Studies on the Sorption of Lipids in Segmented Polyurethanes. II. Effect of Hard-Segment Content

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SYNOPSIS

Diffusion and absorption, of a few representative components found in blood, in segmented polyurethane are studied. The absorption of the components, confined to the soft segment, is found to be Fickian. Both diffusion coefficients and equilibrium absorption was found to decrease with % hard-segment content. An empirical equation has been proposed to visualize the absorption behavior with soft/hard-segment content.

INTRODUCTION

Segmented polyurethanes, due to the unique properties arising from the phase segregation, are one of the widely sought materials for medical applications.[1-4] Largely due to the extensive blood contacting applications, the behavior of this class of materials in the bioenvironment has been a subject of wide attention.[5-7] One aspect that has seldom been addressed in this connection is the diffusion of small molecules found in body fluids. Recently, Hyashi et al.[8] and Takahara et al.[9] reported the absorption of lipids by polyurethanes and the consequent alteration in the mechanical characteristics of the materials. Lipid absorption has also been hypothesized as a causative factor of the calcification of polyurethanes.[10,11]

Diffusion of small molecules, largely organic vapors and gases, through segmented polyurethanes in order to understand the structural intricacies of the materials has been reported.[12-14] Gases are often chosen for the diffusion studies since they scale with microdomains of the polymers. Our understanding, however, on the combined morphology and the diffusion of biological components is scanty. The aim of the present work was to understand the diffusional behavior of some of the representative components found in blood through segmented polyurethanes based on methylene bis(*p*-cyclohexyl isocyanate) in connection with the microstructure.

EXPERIMENTAL

Materials

The soft segment of the polymers used in this study consists of a 990 molecular weight poly(tetramethylene glycol) (PTMEG) and the hard segment consists of methylene bis(2-cyclohexyl isocyanate) (H_{12}MDI) and 1,4-butanediol (BD). By varying the molecular composition of H_{12}MDI/BD/PTMEG, polymers having varied hard/soft segments were synthesized. The synthesis and characterization of the polymers were detailed in Part I of this study.[15] The relevant parameters are summarized in Table I.

Stearic acid, methyl palmitate, butyl oleiate, triolein, cholesterol, and cholesteryl acetate (all from Sigma) was used as representative diffusants. GLC-grade silicone oil (BDH, Poole, UK) was used for dissolving the components.

A Model 597 Perkin-Elmer IR spectrophotometer was used for recording IR spectra using a matched pair (0.2 mm) of NaCl cells. A Model 35A Nikon optical microscope was used for obtaining the optical microphotographs.

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Table I Relevant Parameters of the Polymer

Polymer	HS Content (%)	Glass Transition Temperature (T_g °C)	M_w	M_n	$D(M_w/M_n)$
PU-0	0	−71	2,02,000	1,00,000	2.02
PU-1	23	−53	2,10,000	1,05,000	2.01
PU-2	33	−42	2,32,000	1,09,000	2.12
PU-3	47	−31	1,63,000	87,000	1.87
PU-4	66	—	1,83,000	84,700	2.16
PU-5	100	—	83,000	37,200	2.23

Silicone oil was used as the medium for dissolving the components as well as for performing the diffusion studies. The extent of diffusion of the components through the polymers was slow, and largely due to this, immersion and weighing rather than the permeation method was adopted for the experiment.[16] Rectangular polymer strips having a 2 cm^2 area and 0.4–0.41 mm thickness were conditioned in silicone oil for several days at the experimental temperature (37°C). These strips after pressing between filter paper, for removing the adhered silicone oil, were weighed and immersed in silicone oil solution containing blood fluid model components at 37°C. At a definite time interval, the strips were taken, pressed in between filter paper, and weighed. The experiments were continued until equilibrium weight was attained. All the diffusion studies were performed at static conditions. Alternatively, IR spectral analysis was also used for estimating the amount of diffusant diffused.

Estimation of Diffusion Coefficient (D)

The diffusion process is quantitatively expressed by Fick's Second Law[16]:

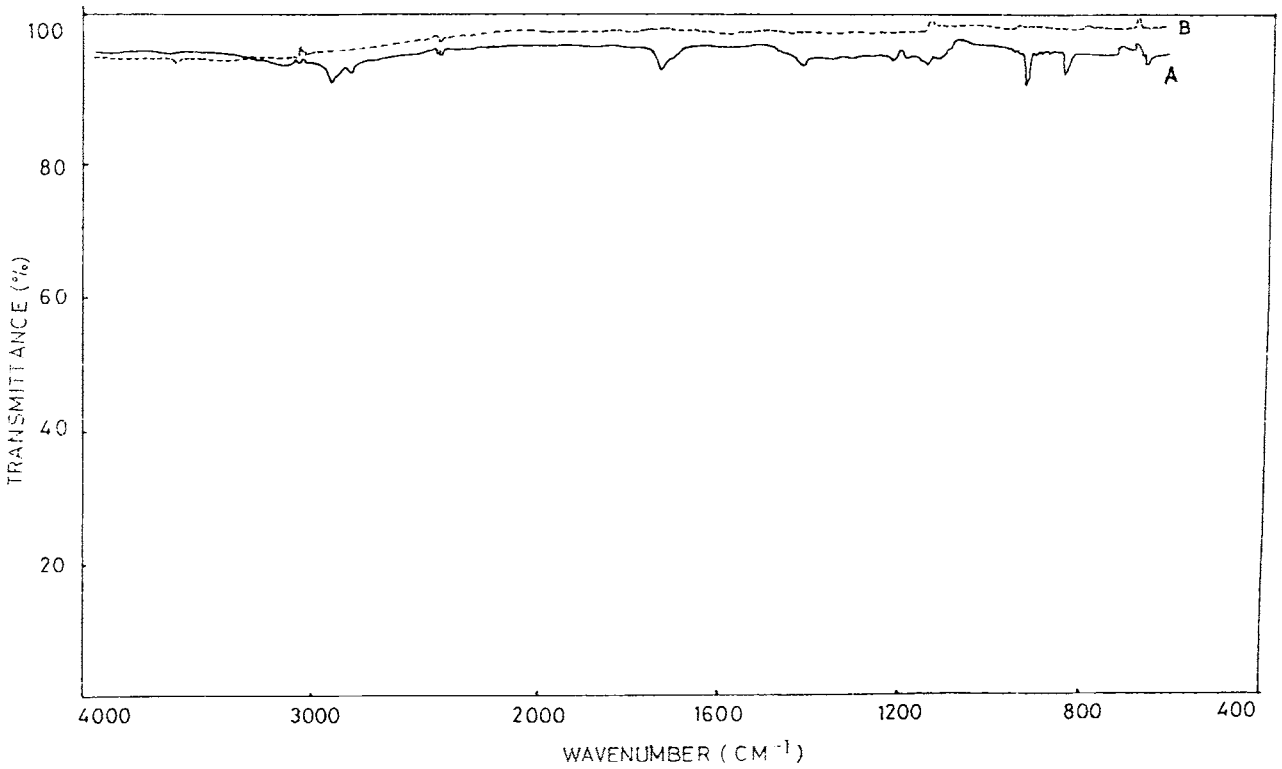

Figure 1 (A) A typical IR-spectrum of carbon tetrachloride extract of PU-2. (B) IR spectrum of CCl4 extract of PU-2 vs. the same solution in the reference.

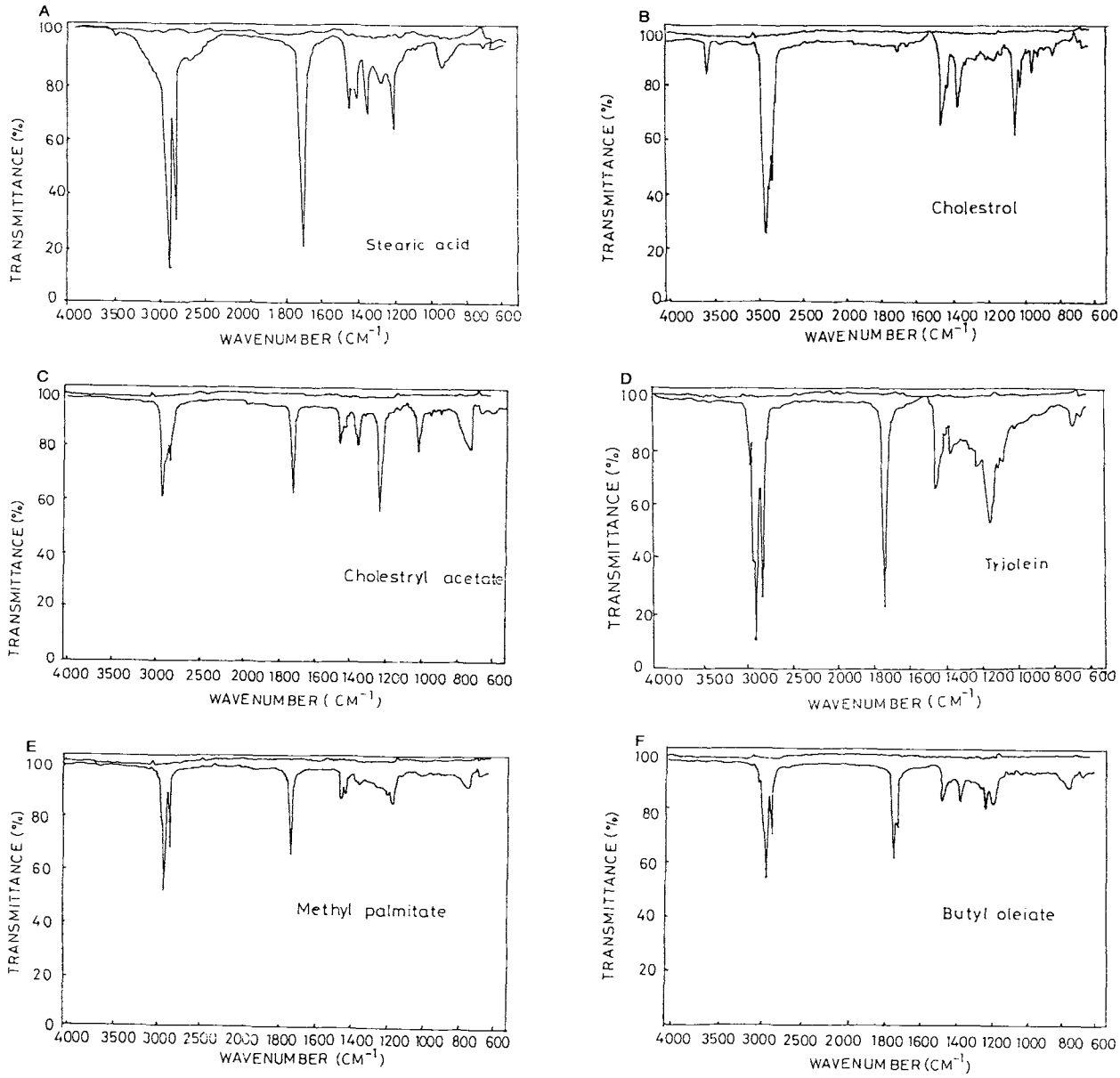

Figure 2 (A) IR spectrum of stearic acid extracted from PU-2. (B) IR spectrum of cholestrol extracted from PU-2. (C) IR spectrum of cholesteryl acetate extracted from PU-2. (D) IR spectrum of triolein extracted from PU-2. (E) IR spectrum of methyl palmitate extracted from PU-2. (F) IR spectrum of butyl oleiate extracted from PU-2.

$$\frac{dc}{dt} = \text{div}(D \text{ grad } C) \qquad (1)$$

where C is the local concentration of the diffusant; t, the time, and D, the diffusion coefficient. Assuming D is constant, independent of the diffusant concentration, a solution to eq. (1) in terms of $M(t)$ (mass uptake at t) is

$$M(t) = 2M_\infty (Dt/L^2)^{1/2} \times \{1/\pi^{1/2} + 2\Sigma_{m=0}^{\infty}(-1)^n \text{ erfc } [nL/(Dt)^{1/2}]\} \qquad (2)$$

where M_∞ is the amount of diffusant absorbed as $t \rightarrow \infty$ and L is the thickness. The form of this equation suggests that a plot of fractional equilibrium uptake, Mt/M_∞ vs. $t^{1/2}$, should be linear at small times and the diffusion coefficient can be calculated from the initial slope. At larger time intervals, another solution to eq. (1) is preferred for the calculation:

$$Q(t) = 1 - (8/\pi^2)\Sigma_{m=0}^{\infty}\{[1/(2m+1)^2] \times \exp[-D(2m+1)^2\pi^2 t/4L^2]\} \qquad (3)$$

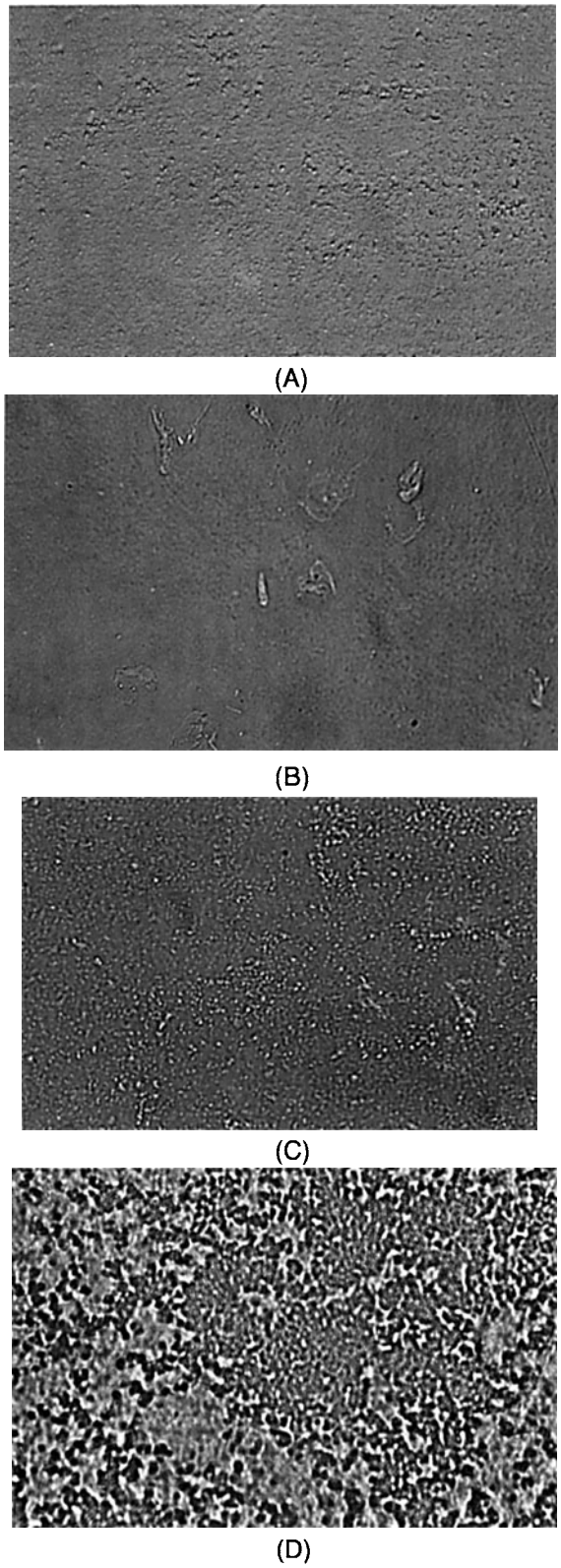

Figure 3 (A) Phase contrast optical micrograph of PU-2. (B) Optical micrograph of PU-2 recovered from cholesteryl acetate solution. (C) Optical micrograph of PU-2 from cholesterol solution. (D) Optical micrograph of PU-2 from stearic solution.

where $Q(t)$ is the mass uptake at time t, which reduces to $\ln[1 - Q(t)] = \ln(8/\pi^2 + (-D/\pi^2 t/4L^2)$ as $t \rightarrow \infty$. Thus, a plot of $\ln(1 - Q(t)$ vs. t should be linear at larger time intervals and, again, the slope is proportional to the diffusion coefficient. Throughout this study, we used the first eq. (2) for estimating D since both these equations gave the same values for D.

RESULTS AND DISCUSSION

In Figure 1(A) is shown a representative infrared spectrum of carbon tetrachloride extract of polyurethane (PU-2) conditioned in silicone oil vs. carbon tetrachloride. The spectrum shows weak absorption bands at the characteristic regions of polyurethane and silicone oil, indicating extraction of the polymer by carbon tetrachloride of presumably oligomeric species and slight absorption of silicone oil by the polymer. Figure 1(B) illustrates the spectrum of silicone oil-conditioned PU-2 extract vs. the same solution in the reference cell. Cancellation of absorption peaks are evident from the spectrum. For recording the spectra of extracts of polymers kept in solution containing the model components, extract of the same polymers strips kept in silicone oil were used as reference. Figure 2(A)–(F) shows the spectra of carbon tetrachloride extract of PU-2 kept in a silicone oil solution of stearic acid, cholesteryl acetate, cholesterol, triolein, methyl palmitate, and butyl oleiate, respectively. All these spectra show characteristic peaks of these components, indicating their diffusion into the bulk of the material.

Figure 3(A) depicts the phase contrast optical microphotograph of a thin slice of PU-2 material kept in silicone oil. Figure 3(B)–(D) are the microphotographs of PU-2 kept in the solution of cholesteryl acetate, cholesterol, and stearic acid recorded in similar fashion. The white patches in the respective photos could be the diffused species, and the concentration of these patches appears to be in the order of steric acid > cholesterol > cholesteryl acetate, which, in fact, agrees well with the equilibrium absorption of these components (See Table III). The spectra and photographs apparently indicate the diffusion of the components deep into the bulk of the polymers.

Diffusion Coefficients

Typical Mt/M_∞ vs. $t^{1/2}$ plots are shown in Figures 4(A) and (B). The Fickian nature of the absorption

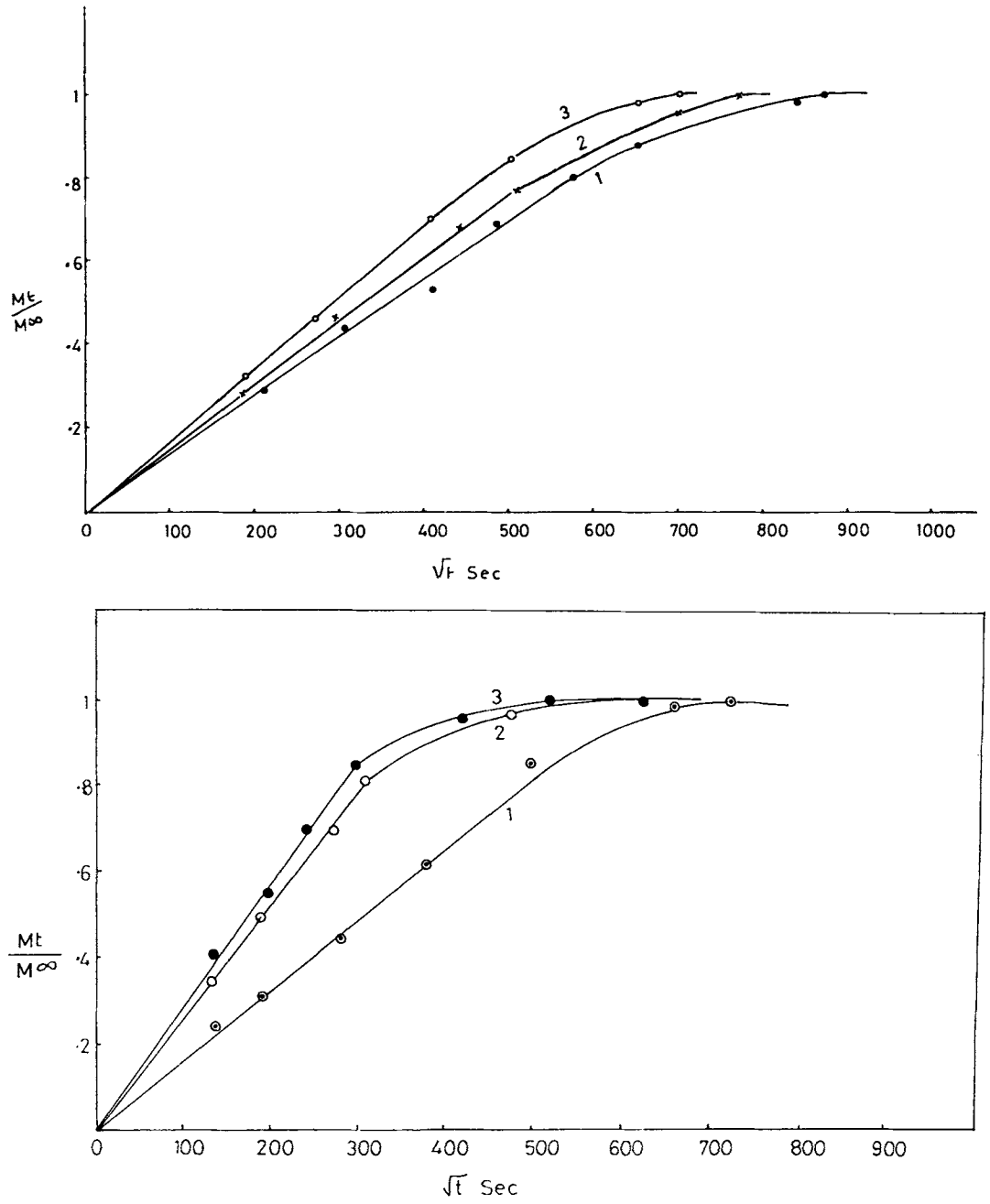

Figure 4 (A) Typical Mt/M_∞ vs. $t^{\frac{1}{2}}$ plots of (1) cholesteryl acetate, (2) cholesterol, and (3) stearic acid in PU-2. (B) Mt/M_∞ vs. $t^{\frac{1}{2}}$ plots of (1) triolein, (2) butyl oleiate, and (3) methyl palmitate in PU-2.

is apparent from these plots. The diffusion coefficient (D) estimated from the initial slope of these plots are summarized in Table II. The diffusion coefficients were found to be independent of the concentration of the diffusants and the thickness of the polymer strip. Zentner et al. reported 0.474×10^{-9} cm^2/s as the diffusion coefficient of progesterone in biomer,[17] a polyurethane, based on MDI, PTMEG, and chain extended by ethyldiamine. Although the present system is different from the reported one,[17] the diffusion coefficients obtained for the steroids are comparable.

It is interesting to see that the diffusion coefficient of a given component, e.g., cholesterol, decreases with % hard-segment (HS) content. D sharply decreases from 100% soft-segment (SS) material to

Table II Variation of Diffusion Coefficient with HS Content at 37°C

Component	Diffusion Coefficient in ($cm^2/s \times 10^9$)					
	PU-0	PU-1	PU-2	PU-3	PU-4	PU-5
Stearic acid	4.87	3.41	2.37	2.01	1.17	—
Cholesteryl acetate	3.37	1.35	0.72	0.57	—	—
Cholesterol	3.83	1.62	1.16	0.63	—	—
Triolein	1.98	0.73	0.56	0.42	—	—
Methyl palmitate	4.38	2.13	1.77	1.18	—	—
Butyl oleiate	3.91	2.01	1.62	0.98	—	—

zero in 100% HS material. In other words, 100% HS material is impermeable to any of the diffusants. Unlike gases and organic vapors, the components studied here are bulky and need more space for their permeation. The unavailability of sufficient space in the HS hinders the diffusion process.

Diffusion in block polymers are known to be affected tremendously by the presence of domains, by the extent and orientation of the domains, and also by the nature of the interfacing region.[18] The presence of impermeable hard domains increases the tortuousity, thereby decreasing the diffusion. Further, dispersed hard domains act as physical crosslinks restricting the SS movement, affecting unfavorably the permeation. The restricted movement can increase the length of the "path of least resistance" of the rigid molecules like cholesterol, which certainly brings down the diffusion coefficient manyfold.

Table III summarizes the equilibrium absorption of the components in the polymers. The absorption also decreases with % HS content. Figure 5 shows the IR spectra of stearic acid extracted from polymers having varied hard/soft-segment content. Apparently, the figure shows reduction in % absorption with % HS content. The variation in absorption may be fit into an empirial equation of the form

$$A = A_0(1 - e - X)^2 \quad (4)$$

where A_0 is a constant for a given component, A is the equilibrium absorption, and X is the fraction of SS. Assuming that the equation holds good for a given component in all the polymers, the constant A_0 was calculated using the absorption values of the diffusants in PU-0; the A_0 values thereby obtained are tabulated in Table IV. Using these A_0 values, the equilibrium absorption of diffusants in other polyurethanes having increased HS content were estimated, and these values are shown in Table IV. A graphical representation of % absorption vs. SS content is shown in Figure 6. The calculated absorption values closely agree with the experimental values in polymer having a higher % of SS (see Table III). However, the calculated absorption % deviates in polymers having more HS content. This could be due to the enhanced phase mixing with the % HS content, which thereby curtailed the SS mobility more than expected. An upward shift in the glass

Table III Effect of SS Content on the Equilibrium Absorption of Diffusents at 37°C

Component	% Absorption in					
	PU-0	PU-1	PU-2	PU-3	PU-4	PU-5
Stearic acid	5.85	4.24	3.35	2.27	0.85	0
Cholesteryl acetate	3.39	2.42	1.57	0.86	—	—
Cholesterol	3.92	2.90	2.04	1.26	—	—
Triolein	2.71	1.8	1.2	0.6	—	—
Methyl palmitate	1.9	0.9	0.73	0.42	—	—
Butyl oleiate	1.74	0.81	0.61	0.37	—	—

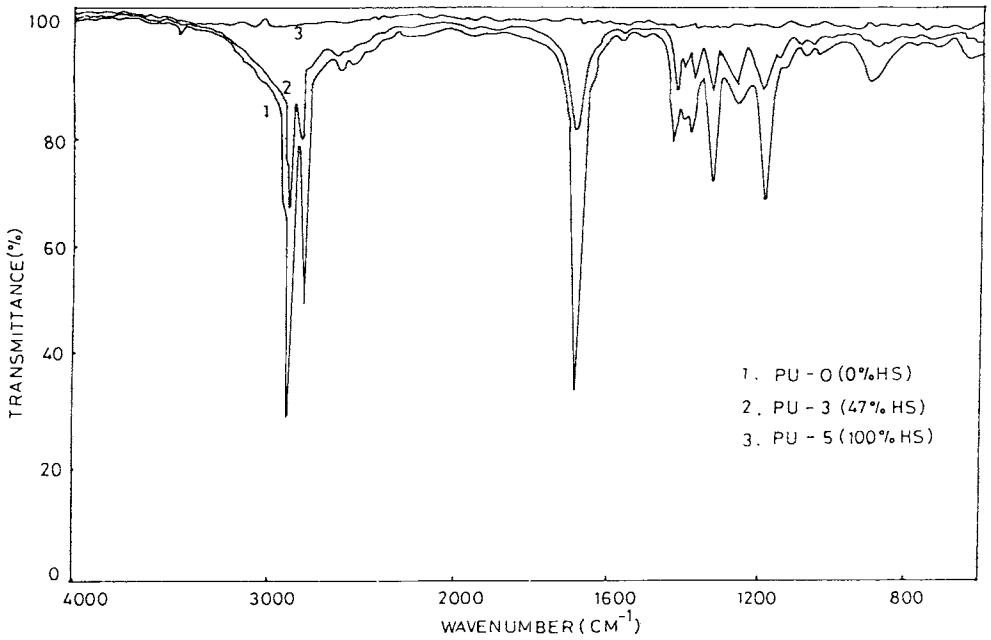

Figure 5 IR spectra of stearic acid extracted from (1) PU-0, (2) PU-3, and (3) PU-5.

transition temperature (T_g) of the SS with HS content (Table I) apparently indicates phase mixing.

To visualize the diffusion in multiphase polymers, an effective medium theory has been proposed.[19] This theory predicts the overall transport properties for randomly inhomogeneous systems and provides acceptable results when the ratios of the pure component diffusivities are large (> 100). It replaces an actual heterogeneous system that exhibits the same steady-state transport properties as does the original composite. The absorption of the components in the present case, however, were found to vary exponentially with SS content rather than linearly. This possibly indicates the presence of a significant interfacial region as well as phase mixing. Van Bogart et al. reported that H_{12}MDI HS inhibit SS crystallization to a greater extent than does MDI-based HS, suggesting that more HS are dispersed in the SS.[20] These authors further reported from small-angle X-ray scattering studies that H_{12}MDI HS are smaller and greater in number than is the MDI HS. More dispersed HS in the SS restricts the mobility of the SS and increases the viscosity of the SS. The increase in T_g of the SS with HS content also favors more phase mixing (see Table I).

Table IV % Absorption of the Components (Calculated)

Component	A_0	PU-1	PU-2	PU-3	PU-4
Stearic acid	14.64	4.22	3.49	2.48	1.21
Cholesteryl acetate	8.48	2.45	2.02	1.44	0.70
Cholesterol	9.81	2.83	2.34	1.66	0.81
Triolein	6.78	1.96	1.62	1.15	0.56
Methyl palmitate	4.75	1.37	1.13	0.80	0.39
Butyl oleiate	4.35	1.25	1.04	0.74	0.36

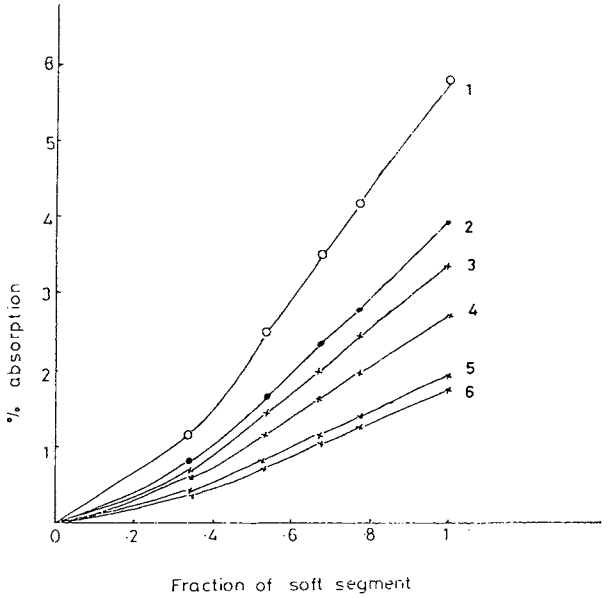

Figure 6 A graphical illustration of % absorption vs. fraction of soft segment. 1, stearic acid; 2, cholestrol; 3, cholestryl acetate; 4, triolein; 5, methyl palmitate; 6, butyl oleiate.

Apart from the polymer morphology, the extent of absorption is also governed by the nature of the diffusants, particularly the size and shape. Among the components studied, stearic acid diffuses more to all the polymers. In methyl palmitate and butyl oleiate, although smaller than steroids, the extent of absorption is rather low. This indicates that the thermodynamic aspects also have a major role. The solubility of these components in silicone oil is extremely high when compared to the other components, presumably due to the closeness in the solubility parameter. The components largely due to this prefer to be in the medium rather than diffusing into polyurethanes. It may be relevant to point out that the absorption of these components in silicone polymer is very high, again due to the closeness of the solubility parameter (unpublished results).

The empirical equation [eq. (4)] indicates possible absorption of all the components by polyurethanes having 66% HS content. However, actually only stearic acid is diffused to this material and all the remaining components are impermeable, reflecting inadequate space available for the diffusion.

CONCLUSION

The diffusion and absorption of components are confined to the SS region. With the increase of HS content, the extent of absorption was found to decrease exponentially, presumably due to more phase mixing.

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