVC sheets plotted against monomer concentrations used for grafting at a radiation dose of 0.25 Mrad. NVP : HEMA = (□) 25 : 75, (+) 50 : 50 and (◇) 75 : 25 (Standard deviations were within 10% and are not known due to overlapping).

The ATR-IR spectra of the grafted surface indicated the absence of the characteristic 1725 cm^{-1} strong band of the –C=O group in the plasticizer. It is substituted by the weak doublet at 1710 and 1730 cm^{-1} characteristic of the carbonyl functions present in NVP and HEMA polymers (Fig. 4). The 1440 cm^{-1} peak is also characteristic of poly(HEMA) and the 1640 cm^{-1} peak is characteristic of poly(NVP). The scanning and phase-contrast optical photomicrographs of the grafted and the ungrafted surfaces of PVC are shown in Figs 5 and 6. It can be seen that the fine layer of graft at the surface alters the morphology of the surface significantly.

The surface energy parameters of the modified and unmodified surfaces are listed in Table I. The hydrophilic nature of the modified surfaces are indicated by the sharp increase in the polar component value (γ^p_{sv}) and decrease in the dispersion component (γ^d_{sv}) for all of the systems. The γ_{sw} value decreases to less than unity even at 1% monomer concentrations in all three systems where the graft yields and the graft water contents are relatively low. The values are very close to zero at 5 and 7% monomer concentrations and, per the minimal interfacial energy hypothesis of Andrade

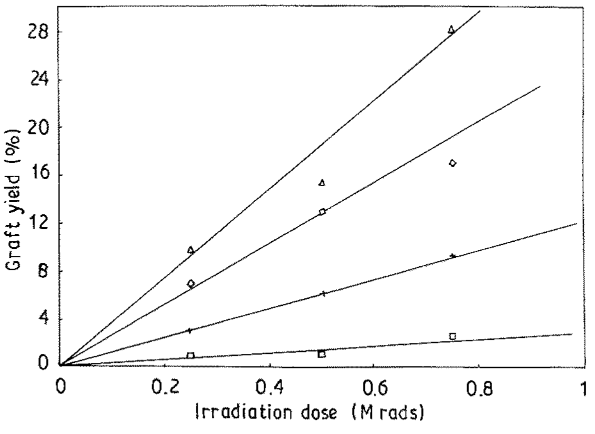


Figure 3 Changes in the percentage graft yield observed on PVC sheets with different radiation doses. NVP : HEMA = 50 : 50; (□) 1, (+) 3, (◇) 5 and (△) 7 vol %.

TABLE I Contact angle and surface energy parameters*

Material	θ_{air}	ϕ_{octane}	γ_{sv}^{d}	γ_{sv}^{p}	γ_{sv}	γ_{sw}†
Ungrafted PVC	60.60	94.86	32.07	14.86	46.93	11.60
1 vol % N25–H75	29.42	158.67	16.15	47.10	63.25	0.45
1 vol % N50–H50	33.08	154.58	15.34	45.73	61.07	0.66
1 vol % N75–H25	29.25	152.92	12.21	45.10	57.31	1.48
3 vol % N25–H75	40.33	165.08	8.92	48.81	57.73	2.77
3 vol % N50–H50	35.92	162.83	11.66	48.28	59.94	1.55
3 vol % N75–H25	32.08	157.58	15.01	46.75	61.76	0.67
5 vol % N25–H75	26.10	139.50	26.63	39.11	65.74	0.99
5 vol % N50–H50	22.50	154.10	21.16	45.58	66.74	0.13
5 vol % N75–H25	20.30	151.00	23.48	44.39	67.87	0.24
7 vol % N25–H75	19.17	162.08	20.08	48.08	68.16	0.06
7 vol % N50–H50	0	165.83	23.17	48.97	72.14	0.04
7 vol % N75–H25	0	180.00	21.60	50.50	72.10	0

*All contact angle values are average of six observations. Standard deviations were within ±5%.

†All units in erg cm^{-2} (1 erg cm^{-2} = 1 mJ m^{-2}).

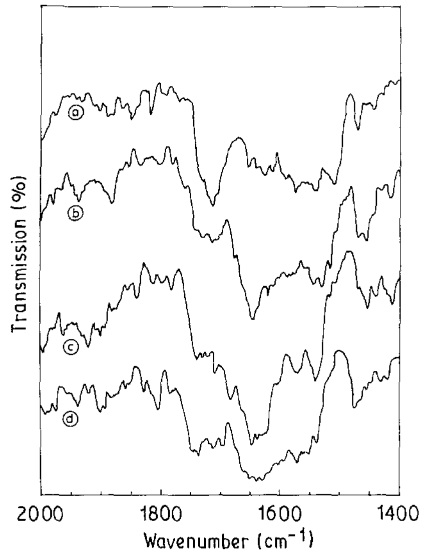


Figure 4 Attenuated total reflectance (ATR) spectra of ungrafted and grafted PVC sheets. (a) Ungrafted, (b) N25–H75 system, (c) N50–H50 system and (d) N75–H25 system. The monomer concentration used in all cases for grafting was 5 vol %.

et al. [33], the protein adsorption should be very low and highly reversible, favouring the material for blood contact applications. However, the γ_{sv} and γ_{sw} values have to be determined by measuring the contact angles with solutions of physiological ionic strength buffered to pH 7.4 before any firm conclusions on protein adsorption and blood compatibility can be drawn. Increasing the NVP content in the monomer systems resulted in lower θ_{air} and higher ϕ_{octane} values, showing a higher degree of hydrophilicity as expected, which is substantiated by decrease in γ_{sw} and increase in γ_{sv}^{p} values. However, the total surface energy values (γ_{sv}) do not seem to show appreciable changes.

The migration behaviour of DEHP in an organic solvent such as n-hexane stored in grafted and ungrafted bags shows a drastic change for all three systems (Figs 7 to 9). The amount of DEHP migrated in the control bag within 5 h is so high (nearly 250 mg) that Fickian behaviour does not hold true for this system, as evidenced by Fig. 10.. The amount that is leached out into n-hexane in modified bags for the N25–H75 and N75–H25 systems is < 20 mg even after 5 h (where grafting concentrations of more than 1% (v/v) have been used), whereas it was as low as 3 to 20 mg in the case of the N50–H50 system. This is only about 2 to 4% of the amount shown by the unmodified bags, which is a drastic reduction in the migration of DEHP. Reduction in leaching was also observed in bags grafted with 1% monomer, but to a slightly higher degree than where higher concentrations of monomer were employed for grafting. All of the grafted bags showed Fickian migration behaviour (Fig. 10), indicating that the migration was diffusion controlled, whereas it was non-Fickian in the case of ungrafted bags. The reason for this drastic reduction in migration in other cases, especially the N50–H50 system, can be attributed to the fact that, in the

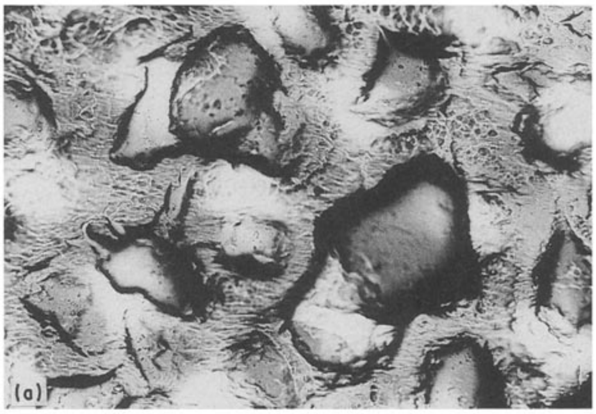
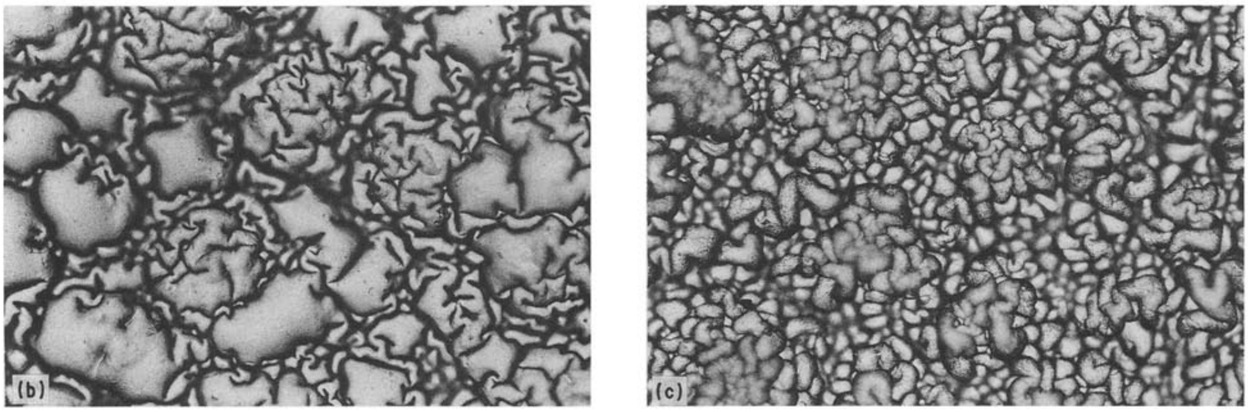


Figure 5 Optical phase contrast photomicrograph of PVC surface grafted using 5% monomer concentration at different NVP : HEMA combinations at 0.25 Mrad: (a) N25 : H75, (b) N50 : H50 and (c) N75 : H25.



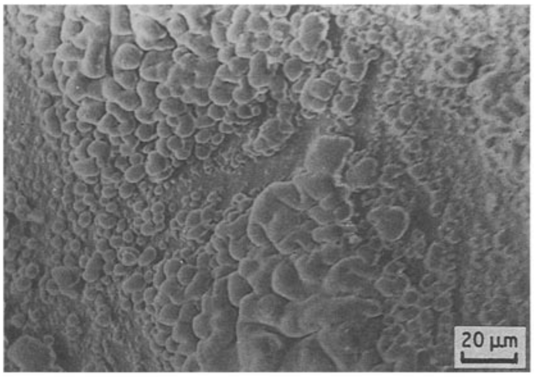


Figure 6 Scanning electron photomicrograph of PVC surface grafted using a 5% monomer concentration (N50:H50) at 0.25 Mrad.

presence of non-polar organic solvents, the hydrophilic network at the surface of the PVC tend to shrink and form a very tightly closed network. However, this does not mean that migration will be faster in polar solvents, as the migration behaviour is also strongly dependent on other factors such as the solubility of the plasticizer in the medium, the temperature, etc.

The N50–H50 system was further chosen (due to its low migration in hexane) to study the behaviour of migration of DEHP in other hydrocarbon solvents such as n-heptane and n-octane, and for accelerated leaching in cotton seed oil and PEG-400, which have been used as simulated biological test extractants for toxicity testing [36]. The leaching behaviour in n-heptane and n-octane was found to be very similar to that in hexane (Fig. 11) for the system studied (5% (v/v)). Fig. 12 illustrates the behaviour of migration into cotton seed oil and PEG-400 from grafted and ungrafted bags at 70° C monitored over a period of 96 h. Ungrafted bags showed a loss of nearly 15 to 20% of the DEHP content after 96 h in both media, whereas grafted sheets did not show any loss of weight in cotton seed oil after 96 h. Grafted sheets showed migration in PEG-400, but to a lesser extent than control after 96 h. The migration phenomena shown in cotton seed oil is extremely interesting and the only reason that can be attributed at present is the same that has been projected in the case of n-hexane. PEG-400, being highly polar and highly miscible with DEHP, may have relaxed the hydrophilic network at the surface to permit migration.

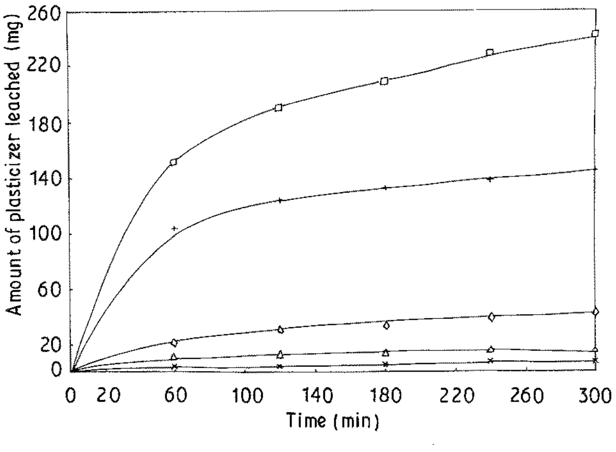


Figure 7 Comparison of the amount of DEHP migrated into n-hexane at 30° C from grafted and ungrafted bags. (□) Ungrafted surface, (+) surface grafted with 1% monomer, (◇) surface grafted with 3% monomer, (△) surface grafted with 5% monomer and (×) surface grafted with 7% monomer. HEMA:NVP = 25:75 was used for grafting in all cases.

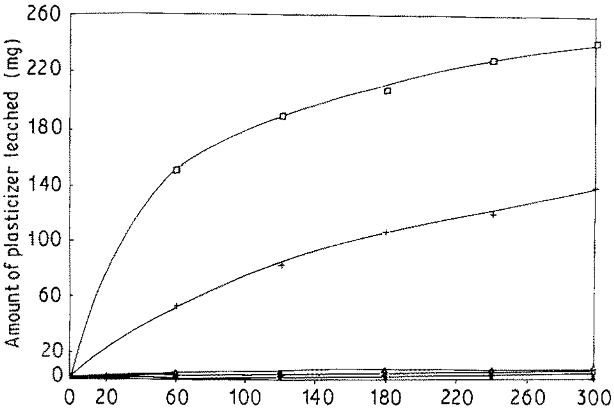


Figure 8 Amount of DEHP migrated into n-hexane at 30° C from grafted and ungrafted bags compared for the N50–H50 system. (□) Ungrafted surface, (+) surface grafted with 1% monomer, (◇) surface grafted with 3% monomer, (△) surface grafted with 5% monomer and (×) surface grafted with 7% monomer.

Increasing the radiation dose also was found to reduce the migration of DEHP for the system studied (5% (v/v)) (Fig. 13). A dose of 0.5 Mrad seems to be optimum for grafting, as it was found to bring the amount of DEHP leached to well below 5% of the control value. Increasing the dose to 0.75 Mrad did not seem to make any appreciable change in the migration.

The atomic absorption estimation of residual copper ion content on the grafted sheets indicated the presence of only 0.25 p.p.m. Cu^{2+} in the aqueous extract, which is well below the acceptable level of 1 p.p.m. This showed conclusively that the use of this metal ion in solution at the concentrations employed for grafting NVP and HEMA combinations on to PVC are acceptable from a toxicological standpoint to prevent homopolymerization of the monomers during grafting.

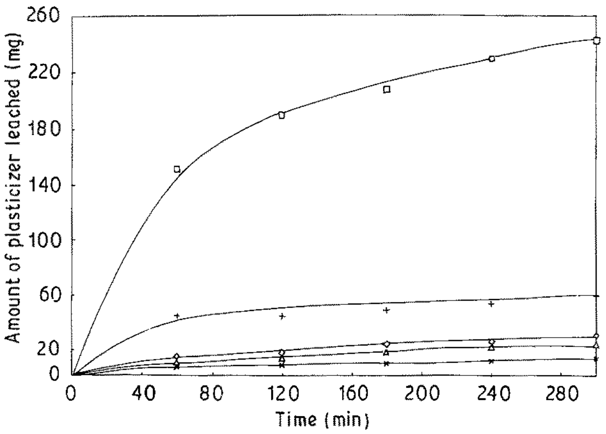


Figure 9 Amount of DEHP migrated into n-hexane at 30° C from grafted and ungrafted bags compared for the N75–H25 system. (□) Ungrafted surface, (+) surface grafted with 1% monomer, (◇) surface grafted with 3% monomer, (△) surface grafted with 5% monomer and (×) surface grafted with 7% monomer.

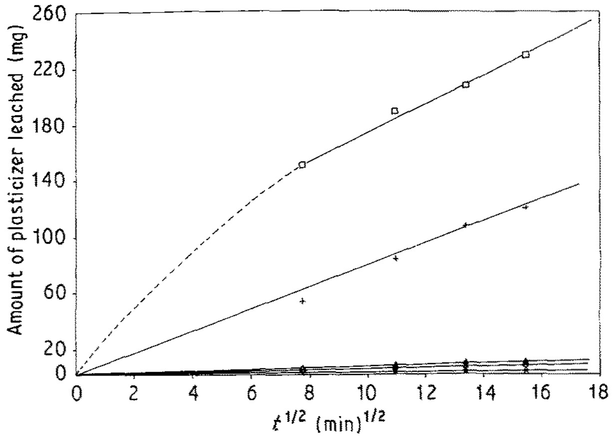


Figure 10 Amount of DEHP migrated plotted against the square root of time for the N50–H50 system, showing the Fickian behaviour of the grafted sheets. (□) Ungrafted surface, (+) surface grafted with 1% monomer, (◇) surface grafted with 3% monomer, (△) surface grafted with 5% monomer and (×) surface grafted with 7% monomer.

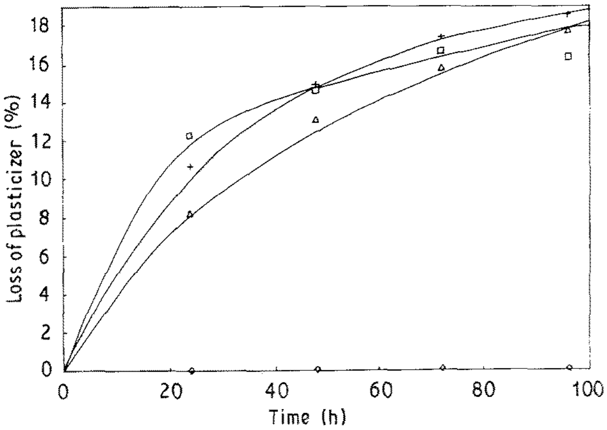


Figure 12 Percentage loss of plasticizer from PVC sheets grafted (0.25 Mrad) using a 5% monomer concentration (N50:H50) at 70° C in cotton seed oil and PEG-400. (□) Cotton seed oil (control), (◇) cotton seed oil (grafted), (+) PEG-400 (control) and (△) PEG-400 (grafted).

Further work on the migration behaviour of DEHP into physiological media such as plasma, blood, etc., and the blood compatibility of the grafted surfaces is in progress and will be reported later.

4. Conclusions

Hydrophilic monomers such as HEMA and NVP can be conveniently grafted on to plasticized PVC by gamma irradiation. The graft yield is found to vary linearly with the monomer concentration and the irradiation dose.

The PVC surface assumes hydrophilic character when modified with even 1% (v/v) monomer combinations of HEMA and NVP, as evidenced by the low γ_{sw} values, low γ_{sv}^{d} values and high γ_{sv}^{p} values. The low interfacial energy exhibited by the grafted surface may make it more blood compatible than unmodified PVC surfaces.

Migration of the plasticizer DEHP from modified bags into organic media is only 2 to 4% of the amount migrated from unmodified bags. A monomer concentration of 5 to 7% seems to be optimum for grafting, as they tend to show minimal leaching. The Fickian behaviour exhibited by all grafted systems indicates that the migration is diffusion controlled, whereas with unmodified samples it exhibits non-Fickian character.

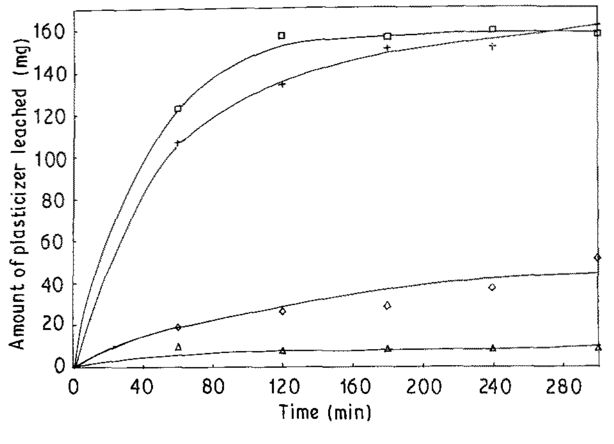


Figure 11 Migration behaviour of DEHP in n-heptane and n-octane from grafted and ungrafted PVC bags at 30° C. The results are shown for 5% monomer concentration of the N50–H50 system. (□) (control), (◇) n-heptane (grafted), (+) n-octane (control) and (△) n-heptane (control) (grafted).

Leaching in cotton seed oil is totally absent, whereas in PEG-400 the behaviour is more similar to that of the control. This seems to suggest a dual character of polarity and solubility of plasticizer in the medium competing for dominance, which may be the determining parameter in deciding the migration behaviour.

The residual copper ion concentration in grafted polymer is well within the safety limits recommended for blood contact applications. The incorporation of cupric ions thus prevents homopolymerization and facilitates cleaning procedure of the grafted material to a great extent.

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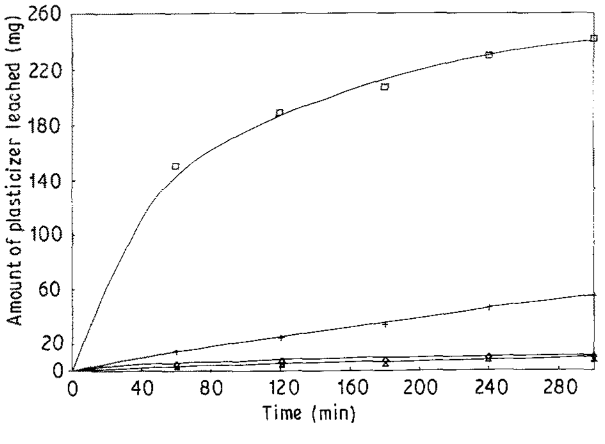

Figure 13 Migration of DEHP into n-hexane with time from PVC sheets grafted using 5% monomer (N50:H50) concentration at various radiation doses. (□) Ungrafted, (+) 0.25 Mrad, (◇) 0.5 Mrad and (△) 0.75 Mrad.

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The above work will form part of the PhD thesis of one of the authors (V.K.K.).

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