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Published in:
Indoor Air Online

Link to article, DOI:
10.1111/ina.12354

Publication date:
2017

Document Version
Peer reviewed version

Citation (APA):
Morrison, G. C., Weschler, C. J., & Beko, G. (2017). Dermal uptake of phthalates from clothing: Comparison of model to human participant results. Indoor Air Online, 27(3), 642-649. DOI: 10.1111/ina.12354

Received Date : 15-Aug-2016

Revised Date : 01-Nov-2016

Accepted Date : 04-Nov-2016

Article type : Original Article

Dermal uptake of phthalates from clothing: comparison of model to human participant results

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ABSTRACT

In this research, we extend a model of transdermal uptake of phthalates to include a layer of clothing. When compared with experimental results, this model better estimates dermal uptake of diethylphthalate (DEP) and di-n-butylphthalate (DnBP) than a previous model. The model predictions are consistent with the observation that previously exposed clothing can increase dermal uptake over that observed in bare-skin participants for the same exposure air concentrations. The model predicts that dermal uptake from clothing of DnBP is a substantial fraction of total uptake from all sources of exposure. For compounds that have high dermal permeability coefficients, dermal uptake is increased for i) thinner clothing, ii) a narrower gap between clothing and skin and iii) longer time intervals between laundering and wearing. Enhanced dermal uptake is most pronounced for compounds with clothing-air partition coefficients between 10^4 and 10^7. In the absence of direct measurements of cotton cloth-air partition coefficients, dermal exposure may be predicted using equilibrium data for compounds in equilibrium with cellulose and water, in combination with computational methods of predicting partition coefficients.

PRACTICAL IMPLICATIONS

This model improves predictions of dermal uptake from clothing for two phthalates. Successful extension of this model to other compounds will improve population exposure estimates.

KEYWORDS

SVOC, model, fabric, skin, absorption, exposure

1 INTRODUCTION

Cotton and other textile materials can accumulate chemicals from their local environment, thereby posing an exposure risk through skin contact and/or mouthing by children. Organic compounds of lower volatility have a stronger affinity for surfaces than higher volatility compounds. Very large equilibrium partitioning between fabrics and air has been observed for phthalates (Morrison et al., 2015a; Cao et al., 2016), dichlorobenzene and naphthalene (Guerrero and Corsi, 2011) and methamphetamine (Morrison et al., 2015b). Strong non-equilibrium uptake has been observed for polybrominated diphenylethers to cotton and polyester (Saini et al., 2016a), nicotine and ethylpyridine on cotton and nylon (Piade et al., 1999) and chlorpyrifos on plush toys (Gurunathan et al., 1998). Body uptake has been observed due to wearing clothing that has been treated with pesticides (Rossbach et al., 2010, 2016; Proctor et al., 2014) and flame retardants (Blum et al., 1978).

Morrison et al. (2016a) observed substantial uptake of DEP and DnBP for a subject wearing clothing that had been allowed to absorb the phthalates for 9 days from chamber air enriched in DEP and DnBP. Uptake observed for the clothed subject was much greater than that observed under otherwise identical exposure conditions for bare-skinned subjects reported in Weschler et al. (2015). Wearing freshly laundered clothing resulted in much lower uptake from phthalate enriched chamber air. A recently developed model of transdermal uptake (Morrison et al., 2016b) produces estimates that reasonably match measurements for bare-skinned subjects. However, compared to measurements, the model substantially overpredicts DnBP uptake from clothing. We believe this is because the model is mechanistically simple, and does not adequately account for the exposure history of the clothing prior to wearing or transport through and uptake within the cloth itself.

The objective of this research is to develop a model for dermal uptake of SVOCs that includes clothing. The model is applied to predict dermal uptake of diethyl phthalate (DEP) and di-n-butyl phthalate (DnBP) for the participant described in Morrison et al. (2016a). It is then extended to make predictions about the impact of clothing on overall body-burden of DEP and DnBP and to better understand the influence of elapsed time between laundering and wearing clothing.

2 MATERIALS/METHODS

The model described in Morrison et al. (2016b) is updated with the addition of a more realistic clothing layer. Transport through clothing is assumed to be controlled by gas-phase diffusion that is retarded by adsorption of an SVOC to fibers in the fabric. The geometry of the fabric is considered to be a slab of uniform thickness and composition. Transport from clothing to skin lipids is assumed to take place through a thin quiescent layer of air between the clothing and the surface of the lipids by gas-phase diffusion. From skin lipids to blood, dermal uptake is modeled as in Morrison et al. (2016b). Advective transport through clothing is assumed to be negligible (Korff et al., 2015). The initial clothing concentration gradient is determined by a separate model that addresses clothing uptake from the gas-phase alone during the time prior to wearing, i.e. from hanging in a closet after laundering.

The model is based on one-dimensional transport through multiple layers including skin layers, air and clothing. To be consistent with the transient models of Gong et al. (2014) and Morrison et al. (2016b) the geometry is identical except for the quiescent gap between cloth and skin and the cloth layer (see Figure 1). The model equations for transport through the stratum corneum (SC) and viable epidermis (VE) are described in Morrison et al. (2016b). The skin surface lipids (SSL) are in contact with both the stratum corneum and the air under clothing.

Accumulation in the SSL layer is matched by the flux into and out of that layer due to flux across the cloth-skin air gap and diffusion into the SC:

$$\frac{\partial C_{ssl}}{\partial t} = \frac{D_g}{L_{gap} L_{ssl}} \left(C_{g,\,L_1} - \frac{C_{ssl}}{K_{ssl\_g}} \right) - \frac{D_{sc}}{L_{ssl}} \frac{\partial C_{sc}}{\partial x} \quad \text{for } t \geq 0 \qquad (1)$$

where C_{ssl} and C_{sc} are the SVOC concentrations in the SSL and SC, respectively, $C_{g,L1}$ is the SVOC concentration in the air at the inner cloth-air gap interface, D_g is the gas-phase diffusivity of the SVOC, $L_1 = L_{ve} + L_{sc} + L_{ssl} + L_{gap}$, L_{ve}, L_{sc}, L_{ssl} and L_{gap} are the thickness of the VE, SC, SSL and air gap, K_{ssl_g} is the SSL-air partition coefficient, and D_{sc} is the effective diffusivity through the SC.

Mass transfer through the cloth of thickness L_{cl} is assumed to occur by Fickian diffusion retarded by partitioning to cloth fibers

$$\frac{\partial C_{cl}}{\partial t} = \frac{\varepsilon D_g}{K_{cl\_g}} \frac{\partial^2 C_{cl}}{\partial x^2} \qquad \text{for } L_1 \leq x \leq L_1 + L_{cl}, \text{ for } t \geq 0 \qquad (2)$$

where C_{cl} is the SVOC concentration within the cloth, ε is the porosity of the fabric and K_{cl_g} is the cloth-air partition coefficient. Mass transfer by advection is neglected because diffusive transport is anticipated to be the dominant transport mechanism (Korff, et al., 2015); details of this analysis can be found in Appendix S1 of Supporting Information. A flux matching condition is applied for the inner cloth-air gap interface:

$$\frac{D_g}{L_{gap}}\left(\frac{C_{cl}}{K_{cl\_g}} - \frac{C_{ssl}}{K_{ssl\_g}}\right) = \frac{\varepsilon D_g}{K_{cl\_g}} \frac{\partial C_{cl}}{\partial x} \qquad \text{for } x = L_1,\ t \geq 0 \qquad (3)$$

Similarly, a flux-matching condition is applied for the outer cloth-room air interface:

$$h_m\left(C_g - \frac{C_{cl}}{K_{cl\_g}}\right) = \frac{\varepsilon D_g}{K_{cl\_g}} \frac{\partial C_{cl}}{\partial x} \qquad \text{for } x = L_1 + L_{cl,},\ t \geq 0 \qquad (4)$$

Where h_m is the mass-transfer coefficient associated with flux from room air to the cloth and C_g is the SVOC concentration in the room air while wearing clothing.

As in simulations (Morrison et al., 2016b) of experiments described in Weschler et al. (2015) and Morrison et al. (2016a), we assume that the initial concentration in skin layers is zero:

$$C_{ve} = 0, C_{sc} = 0 \qquad \text{for } 0 \leq x \leq L_{sc} + L_{ve}, t=0 \qquad (5)$$

$$C_{ssl} = 0 \qquad \text{at } t=0 \qquad (6)$$

The total mass transferred to blood, m, is given by the time integral of the flux at the blood-VE boundary times the body surface area, A:

$$m = -A \int_0^t D_{ve} \frac{\partial C_{ve}}{\partial x} dt \qquad \text{for } x = 0 \qquad (7)$$

The model was solved using a finite-difference approach in Matlab.

The initial concentration profile in clothing is dependent on the clothing's prior history, specifically exposure time between laundering and wearing, t_{lw}, (e.g. time hanging in a closet) and the local air concentration, C_{g_lw}. Fickian transport within the cloth is calculated in a separate simulation. Flux from air to cloth between laundering and wearing is controlled by an external mass transfer coefficient, h_{m_lw}. For constant values of C_{g_lw}, h_{m_lw} and D_g, this system has an analytical solution (see Appendix S2 in Supporting Information).

Model parameters and simulations

Simulations of chamber exposure

All model inputs are independently determined, measured or estimated. Dermal parameters are identical to those in Morrison et al. (2016b). New parameters for this model and external mass transport are shown in Table 1 for specific simulations. Model simulations were performed to match conditions and experimental protocols described in Morrison et al. (2016a). The subject wore cotton clothing for 6 hours that was either freshly washed or had been allowed to adsorb the two phthalates from air in the exposure chamber. After this, the participant changed into fresh clothing. Fresh clothing, worn during or after the chamber exposure period, is assumed to have a zero initial concentration, $C_{cl} = 0$, but may accumulate phthalates while worn. Air concentrations, C_{g_lw}, were measured during days 4 and 5 of the 9-day cloth sorption time, t_{lw} (exposed clothing); the average values were 242 and 119 $\mu g/m^3$ for DEP and DnBP respectively. The air concentrations during the 6 h chamber experiments while wearing the exposed clothing are shown in Table 1. After exposure, participants are assumed to be exposed to clean air and $C_g = 0$.

During the cloth sorption time, t_{lw}, a fan was positioned near the clothing (but not directed at clothing), and there was sufficient air movement for clothing to visibly move with air currents. To consider a range of conditions, the external mass transfer coefficient was assumed to be either slightly higher than that induced by convective mass transfer to bare skin (4 m/h) or much greater (10 m/h).

Clothing thickness was estimated using microscope images of razor cut edges from clothing used in Morrison et al. (2015a and 2016a). The distance between skin and clothing, L_{gap}, is an adjustable parameter in the model and is estimated to range from 0.01 cm (approximately the thickness of a human hair) to 1.0 cm for loosely fitting clothing. Cloth-air partition coefficients, K_{cl_g}, for the clothing used in Morrison et al. (2016a) were measured and reported in Morrison et al. (2015a). They suggest that the K_{cl_g} value reported for DnBP is a lower limit at 25ºC because the cloth may not have achieved equilibrium during the 10 day experiment. However, Cao et al. (2016) measured a partition coefficient for DnBP and cotton that was similar to Morrison et al. (2015a), when converted to a cloth-mass basis. Therefore the average K_{cl_g} values reported in Morrison et al. (2015a) are used in simulations of the chamber exposure (2.5×10^5 and 4×10^6 for DEP and DnBP, respectively). Porosity, ε, is assumed to be 0.6 based on measurements by Morrison et al. (2015a).

Simulations of uptake for a daily wear cycle

To simulate the impact of the launder-wear interval on uptake of these two phthalates during normal wear, we performed simulations of a repeated daily cycle. Cotton clothing, 1 mm thick, is assumed to be phthalate free immediately after washing and then allowed to accumulate phthalates from room air for launder-wear intervals, t_{lw}, ranging from several hours to months. The room air concentration is assumed to be 0.4 μg/m^3 and 0.2 μg/m^3 for DEP and DnBP respectively (based on median values reported in US homes in Sheldon et al., 1992, Rudel et al., 2003 and Rudel et al., 2010; see Appendix S3 in Supporting Information). In the present conservative simulation, an individual wears exposed clothing for 12 hours and then dons clean clothing that has no sorbed DEP or DnBP, wearing this clothing for the following 12 hours. After a 24 h simulated cycle, dermal layers will retain some phthalates and start at a non-zero concentration condition the next day. To arrive at a day where the cycles have stabilized, 8 daily cycles are simulated; each day, the individual wears a new set of clothing that has been exposed for the same launder-wear interval (See more in Appendix S4 in Supporting Information). This was sufficient to reach steady-cycle results, which are reported as mass transferred to blood in a 24h period. The last daily cycle is assumed to be representative of a typical day for a repeated daily schedule. Mass transferred to blood is converted to urinary metabolite concentrations by dividing daily uptake by average urine volume for an adult male (1.3 L/day; Hays et al., 2015) and multiplying simulated mass uptake for both phthalates by 0.84 based on ingestion metabolism efficiency reported by Koch et al. 2012. The influence of skin-lipid transfer to clothing is discussed, but not directly simulated. For this and the following set of simulations, the partition coefficient for DEP is taken from Morrison et al. (2015a) and that for DnBP is the average of the Cao et al. (2016) and Morrison et al. (2015a) values.

Influence of cloth thickness, cloth-skin gap, launder-wear interval and cloth-air partition coefficient

The influence of cloth thickness, cloth-skin gap, launder-wear interval and the cloth-air partition coefficient are estimated in a series of simulations independent of dermal resistance. To place the focus on these parameters, we assume dermal resistance is lower than the resistance associated with transport of an SVOC from cloth to skin with a 3 mm gap (~0.17 h/m; see more detail in Supporting Information, Appendix S5). A list of compounds that meet this criterion (as well as compounds with a larger, but still small dermal resistance) is found in Supporting Information, Appendix S6. This excerpts and expands on the list of Weschler and Nazaroff (2012). In these simulations, the air concentration during cloth loading is assumed to be 1 $\mu g/m^3$, clothing is worn for 12 hours per day and the body surface area is 1 m^2. Therefore, the results can be read as "mass transferred to skin, per $\mu g/m^3$, per m^2 body area, per day".

RESULTS

Simulations of chamber exposure

Shown in Figure 2a are three simulations of DEP mass delivered to blood vs. the cloth-skin gap: i) the Morrison et al. (2016b) model, ii) the updated model with 4 m/h for h_{m_lw}, and iii) the updated model with 10 m/h for h_{m_lw}. Figure 2b is analogous, but for DnBP. Also shown (horizontal line in each figure) is the estimated uptake of the two phthalates based on measurements of urinary metabolites in Morrison et al. (2016a) (hereafter known as "measured"). As shown in the figure, the models are sensitive to the gap between skin and clothing. For example, assuming $h_{m\_lw} =$ 10 m/h, new model predictions of DEP and DnBP uptake are 7.6 and 13.8 mg respectively for tight fitting clothing (0.2 mm gap between skin and cloth) and 3.0 and 1.8 mg respectively for loose fitting clothing (10 mm gap). Measured cumulative uptake of DEP and DnBP were 4.7 and 3.3 mg, respectively. Model results for a gap ranging between 3 and 7 mm appear to match the measurements reasonably well, and the deviation from measured values are modest in this region (<40% for either phthalate). In other words, uptake is only weakly sensitive to the gap over a relatively wide range. For both compounds, the modeled estimate ($h_{m\_lw} =$ 10 m/h) is equal to the measured value when $L_{gap} \sim$ 4-5 mm.

The previous model (Morrison et al., 2016b) treated clothing in a simplified manner by assuming that after nine days in the chamber, the air concentration adjacent to the inside of the cloth was equal to the air concentration in the chamber (i.e., in equilibrium). The previous model overestimates uptake for DnBP for all gap distances up to about 10 mm, but the prediction is not substantially different for DEP. For DEP, cloth approaches equilibrium with air rapidly and the assumption of equilibrium after nine days in the previous model was acceptable. However, it takes much longer than nine days for the clothing to approach equilibrium for DnBP. The consequence is that when the subject first puts on the clothing, the concentration of

DnBP adjacent to the clothing surface is lower than the exposure (chamber) concentration. This results in a lower flux from clothing to skin, relative to the flux resulting from an equilibrium assumption.

Simulations of uptake for a daily wear cycle

Shown in Figure 3 are steady-cycle simulated urine concentrations for a person wearing cotton clothing that has been exposed to typical indoor air concentrations of DEP and DnBP for launder-wear intervals ranging from 0.1 to 100 days after washing. DEP reaches its maximum urine concentration with ~7 days of sorption, but it takes ~40 days between laundering and wearing before DnBP reaches 95% of its maximum urine concentration. This difference is due to the fact that cotton has a higher sorptive capacity for DnBP than DEP and it takes much longer to reach equilibrium for equivalent mass-transfer conditions. For a launder-wear interval of 10 days, dermal uptake from clothing results in a simulated urine concentration that is 10-20% of the geometric mean urine concentration of MEP reported in the NHANES survey for years 2009/2010 (CDC, 2015). For MnBP, assuming the same launder-wear interval, uptake from clothing results in a simulated urine concentration that is roughly 70% of the reported NHANES value for a gap of 1mm and 25% of the reported value for a gap of 5 mm. The impact of dermal uptake from clothing on total DnBP body burden is quite sensitive to the time interval between washing; for a reasonable range of washing intervals (1 to 30 days), uptake from clothing could range from a very small source to a dominant source.

Figure 3 is based on simulations using what we consider reasonable parameter values reported in previous publications (Gong et al., 2014; Weschler and Nazaroff, 2012; Morrison et al., 2016b). However, uncertainty in parameters such as the thickness of skin layers or their partition coefficients results in uncertainty in the overall permeability of the skin. A sensitivity analysis of this model showed that uptake would vary modestly for a typical range of parameter values (Morrison et al., 2016b). Further, participants exposed to DnBP in air under identical conditions (Weschler et al., 2015) experienced uptake that ranged from 0.1 to 0.7 mg. While we predict that DnBP uptake from clothing could be a substantial fraction of total uptake, an investigation of in-situ dermal uptake and quantification of SVOCs sorbed to in-use clothing will be necessary to verify this prediction.

Simulations under assumption of negligible dermal resistance

Shown in Figure 4 are results for simulations focused on revealing the influence of cloth thickness, cloth-skin gap, cloth partition coefficient and launder-wear interval on the dermal uptake of SVOCs mediated by clothing. Dermal resistance is considered negligible for these simulations to highlight the influence of parameters external to the skin (See Appendix S5 in Supporting Information). There are several observations of note:

1) Dermal uptake is higher for a smaller cloth-skin gap and longer intervals between laundering and wear.
2) Dermal uptake is higher for compounds whose partition coefficient, $\log_{10}(K_{cl\_g})$, ranges between 5 and 7, but the peak for uptake depends on other conditions as well. For a smaller cloth-skin gap there is a more pronounced peak for $\log_{10}(K_{cl\_g})$ between 6 and 6.5, but for a larger gap the peak is more broad; therefore, over a wide range of partition coefficients a (normalized) uptake of similar magnitude is expected.
3) At lower values of K_{cl_g}, less than about 10^5, results are not strongly influenced by the launder-wear interval. At higher values of this partition coefficient, the launder-wear interval has a very strong influence on uptake. For example, for SVOCs with higher values for K_{cl_g}, a launder-wear interval of 28 days results in at least one order of magnitude larger uptake than a launder-wear interval of 1 day.
4) Cloth thickness has a modest effect on dermal uptake, but the impact depends on K_{cl_g}. For middle to high values of K_{cl_g}, dermal uptake *increases* by as much as factor of three as the cloth thickness decreases from 2 to 0.5 mm. For values of K_{cl_g} less than 10^5, dermal uptake *decreases* by as much as a factor of three as the cloth thickness decreases from 2 to 0.5 mm.

DISCUSSION

The updated model accounts for the dynamics of DnBP adsorbing onto clothing and subsequently diffusing from exposed fibers to interior fibers prior to the subject donning clothing. This accounts for most of the difference observed between the present and the previous (Morrison et al., 2016b) model and results in a better match with observed uptake. However, Figure 4 demonstrates that the model is sensitive to uncertainty in parameters such as partition coefficient and launder wear interval. For example, for K_{cl_g} ranging from 10^6 to 10^7, the highest normalized uptake (thin cloth, thin gap and long launder-wear interval) is nearly three orders of magnitude greater than the lowest (thick cloth, wide gap, short launder-wear interval). Therefore, quantifying these parameters for the typical range of actual conditions is vitally important for applying the model to population exposure estimates.

An important assumption applied in these simulations is that SVOCs are removed completely after laundering. Gong et al., (2016) found that approximately 80% and 30% of DEP and DnBP respectively were removed in laundering cotton jeans. Larger molecular weight phthalates were removed less efficiently, and they observed an inverse relationship between removal fraction and $\log_{10} K_{ow}$. However, the laundered clothing described in Gong et al. (2016) was dried by hanging in the air. Had the clothing been tumble-dried in a hot air dryer, the removal efficiency of DEP and DnBP would likely have been higher. Saini et al. (2016b) observed post-laundering retention of higher molecular weight phthalates, organophosphate esters and polybrominated diphenyl ethers even after laundering and hot-air drying. However, less than 20% of DnBP was retained on the clothing after washing. Based on the findings of Gong et al. (2016) and Saini et al. (2016b), and the fact that the clothing in Morrison et al. (2016a) was washed and hot air tumble-dried, we anticipate that most of the DEP and DnBP was removed prior to the nine-day exposure interval. In general, incomplete removal of SVOCs after laundering will increase the initial concentration in the fabric, thereby hastening the approach to equilibrium during the launder-wear interval and potentially increasing exposure. The impact is greatest for those compounds with higher values for K_{cl_g}, which require a longer loading time to approach equilibrium with the surrounding environment.

For simulations shown in Fig 4, the external mass-transfer coefficient associated with adsorption of an SVOC to clothing was chosen to be 3 m/h, during the period between laundering and wearing. It is easy to envision scenarios where adsorption can occur much more slowly or much more quickly. For example, a set of freshly laundered clothing that is folded and stacked in a drawer will only slowly accumulate SVOCs from its local environment. Alternatively, a freshly laundered shirt that is hung between shirts that have not been laundered for many weeks may rapidly accumulate SVOCs from the adjacent shirt "reservoirs". Therefore, accounting for differences in how clothing is stored between laundering and wear will be an important next step in using the model for exposure analysis.

While the assumption of negligible dermal resistance (Figure 4) does not apply generally, many compounds appear to fit this criterion (See Supporting Information Appendix S6). To apply Figure 4 broadly, it is necessary to have a measured or estimated value of K_{cl_g}. Only a few measurements are available (Morrison et al., 2015a; Morrison et al., 2015b; Cao et al., 2016). Measurements of partition coefficients over appropriate environmental conditions will be time consuming to acquire for the large number of commercial fabrics paired with the many SVOCs common in buildings. Direct measurements are vital, but validated methods of estimating partition coefficients from other kinds of measurements or computational methods could help more rapidly estimate the body burden of SVOCs associated with dermal uptake from clothing.

To estimate partition coefficients in cotton, the most widely used material used to make clothing, we hypothesize that partition coefficients determined for cellulose and other constituents may be used as a surrogate. Cellulose is the primary constituent of cotton (88-96%; Kirk-Othmer, 2004). Non-cellulosic organics (e.g. waxes and proteins) constitute ~1-3% of components in processed cotton. This does not include organics or other constituents that accumulate from soiling, laundering, sizing or other processes. A small amount of minerals and water are also present.

For a wide variety of chemical compounds Hung et al. (2010) measured partition coefficients between carbohydrates (cellulose and starch) and water. The cellulose-water partition coefficient, $K_{cellulose\text{-}water}$, can be converted to the cellulose-air partition coefficient, $K_{cellulose\text{-}air}$, via the air-water partition, $K_{air\text{-}water}$:

$$K_{cellulose-air} = \frac{K_{cellulose-water}}{K_{air-water}}. \tag{8}$$

Henry's law coefficient (H) can be used to calculate $K_{air\text{-}water}$:

$$K_{air=water} = \frac{1}{H\mathrm{RT}} \tag{9}$$

where we are using H with units of M atm^{-1}, R is the universal gas constant (0.0821 atm M^{-1} K^{-1}) and T is temperature (K). Shown in Appendix S7 of the Supporting Information are the calculated $\log_{10} K_{air\text{-}water}$ based on reported values of H, predicted $\log_{10} K_{cellulose\text{-}air}$, $\log_{10} K_{cl\_g}$ and available measurements of $\log_{10} K_{cl\_\mathrm{g}}$. To make a direct comparison on a mass basis, we converted the unitless K_{cl_g} reported by Morrison et al., 2015 and Cao et al., 2016 to units of l/kg by dividing their values of K_{cl_g} by the bulk density of the fabric. For DEP and DnBP the values of $\log_{10} K_{cellulose\text{-}air}$ estimated from Hung et al. 2010 are lower by 0.3 to 0.8 log units than measured values. Since these estimates are based on values obtained in water, the cellulose should be considered “fully hydrated”. In air, the cellulose in cotton would be less than fully hydrated and resulting partition coefficients for low-polarity compounds like DEP and DnBP may be somewhat higher.

Computational methods may also allow for estimating partition coefficients for those SVOC-fabric pairs that have not been investigated experimentally (e.g. Saini et al., 2016c). Goss (2011) applied several computational methods to estimate $K_{cellulose\text{-}water}$ and found that their results correlated well with most measurements reported by Hung et al. 2010. Note that DEP and DnBP were excluded from their correlation because their predictions deviated significantly from the Hung et al. 2010 results. However, by converting predicted values for dry cellulose and cellulose with 20% water (obtained by personal communication with Goss, 2016) and using correlations in Goss (2011), we find that predicted values for DEP and DnBP overlap with cotton-clothing measurements and differ by no more than 0.4 log units. This proof of principle comparison suggests that the correlations based on measured values in water could be used, with caution, to estimate K_{cl_g} for compounds within some chemical classes, i.e. aromatics, halogenated alkanes and benzenes, chlorinated alkanes and biphenyls, phthalates and anilines.

To demonstrate the application of this method beyond the two phthalates discussed already, we consider benzo(a)pyrene (BaP). Figure 4 can be used to estimate the daily uptake of BaP since it is predicted to have a high dermal permeability coefficient as shown in Appendix S6 of Supporting Information (17 m/h). Using the method of Goss (2011) the predicted $\log_{10}K_{cl\_g}$ for BaP is 6.3 for either dry cellulose or cellulose with 20% water. The normalized dermal uptake factor from Figure 4 is 0.22 mg/(μg/m^3)/m^2/day for 1 mm thick fabric, a 1 mm gap and 7 day launder-wear interval. In a survey of 150 US homes, the median gas-phase concentration of BaP was 0.00155 ng/m^3 (Nuamova et al., 2003; HEI, 2016). For an individual wearing clothes covering 1.5 m^2 of skin area, the daily uptake due to gas-phase BaP accumulation on clothing and subsequent transfer to skin is estimated to be 0.5 ng/day. This can be compared to the daily inhalation intake. For a typical breathing rate (0.7 m^3/h; US EPA, 2011) and combining the median gas-phase and particle phase concentration of BaP (0.00155 ng/m^3 and 0.0455 ng/m^3; HEI, 2016), the daily intake is 0.8 ng/day. Therefore, dermal uptake from clothing is similar to that by inhalation. Dermal uptake may even be greater if enhanced deposition to clothing occurs due to net transfer of SVOCs to the gas phase within the concentration boundary layer adjacent to the clothing surface (Liu et al., 2012).

However, the case of BaP is also emblematic of a potential limitation in the current model – namely, that it does not consider the time required to clear molecules from the dermis. The model simply assumes that the concentration at the interface between the viable epidermis and dermis is zero. Gong et al. (2014) noted that the viable epidermis/dermis interface is not actually where compounds are cleared from the skin and that their model would be improved if it explicitly included clearance for at least the first 100 μm of the dermis. This limitation also applies to the present model, which has extended the Gong model with the addition of a skin surface lipid layer (Morrison et al., 2016b) and clothing (present paper). The failure to account for dermal clearance is expected to have the largest impact on highly lipophilic chemicals that largely exist in the dermis bound to proteins rather than in free form. BaP is anticipated to be such a compound. Models that can be used to estimate dermal clearance for a range of compounds have been published (Ibrahim et al., 2013; Kapoor et al., 2016) and, going forward, could be added to the present model.

The model can be further enhanced by including advection. In Appendix S1 of Supporting Information, we argue that advection through cloth and across the cloth-skin gap can be ignored for most indoor situations where an occupant is not moving vigorously. However, advection can be included in future versions to extend the reach of the model beyond typical indoor conditions or for outdoor exposure. This exercise should be relatively straightforward because much of the groundwork for including advection in clothing models has already been laid by researchers studying thermal comfort and heat transfer from the skin surface (e.g. Ghali et al., 2002).

5 CONCLUSIONS

The present model steps us further towards a full mechanistic model of SVOC uptake as it is influenced by clothing. A key challenge will be improving parameter values for the model, including partition coefficients with clothing as influenced by environmental conditions, history of use, laundering frequency, laundering methods and the composition and morphology of the fabric.

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Table 1. Parameters used in current model simulations of human participant studies described in Morrison et al. (2015).

		DEP	**DnBP**
h_m, while wearing clothing	m/h	3.4	3.1
h_m during cloth loading	m/h	4 -10	4 - 10
K_{cl_g}	1	2.5×10^5	4.0×10^6
K_{ssl_g}	1	2.2×10^7	2.2×10^8
K_{sc_g}	1	7.1×10^6	2.7×10^7
K_{ve_g}	1	7.6×10^5	3.3×10^6
D_g	m²/s	5.5×10^{-6}	4.7×10^{-6}
D_{sc}	m²/s	2.6×10^{-15}	4.2×10^{-15}
D_{ve}	m²/s	6.3×10^{-11}	6.4×10^{-12}
L_{cl}	cm	0.1-0.2	0.1-0.2
L_{gap}	cm	0.01 – 1.0	0.01 – 1.0
L_{ssl}	μm	1.2	1.2
L_{sc}	μm	23	23

L_{ve}	μm	100	100
t_{lw}	days	9	9
C_{g_lw}	μg/m^3	244	119
C_g	μg/m^3	295	142

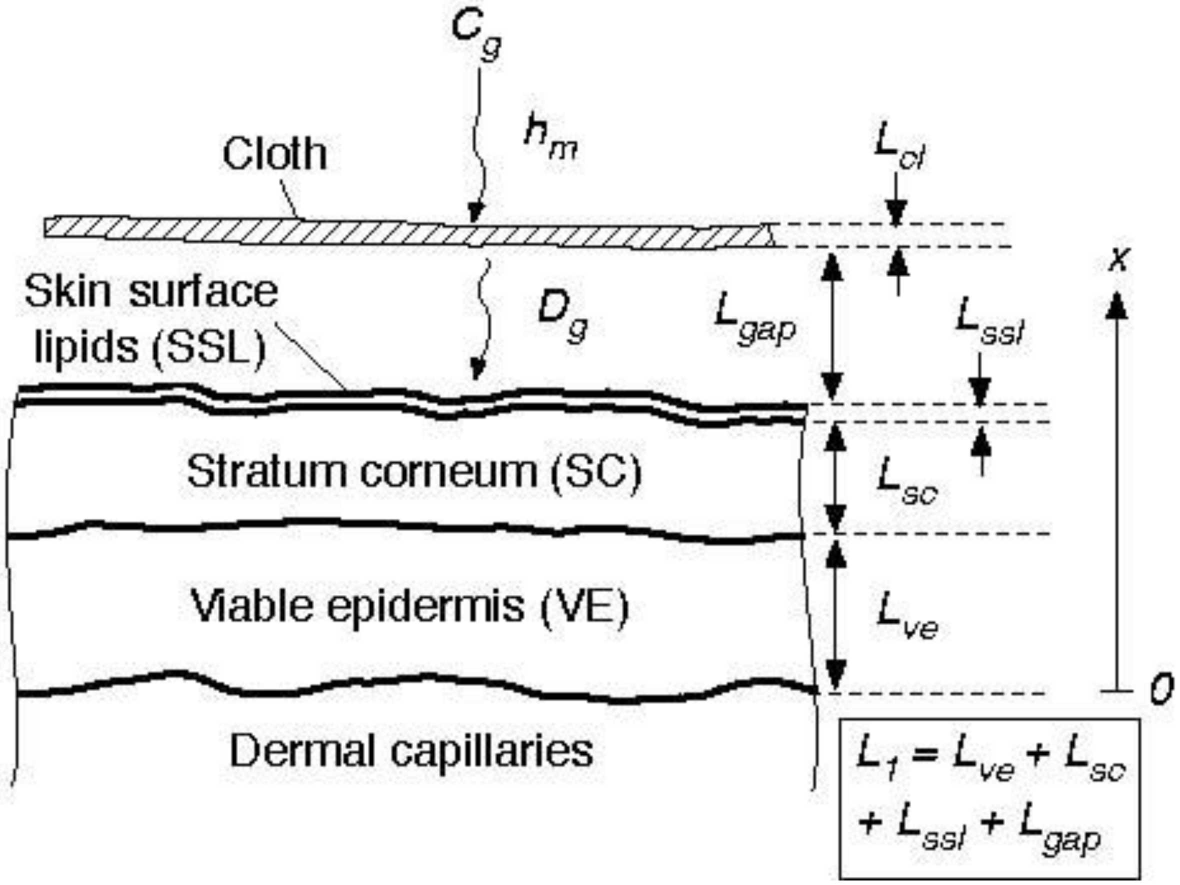
[1] dimensionless

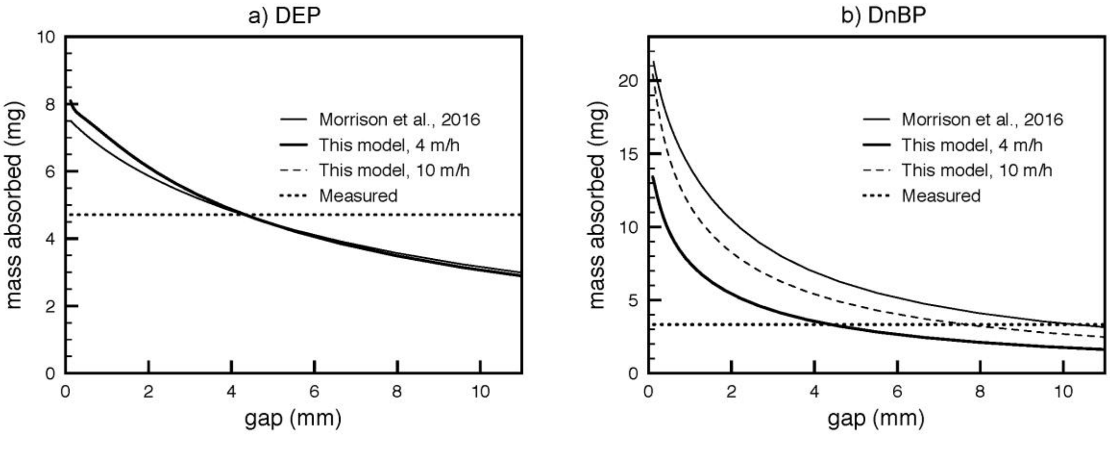
Figure 1. Geometry of dermal uptake model as influenced by clothing

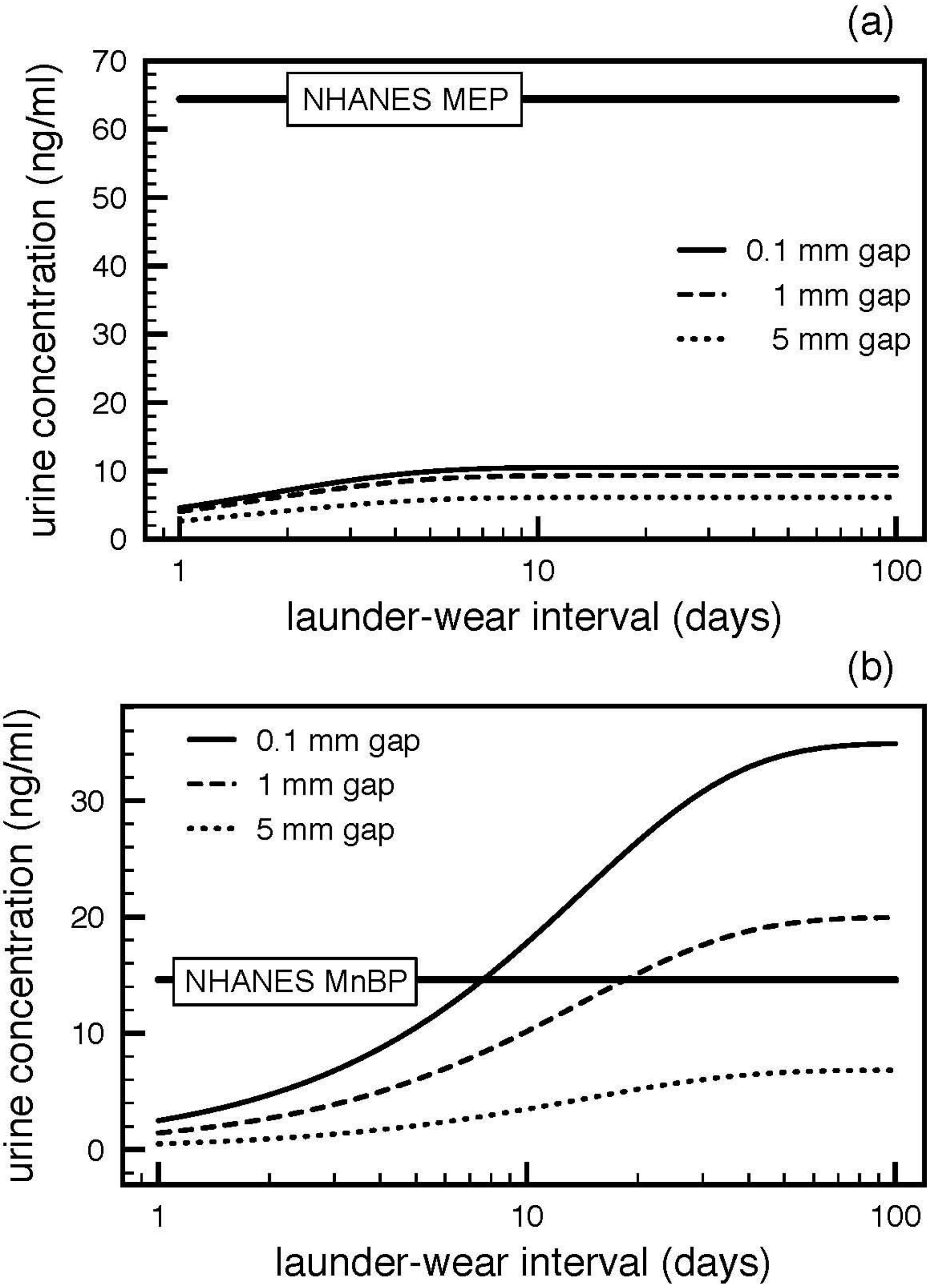
Figure 2. Simulations of phthalate uptake for the single participant described in Morrison et al. (2016a). Mass DEP (a) and DnBP (b) delivered to blood vs cloth-skin gap for previous model (Morrison et al., 2016b) and new model with two different mass-transfer coefficients.

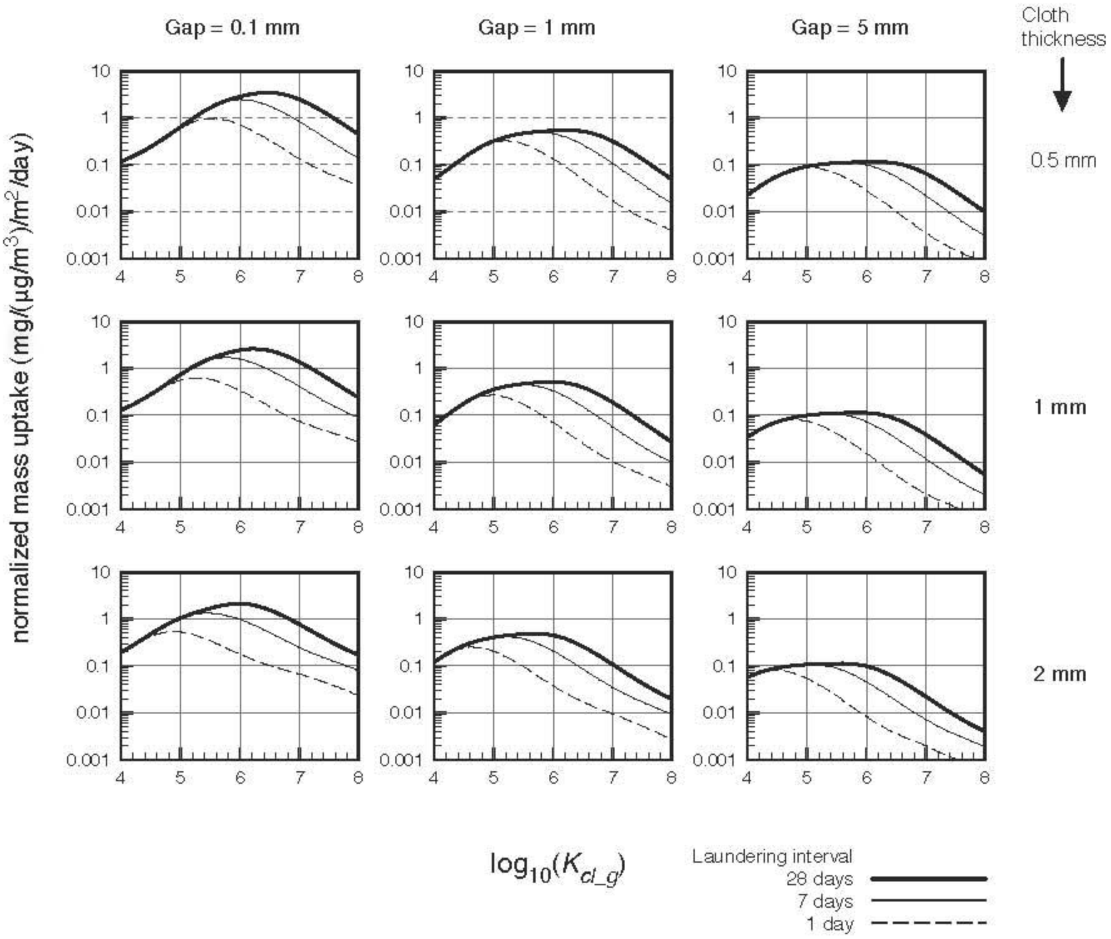
Figure 3. Steady-cycle simulations of MEP (a) and MnBP (b) urine concentrations based on 12-h of wear per day for clothing exposed to room air from 0.1 to 100 days (loading time) after washing. Heavy solid lines are the geometric mean urine concentrations from the 2009/2010 period of the National Health and Nutrition Examination Survey (NHANES; CDC, 2015).

Figure 4. Simulations of normalized mass uptake that are focused on revealing the influence of cloth thickness, cloth-skin gap, cloth partition coefficient and launder-wear interval on dermal uptake mediated by clothing. Dermal resistance is assumed to be negligible.


C_g
h_m
Cloth
L_{cl}
x
Skin surface lipids (SSL)
D_g
L_{gap}
L_{ssl}
Stratum corneum (SC)
L_{sc}
Viable epidermis (VE)
L_{ve}
0
Dermal capillaries
$L_1 = L_{ve} + L_{sc} + L_{ssl} + L_{gap}$


a) DEP
b) DnBP
mass absorbed (mg)
gap (mm)
0
2
4
6
8
10
0
5
10
15
20
Morrison et al., 2016
This model, 4 m/h
This model, 10 m/h
Measured


(a)
70
60
50
40
30
20
10
0
urine concentration (ng/ml)
NHANES MEP
0.1 mm gap
1 mm gap
5 mm gap
1
10
100
launder-wear interval (days)
(b)
30
20
10
0
urine concentration (ng/ml)
0.1 mm gap
1 mm gap
5 mm gap
NHANES MnBP
1
10
100
launder-wear interval (days)


Gap = 0.1 mm
Gap = 1 mm
Gap = 5 mm
Cloth thickness
0.5 mm
1 mm
2 mm
normalized mass uptake (mg/(µg/m³)/m²/day)
10
1
0.1
0.01
0.001
4
5
6
7
8
log10(Kcl_g)
Laundering interval
28 days
7 days
1 day