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Effects of time, temperature, and sebum layer on migration rate of plasticizers in polyvinyl chloride products

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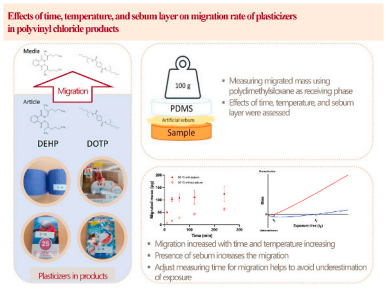
HIGHLIGHTS

- Dermal migration of plasticizers is affected by time, temperature, and sebum.
- Sebum should be considered when measuring dermal migration.
- Modification of measuring time with exposure scenario is needed.

GRAPHICAL ABSTRACT



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ABSTRACT

Large amounts of plasticizers, such as di(2-ethylhexyl) phthalate (DEHP) and dioctyl terephthalate (DOTP), are added to various polyvinyl chloride (PVC) products. To assess the human exposure to these plasticizers on using PVC products, it is important to know their migration rate. However, conventional migration tests conducted at a fixed time and temperature are often insufficient for determining possible variations in migration rates with respect to time, temperature, and sebum layer. In this study, the migration rates of DEHP and DOTP from five PVC products were measured using a polydimethylsiloxane (PDMS) sampler at different times and temperatures, in the presence and absence of artificial sebum. Although the migrated mass of the plasticizers increased over time, the average migration rate decreased. The average migration rates increased with increasing temperature and in the presence of an artificial sebum layer between the product and the PDMS sampler. When the artificial sebum layer was added, the average migration rate increased considerably by a factor of 1.5–14, suggesting that sebum should be considered to avoid the underestimation of dermal exposure to highly hydrophobic plasticizers, such as DEHP and DOTP. Based on the measured values, a conceptual analysis was conducted to quantitatively assess the difference in the migration rate of plasticizers caused by the difference between the time set for the migration test and the exposure time when the product is used. To reduce uncertainties and the potential underestimation of dermal exposure, an appropriate time for the experiment should be set to simulate the exposure scenario of a given product.

Abbreviations: DEHA, di(2-ethylhexyl) adipate; DEHP, di(2-ethylhexyl) phthalate; DINCH, 1,2-cyclohexane dicarboxylic acid diisononyl ester; DOTP, dioctyl terephthalate; PDMS, polydimethylsiloxane; PVC, polyvinyl chloride.

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1. Introduction

Phthalate plasticizers are commonly used in the manufacture of polyvinyl chloride (PVC) products to enhance their physical properties, such as durability and elasticity (Graham, 1973; Sperling, 2005). The use of low molecular weight phthalate esters has been banned since the 1990s because of their toxicity, and the use of di(2-ethylhexyl) phthalate (DEHP) has increased over the past decades (Gao et al., 2018). DEHP is a potential endocrine-disrupting chemical and affects child development, which has led to the replacement of DEHP with more benign additives (Kamrin, 2009; Matsumoto et al., 2008). Many alternatives, such as dioctyl terephthalate (DOTP), di(2-ethylhexyl) adipate (DEHA), and 1, 2-cyclohexane dicarboxylic acid diisononyl ester (DINCH), are used instead of DEHP (Nehring et al., 2020; Van Vliet et al., 2011). However, these alternatives cause reduced body weight gain or anti-androgenic effects in rats (Kwon and Ji, 2016). These phthalate plasticizers and alternatives are widely used in PVC products, including products for children, and their content has been quantified in several studies (Babich et al., 2020; Bouma and Schakel, 2002; Gill et al., 2010; Kim et al., 2020; Xie et al., 2016).

Human exposure to plasticizers occurs via dermal, oral, and inhalation pathways. In the case of dermal exposure, people touch the products directly, and plasticizers migrate out of the products and are absorbed through the epidermis. The migration rate is an important parameter for assessing exposure to plasticizers but has great uncertainty. The default values assumed in exposure models under various exposure scenarios are often insufficient for obtaining reasonable estimates of migration rate (Kim et al., 2020). To reduce these uncertainties, experimentally measured migration rates at a certain time and temperature may be used (Danish Environmental Protection Agency,). These experimental values are often three to five orders of magnitude lower than the default values used in consumer exposure models (U.S. EPA, 2019). However, the experimentally measured migration rates under one condition cannot be applied to other conditions because the migration rate is significantly affected by time, temperature, and the surrounding matrix (Gong et al., 2014; Zeng et al., 2019). A sebum layer on the surface of the human epidermis may affect the migration of lipophilic plasticizers because sebum contains lipids and its derivatives that act as carriers of these compounds (Frederiksen et al., 2016). Moreover, a large number of PVC consumer products are available in the market requiring the exposure assessment for plasticizers. Physicochemical parameters, such as the diffusion coefficient of plasticizers in PVC products and the activation enthalpy of diffusion, are also important for extending the limited experimentally measured migration rates to various exposure conditions using diverse consumer products.

In this study, the migration rates of two plasticizers DEHP and DOTP from five PVC products were measured using a polydimethylsiloxane (PDMS) passive sampler at 20, 40, and 60 °C, in the presence and absence of artificial sebum to evaluate the effects of time, temperature, and artificial sebum on migration rate. The diffusion coefficients (D) of DEHP and DOTP in PVC products were obtained by assuming one-dimensional Fickian diffusion. The activation enthalpy of diffusion was also obtained using D values at 20, 40, and 60 °C. To evaluate uncertainties associated with the time set for migration tests, a conceptual analysis was conducted to assess the underestimation or overestimation of dermal exposure to plasticizers for the given exposure scenarios, based on the experimentally measured migration rate at a fixed time.

2. Material and methods

2.1. PVC products

Five PVC products were purchased from online stores in 2020. They comprised a yoga mat (S-15), a steering wheel cover with two differently colored parts (S–17B for the black colored part and S-17R for the red colored part), two air-pumping children swimming pools (S-23 and S-24), and a swimming vest for children (S-25). Photos of the products were shown in Fig. S1. The DEHP and DOTP contents of the products were analyzed using a standard analytical method (U.S. Consumer Product Safety Commission, 2018). Shore hardness, tensile strength, and elongation of products were analyzed and the results are shown in Table S1.

2.2. Materials

DEHP (certified reference material grade) and DOTP (pharmaceutical primary standard grade) were purchased from Supelco (Bellefonte, PA, USA) and Merck (Kenilworth, NJ, USA), respectively. Fluoranthene-d_{10} was chosen as the internal standard for instrumental analysis and was purchased from Sigma-Aldrich (St. Louis, MO, USA). PDMS is widely used as a passive sampler for hydrophobic organic chemicals (HOCs) because it is nonpolar and diffusion of HOCs in PDMS does not limit the overall mass transfer (e.g., Kwon and Escher, 2008; Rusina et al., 2010). In addition, PDMS is not permeable to ionic constituents in the artificial sebum, making it an ideal sampler for plasticizers migrated from PVC products. PDMS sheets with a thickness of 1 mm and a density of 1.16 g cm^{-3} were purchased from Shielding Solutions Ltd. (Great Notley, UK). The sheets were cut into disks, using a hole punch with a diameter of 1 cm, which were then cleaned with n-hexane for 1 d, dried in a fume hood, and stored in methanol until use. The artificial sebum used in this study was composed of a mixture of lipids (124 mg of squalene, 250 mg of jojoba oil, 447 mg of triglyceride, and 170 mg of oleic acid) (Wertz, 2009), which were purchased from Sigma-Aldrich (St. Louis, MO, USA).

2.3. Measurement of migration of plasticizers from PVC products using PDMS sampler

Before measuring the migration of plasticizers, all sample products were stored in an incubator at 60 °C for 12 h to ensure that the plasticizers were distributed homogeneously in the PVC products. The PDMS disk was removed from methanol and dried quickly using a gentle stream of nitrogen gas. To evaluate the effects of sebum on the migration of plasticizers, an artificial sebum solution was prepared by dissolving the artificial sebum in n-hexane (1:50, v/v). Then, 30 μL of the artificial sebum solution was spread on the surface of the PDMS disk, and the disk was dried to remove n-hexane. The PDMS disk was attached to the sample product and pressed with a 100 g weight that covered the entire contact surface area. The different temperatures and times used for the assessment of migration rates were 20, 40, and 60 °C; and 10, 30, 60, 120, and 240 min, respectively. The temperature range was chosen considering possible temperature of PVC products contacting with skin. After the experiment, each PDMS sampler was detached and any remaining artificial sebum on the surfaces of PDMS disk was removed using a lint-free tissue. Because the migration time was no longer than 240 min, significant loss of sebum was not observed. Then, the plasticizers that migrated into the PDMS disk were extracted with 4 mL of n-hexane and incubation for 24 h at 25 °C and 150 rpm in a shaking incubator. The quantified migrated mass (μg) was converted to migration rate (μg cm^{-2} min^{-1}) using Equation (1):

$$\text{migration rate} = \frac{\text{migrated mass}}{\text{migrated area} \times \text{migrated time}} \quad (1)$$

2.4. Instrumental analysis

The plasticizers that migrated from the PVC products were quantified using gas chromatography-mass spectrometry (GC-MS). One microliter of the extracted sample was injected into a GC-MS system equipped with Agilent (Santa Clara, CA, USA) 7890A GC system with Agilent 5975C inert XL MSD and Agilent 7683B series autosampler. The mixture of plasticizers was separated on an Agilent HP-5 column (30 m

× 0.25 mm internal diameter, 0.25 μm film thickness). The inlet temperature was set at 300 °C, the pressure was 10.523 psi, and the initial oven temperature was 100 °C. The temperature was then increased at a rate of 15 °C min^{-1} for 6.67 min until it reached 200 °C and was then increased at a rate of 5 °C min^{-1} until it reached 270 °C. The total run time for each sample was 36.67 min. The DOTP and DEHP concentrations were quantified using fluoranthene-d_{10} as the internal standard. Five concentrations of external standards were selected, ranging from 0.1 ng mL^{-1} to 50 ng mL^{-1}. The coefficients of determination for the calibration were greater than 0.99. Mass-to-charge ratios (m/z) of DOTP, DEHP, and fluoranthene-d_{10} were selected as 149, 261 for DOTP, 149, 167 for DEHP, and 212, 213 for fluoranthene-d_{10}, respectively. The chromatographic separation is shown in Figs. S2 and S3 as examples. All samples were analyzed in triplicate. For quality control, a standard sample of 5.0 ng mL^{-1} was analyzed after every 12 samples. All signals from all samples are higher than the signal of the lowest concentration used in calibration curve.

2.5. Calculation of diffusion coefficient and activation enthalpy

In this experimental system, the plasticizers diffused between two (product and PDMS disks) or three media (product, artificial sebum, and PDMS disks). For highly hydrophobic plasticizers, diffusion in the PDMS disk and artificial sebum is substantially faster than diffusion in a PVC product (Frederiksen et al., 2016). In addition, the plasticizer content in the products is very high, which makes the concentration of the plasticizer at the surface of the PVC product constant after migration. Under the experimental conditions, the total migrated amount M_t of the diffusing substance through the contact area at time t can be simplified as follows (Crank, 1975):

$$M_t = 2C_0\left(\frac{Dt}{\pi}\right)^{\frac{1}{2}} \quad (2)$$

where M_t is the migrated mass through the contact area at time t (μg cm^{-2}), C_0 is the initial concentration of the plasticizer in the PVC product (μg cm^{-3}), D is the diffusion coefficient (cm^2 s^{-1}), and t is the experimental time (s). Thus, D was obtained from non-linear regression between M_t and t. The diffusion coefficient of plasticizers in PVC products depends on temperature, and therefore, the activation enthalpy of diffusion can be calculated by plotting the natural logarithm of D ($\ln D$) versus the inverse of temperature ($1/T$) using the van't Hoff equation:

$$\ln D = -\frac{H^*}{R} \times \frac{1}{T} + C \quad (3)$$

where T is the absolute temperature (K), H^* is the activation enthalpy of diffusion (kJ mol^{-1}), R is the gas constant (8.3145 J mol^{-1} K^{-1}), and C is a constant.

2.6. Estimation of dermal exposure

The migrated mass of plasticizers from the PVC products was estimated using the fitted D and Equation (2). According to Equation (2), the migration rate decreased as time increased, and therefore, the estimated migrated mass changed with time compared with the linear estimated migrated mass using migration rates at fixed durations of 30 and 240 min, respectively. To avoid underestimation of exposure, the optimal time to measure migration rates was determined.

3. Results and discussion

3.1. Migration of DEHP and DOTP at different times, temperatures, and skin conditions

Fig. 1 shows the migrated mass (μg) of DOTP in S-15 over time at 20, 40, and 60 °C with and without the sebum layer as examples. All other results are shown in the Supplementary material (Fig. S4). The results for all samples are shown in Table 1. The migration of DEHP and DOTP increased with time in all the samples, but the average migration rate decreased with time. Although a few data at 40 °C showed that the

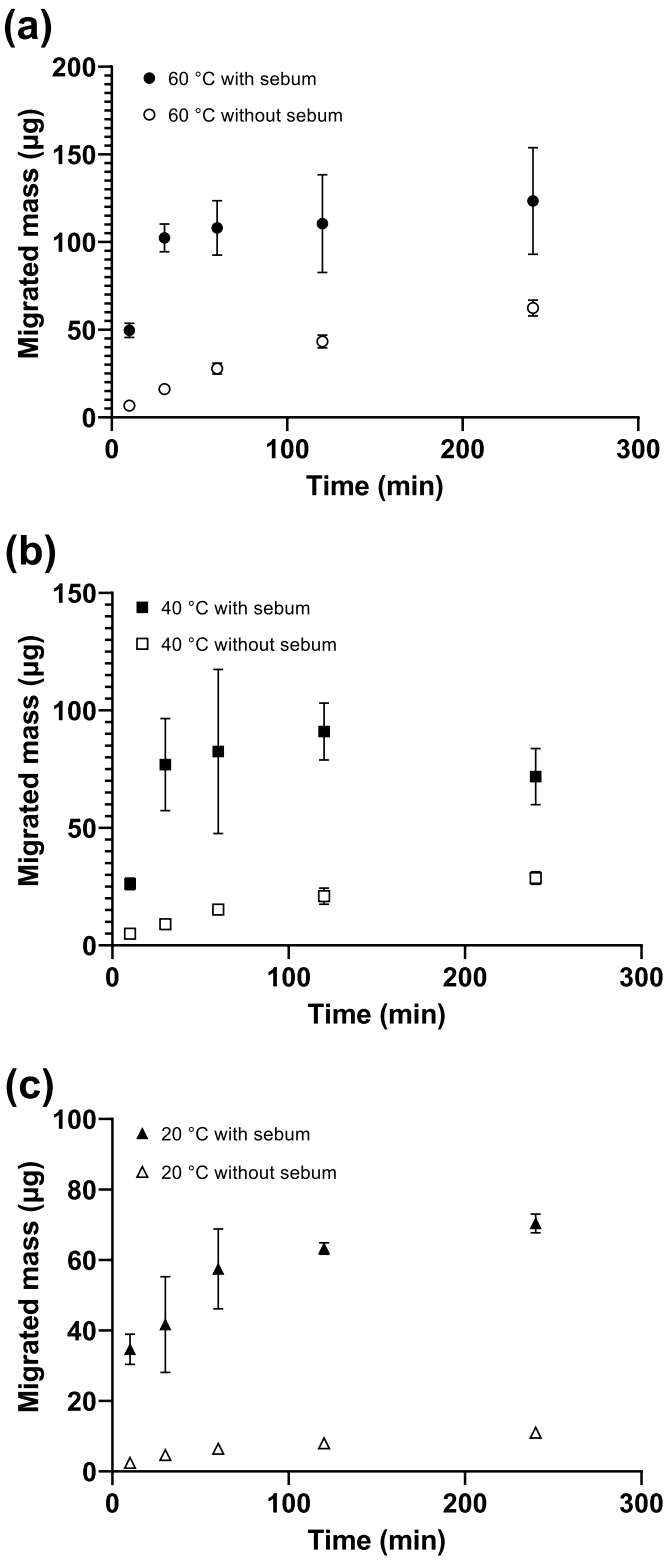

Fig. 1. Cumulative migrated mass (μg) of DOTP in S-15 over time with artificial sebum (solid) and without artificial sebum (empty) at different temperatures: (a) 60 °C, (b) 40 °C, and (c) 20 °C. All samples repeated 3 times and error bars are standard deviation.

Table 1
Measured migrated mass of dioctyl terephthalate (DOTP) and di(2-ethylhexyl) phthalate (DEHP) in all samples over time at different temperatures with and without artificial sebum.

Sample	Sample type	Chemical	Content (%)	Time (min)	Temperature (°C)					
					20		40		60	
					Migration (μg)					
					w/o sebum	w/sebum	w/o sebum	w/sebum	w/o sebum	w/sebum
S-15	Yoga mat	DOTP	12.21	10	2.45 ± 0.75	34.64 ± 4.3	4.97 ± 0.34	26.18 ± 2.46	6.72 ± 1.1	49.59 ± 4.03
				30	4.66 ± 0.24	41.67 ± 13.57	8.98 ± 1.62	76.92 ± 19.58	16.12 ± 0.72	102.32 ± 7.9
				60	6.42 ± 0.97	57.47 ± 11.32	15.24 ± 1.5	82.49 ± 34.91	27.85 ± 3.12	108.04 ± 15.51
				120	7.98 ± 0.42	63.23 ± 1.64	20.91 ± 3.48	91 ± 12.14	43.24 ± 3.67	110.45 ± 27.89
				240	10.99 ± 1.37	70.35 ± 2.68	28.63 ± 2.7	71.81 ± 11.93	62.38 ± 4.52	123.39 ± 30.44
S–17B	Steering wheel cover (black part)		2.21	10	1.22 ± 1.75	3.16 ± 0.98	0.85 ± 0.99	5 ± 4.02	0.2 ± 0.09	7.15 ± 10.05
				30	1.52 ± 1.95	6.41 ± 4.7	0.48 ± 0.15	12.95 ± 5.59	2.27 ± 2.9	7.41 ± 3.6
				60	1.36 ± 1.47	7.8 ± 4.71	0.45 ± 0.25	16.44 ± 9.38	3.77 ± 2.46	15.6 ± 6.1
				120	1.17 ± 1.15	13.91 ± 4.56	1 ± 0.46	14.82 ± 7.46	4.47 ± 2.38	18.72 ± 9.86
				240	0.49 ± 0.12	14.35 ± 7.85	2.52 ± 0.53	24.96 ± 3.76	9.91 ± 2.41	32.73 ± 17.04
S-17R	Steering wheel cover (red part)		2.21	10	0.58 ± 0.26	7.1 ± 6.11	0.73 ± 0.46	18.46 ± 1.33	0.66 ± 0.09	17.31 ± 16.25
				30	1.76 ± 0.76	14.76 ± 8.46	3.31 ± 2.5	20.02 ± 7.55	2.48 ± 0.83	31.39 ± 13.65
				60	3.01 ± 0.57	21.15 ± 13.01	4.98 ± 0.3	28.59 ± 16.25	7.16 ± 6.58	26.27 ± 11.63
				120	4.59 ± 0.57	28.41 ± 8.41	8.19 ± 3.22	36.97 ± 13.58	11 ± 5.84	47.75 ± 18.64
				240	5.37 ± 2.29	39.31 ± 7.58	11.52 ± 5.03	35.55 ± 14.25	10.7 ± 2.6	73.33 ± 4.79
S-23	Children swimming pool		13.09	10	9.58 ± 7	40.3 ± 42.18	9.3 ± 6.93	79.92 ± 5.38	25.07 ± 11.83	115.52 ± 12.26
				30	4.46 ± 3.35	72.38 ± 38.99	22.94 ± 26.12	130.74 ± 10.73	22.51 ± 16.87	139.08 ± 98.28
				60	18.24 ± 9.95	128.88 ± 9.97	46.01 ± 12.04	154.4 ± 18.88	67.99 ± 19.19	194.91 ± 6.92
				120	29.69 ± 16.22	67.73 ± 71.93	100.48 ± 7.03	193.81 ± 38.96	122.66 ± 42.59	208.33 ± 91.05
				240	46.47 ± 10.2	121.18 ± 103.82	109.67 ± 57.72	147.69 ± 90.46	193.77 ± 38.41	326.91 ± 36.95
S-24	Children swimming pool		6.67	10	6.23 ± 3.15	63.11 ± 0.81	14.17 ± 4.73	59 ± 33.36	28.98 ± 8.69	89.62 ± 48.27
				30	7.87 ± 9.37	74.29 ± 46.67	15.7 ± 12.05	141.71 ± 12.91	53.25 ± 5.07	152.98 ± 48.05
				60	18.43 ± 2.62	72.44 ± 46.14	45.07 ± 12.56	198.04 ± 9.59	68.5 ± 44.84	224.24 ± 5.81
				120	26.28 ± 14.54	117.59 ± 56.58	59.44 ± 32.21	226.56 ± 19.66	113.55 ± 79	246.74 ± 105.17
				240	26.55 ± 26.55	167.41 ± 15.22	103.1 ± 11.49	196.3 ± 50.34	179.69 ± 90.45	259.35 ± 98.33
S-25	Children swim vest		10.04	10	3.13 ± 0.84	34.18 ± 4.98	4.4 ± 1.76	54.27 ± 32.45	4.62 ± 2.39	52.97 ± 23.12
				30	3.24 ± 0.5	35.23 ± 21.62	5.59 ± 4.64	56.01 ± 22.06	9.02 ± 6.24	77.09 ± 31.89
				60	3.81 ± 1.2	50.57 ± 19.89	6.73 ± 3.64	63.42 ± 24.78	14.14 ± 10.06	82.13 ± 27.1
				120	3.13 ± 1.09	75.69 ± 22.82	10.44 ± 5.97	28.84 ± 6.52	24.47 ± 11.68	81.94 ± 19.14
				240	10.79 ± 2.35	76.51 ± 32.88	13.15 ± 7.89	67.33 ± 49.03	40.08 ± 32.94	105.42 ± 37.88
S–17B	Steering wheel cover (black part)	DEHP	1.78	10	0.28 ± 0.23	2.55 ± 0.74	0.25 ± 0.06	3.59 ± 2.54	0.36 ± 0.33	1.65 ± 1.43
				30	0.58 ± 0.29	2.84 ± 1.68	0.4 ± 0.1	8.46 ± 3.12	1.01 ± 0.28	4.99 ± 2.03
				60	0.36 ± 0.08	5.43 ± 3.09	0.42 ± 0.22	11.42 ± 6.28	1.53 ± 0.54	10.54 ± 5.31
				120	0.52 ± 0.18	8.62 ± 2.82	0.82 ± 0.51	7.46 ± 6.47	4.49 ± 2.43	12.36 ± 8.1
				240	0.37 ± 0.12	9.06 ± 4.3	2.37 ± 0.4	16.25 ± 3.83	8.97 ± 4.1	24.09 ± 13.23
S-17R	Steering wheel cover (red part)		1.78	10	0.76 ± 0.35	16.15 ± 6.73	0.98 ± 0.61	24 ± 3.03	0.98 ± 0.15	19.14 ± 16.25
				30	2.27 ± 1.21	18.83 ± 10.54	5.48 ± 5.26	27.87 ± 10.09	3.81 ± 1.4	41.36 ± 16.03
				60	3.97 ± 0.73	26.93 ± 16.57	6.46 ± 0.21	39.09 ± 21.76	10.37 ± 8.48	36.45 ± 15.34
				120	6 ± 0.71	35.18 ± 10.23	11.39 ± 4.34	49.95 ± 18.5	19.13 ± 10.31	61.47 ± 21.35
				240	6.91 ± 3	52.02 ± 9.73	16.54 ± 6.21	49.21 ± 18.92	19.62 ± 4.54	102.79 ± 7.41

cumulative migrated mass of plasticizers slightly decreased at 240 min, the difference between values at 120 and 240 min was not statistically significant and considered within experimental uncertainties. According to most protocols for determining the migration rate of plasticizers, the migration rate is measured at a fixed time and the dermal exposure is calculated for simplicity (Danish Environmental Protection Agency,). However, when the contact time of the product under the exposure scenario is relatively short (e.g., 10 min in this experiment), the dermal exposure obtained using a longer duration (e.g., 30 min) might underestimate the actual exposure.

The results demonstrate that the migration rates of the plasticizers were affected by temperature and the artificial sebum (Table 1). Typical human skin temperature is 28.1–34.7 °C (Benedict et al., 1919) and human epidermis is damaged above 44 °C (Xu et al., 2012). The temperature used in this study was a reasonable ambient temperature for assessing migration rate of plasticizers when humans are in contact with PVC products. When temperature was increased from 20 to 60 °C, the migration rate increased up to 2.6 times in sample S-15. Diffusion in a product determines the migration rate of plasticizers, and therefore, it is important to define the temperature at which diffusion occurs. When skin is in contact with a product, a thermal gradient develops, and the temperature at the surface of the product changes with increase in the contact time. For example, a strong thermal gradient develops when a portable PVC hot pack is used to warm hands. Since it is very complex to incorporate changes in the temperature of the product in the evaluation of the migration rate of a plasticizer, the initial temperature of the product before contact should be considered.

The impact of artificial sebum on increasing migration rate is more significant than that of temperature. When artificial sebum was added, migration rate increased up to 14 times compared to that at the same migration time but without sebum. Lipophilic plasticizers tend to dissolve in artificial sebum easily when the artificial sebum layer is in contact with a PVC product. Once plasticizers migrate to the sebum layer, migration to the PDMS sampler would be faster than migration directly from the PVC products. Artificial sebum is composed of a mixture of lipids including fatty acids, which act as plasticizers in polymers. When low molecular weight lipids were added to PVC, an increase in elongation at break was reported, indicating that PVC became softer (da Silva et al., 2011). In this study, the lipids present in the artificial sebum were not detected in the PDMS disks, and therefore, PDMS was regarded as impermeable to polar lipids in the sebum. However, they may penetrate PVC material and alter the diffusivity of plasticizers. Generally, pure PVC has good resistance to these fatty acids; however, plasticized PVC products readily absorb lipids (Schwab and Wingrave, 1981). Therefore, artificial sebum may accelerate the migration of plasticizers, particularly softer PVC. The migration rate varied with contact time and temperature with and without artificial sebum, which suggests that these exposure conditions should be considered when estimating dermal exposure to plasticizers.

3.2. Diffusion coefficient and the activation enthalpy of DEHP and DOTP

Table 2 shows the diffusion coefficients and activation enthalpies of all samples at different temperatures with and without artificial sebum. The diffusion coefficient increased as temperature increased and ln D is linearly related with $1/T$ and the activation enthalpy of diffusion was calculated as a slope (see Fig. 2 for an example of S-15). The values of diffusion coefficients at different temperatures without artificial sebum ranged within one or two orders of magnitude when compared with the values of other studies (Reynier et al., 2001; Tüzüm Demir and Ulutan, 2012; Wang et al., 2015). When artificial sebum was added, the diffusion coefficient increased by a factor of 4–268. Notably, the effects of artificial sebum were more significant at lower temperatures, having smaller activation enthalpy of diffusion. Estimated diffusion coefficients and activation enthalpies have no significant relationship with the concentration of plasticizer in PVC products (Wei et al., 2019). Physical

Table 2
Calculated diffusion coefficient (D) and activation enthalpy (H^*) of dioctyl terephthalate (DOTP) and di(2-ethylhexyl) phthalate (DEHP) in consumer products at different temperatures with and without artificial sebum.

Sample	chemical	Temperature (°C)	W/o sebum		W/sebum	
			D (cm^2/s)	H^* (KJ/mol)	D (cm^2/s)	H^* (KJ/mol)
S-15	DOTP	20	4.70×10^{-13}	67	2.66×10^{-11}	24
		40	2.96×10^{-12}		4.28×10^{-11}	
		60	1.26×10^{-11}		8.85×10^{-11}	
S–17B		20	2.29×10^{-13}	69	2.84×10^{-11}	26
		40	4.27×10^{-13}		7.19×10^{-11}	
		60	7.39×10^{-12}		9.91×10^{-11}	
S-17R		20	3.49×10^{-12}	31	1.74×10^{-10}	23
		40	1.32×10^{-11}		2.23×10^{-10}	
		60	1.58×10^{-11}		5.39×10^{-10}	
S-23		20	5.42×10^{-12}	57	6.03×10^{-11}	36
		40	3.86×10^{-11}		1.52×10^{-10}	
		60	9.06×10^{-11}		3.51×10^{-10}	
S-24		20	1.11×10^{-11}	69	3.45×10^{-10}	26
		40	1.10×10^{-10}		8.71×10^{-10}	
		60	3.31×10^{-09}		1.24×10^{-09}	
S-25		20	4.00×10^{-13}	57	4.38×10^{-11}	13
		40	1.03×10^{-12}		3.24×10^{-11}	
		60	6.75×10^{-12}		8.44×10^{-11}	
S–17B	DEHP	20	6.40×10^{-14}	98	1.72×10^{-11}	30
		40	5.15×10^{-13}		4.38×10^{-11}	
		60	8.12×10^{-12}		7.38×10^{-11}	
S-17R		20	9.08×10^{-12}	42	4.59×10^{-10}	24
		40	4.10×10^{-11}		6.45×10^{-10}	
		60	7.26×10^{-11}		1.53×10^{-09}	

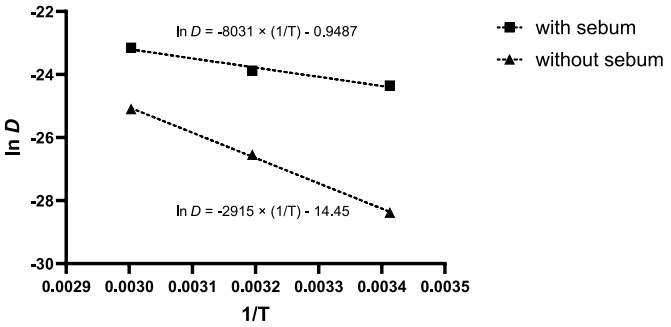

Fig. 2. Linear regression between the logarithm of diffusion coefficient (D) of DOTP and inverse of temperature ($1/T$) with artificial sebum (solid square) and without artificial sebum (solid triangle) using S-15. Dashed lines are least squares regression lines.

properties, such as the softness or surface finish of the product might affect the diffusivity of a plasticizer rather than the content of the plasticizer. However, no correlations were observed between diffusion coefficient and shore hardness, tensile strength, and elongation of five PVC products (Table S1).

The migration rate of plasticizers from PVC products varied with contact time, temperature, and the presence of sebum. The loss of plasticizers from PVC products under typical use conditions is negligible unless the products are exposed to extremely harsh conditions, such as high temperatures and high doses of ultraviolet light (Ito and Nagai, 2007; Wei et al., 2019). Therefore, it is reasonable to assume that plasticizers are evenly distributed within the PVC product, and that migration by skin contact can be repeated when the product is newly manufactured.

3.3. Estimation of dermal exposure

The migration of plasticizers from PVC products is time dependent, although migration experiments are usually conducted at one time point (Danish Environmental Protection Agency,). To generalize the deviation of the extrapolated migration rate based on these experiments, a conceptual analysis was conducted. In Fig. 3a, the solid line represents the theoretical amount of plasticizer that migrated from the product with time, calculated using Equation (2). If experimental measurements were conducted at t_1 or t_2, the dashdotted and dotted lines indicate the extrapolated amounts of plasticizer based on the measured migration rate at time t_1 or t_2. For a given exposure time (t_E), a possible overestimation is expected when using migration rate at t_1 ($t_E > t_1$), whereas a possible underestimation is expected when using migration rate at t_2 ($t_E < t_2$). Consequently, the best practice to minimize estimation bias is to set the time of the experiment close to the exposure time under the exposure scenario. However, it is very difficult in practice to adjust the time for migration tests for diverse exposure scenarios of product uses. In Fig. 3b, the differences between the solid line and dashdotted or dotted lines in Fig. 3a are expressed as over- or under-estimation bias. For example, in the exposure scenario when using a yoga mat (S-15), t_1 is 30 min and t_2 is 240 min, which are reasonable short and long practice times, respectively. When t_E is shorter than 30 min, both migration rates measured at t_1 and t_2 underestimate the exposure, requiring a shorter time for the experiment. As shown in Equation (2), the diffusion coefficient of the plasticizer in the product determines the shape of the migration curve. Experimental diffusion coefficients of plasticizers in PVC products are highly varied, ranging from 2.3×10^{-15} to 3.8×10^{-11} $cm^2\ s^{-1}$ (Reynier et al., 2001; Tüzüm Demir and Ulutan, 2012; Wang et al., 2015). They are also strongly affected by temperature and the presence of sebum, as shown in this study. Therefore, fixing a standard time for the experiment is not desired, but is recommended for determining the duration of the experiment shorter than the exposure time under the use scenario of the product to avoid a potential underestimation of exposure, particularly at the screening stage. Typical use scenarios for dermal contacts assume a contact time in the order of minutes to hours, and therefore, two experimental times (e.g., 20 min and 2 h) should be used for routinely testing the migration of such additives. Refined migration rates would reduce uncertainties in dermal exposure assessment when coupled with reliable dermal absorption rate.

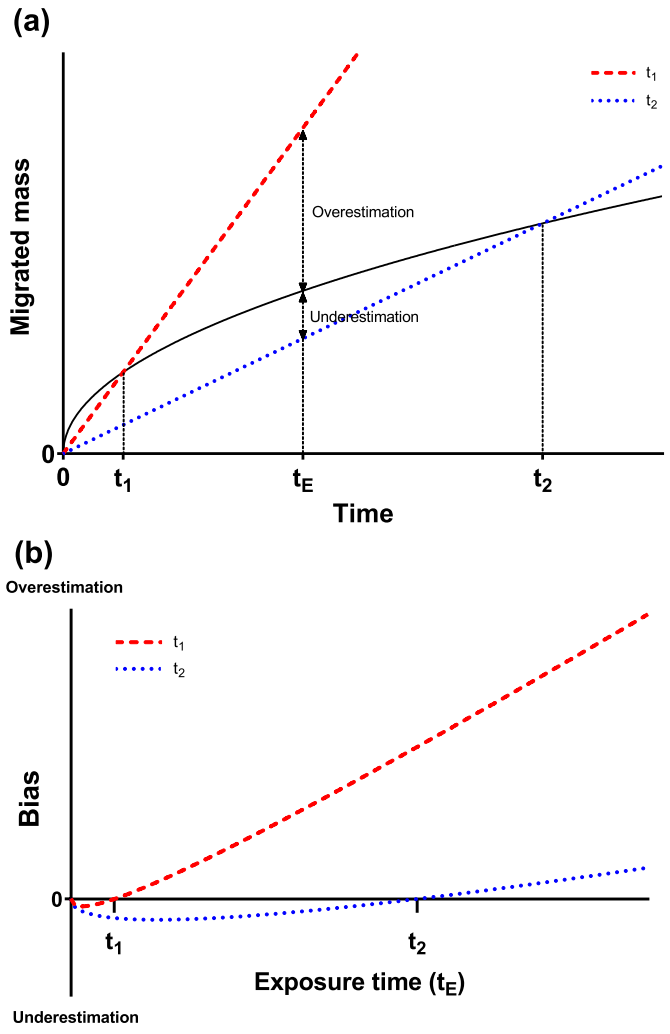

Fig. 3. Conceptual diagram showing (a) theoretical amount of migrated mass (solid line) and extrapolated lines with migration rate measured at t_1 (dashdotted line) and t_2 (dotted line) showing over and underestimation at exposure time, t_E and (b) over and underestimation bias between solid line and long- or short-dashed lines in (a).

4. Conclusions

The migration rates of DEHP and DOTP in PVC products was measured at different times and temperatures with and without artificial sebum, and using PDMS as the receiving phase. As migration time increased, the total amount of migration increased, but the average migration rate decreased significantly. When assessing dermal exposure through contact with products, the exposure time should be considered to prevent potential underestimation, particularly at the screening assessment stage. Both the increase in temperature and the presence of artificial sebum markedly enhanced the migration rates of the plasticizers from the PVC products. Migration increased by up to 14 times with artificial sebum, suggesting that the addition of the sebum layer is necessary to avoid underestimation of the migration of plasticizers from a product. The estimated diffusion coefficient values were similar to the values (without sebum) found in previous studies, but were four to 268 times higher when the sebum layer was added. The estimated dermal exposure using migration experiments suggested measuring migration at a shorter time than the expected exposure time to prevent the underestimation of exposure.

Credit author statement

Du Yung Kim: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing- Original Draft, Writing-Review & Editing, Visualization **Stefana Sochichiu:** Investigation, Data curation **Jung-Hwan Kwon:** Conceptualization, Resources, Writing-Review & Editing, Supervision, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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