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Occupational and Environmental Exposures of Skin to Chemicals - 2005

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Abstract for Poster 40

The multiple transient dermal dose problem: theory

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Background

Typical workplace dermal exposures can be characterized as multiple transient or intermittent dermal contacts. In this scenario, a given amount of contaminant is in contact with a given area of skin for a given period of time. This cycle is repeated throughout the work day with, in general, different amounts of contaminant in contact with different areas of skin over different time intervals.

Here we present solutions for concentration, flux and total mass accumulation for this problem, in which we consider the skin to be a single homogeneous membrane. Analytical solutions are derived in the Laplace domain; numerical methods are required to transform these solutions to the time domain. We show that a simple steady-state solution exists for the total accumulation of contaminant, which is analogous to total systemic uptake. This is the main quantity of interest for dermal risk assessment.

Methods

Statement of problem

We wish to solve the partial differential equation, with boundary conditions to be specified:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} \qquad (1)$$

in the region $0 \leq x \leq h$. C is concentration, D is diffusivity and t is time. Taking the Laplace transform of eq. (1) with the initial condition $C(x, 0) = 0$, and rearranging yields:

$$\frac{d^2\hat{C}}{dx^2} - \lambda^2\hat{C} = 0 \tag{2}$$

where $\lambda = \sqrt{s/D}$. The solution to eq. (2) is:

$$\hat{C}(x) = a\sinh(\lambda x) + b\cosh(\lambda x) \tag{3}$$

with the constants a and b to be determined from the boundary conditions.

Boundary conditions

For the case of multiple transient dermal doses, the boundary condition at $x = 0$ is:

$$C(0,t) = K_{mv}C_1\big(u(t-\tau_1) - u(t-(\tau_1+t_1))\big) +$$
$$K_{mv}C_2\big(u(t-\tau_2) - u(t-(\tau_2+t_2))\big) + \dots \tag{4}$$

where K_{mv} is the membrane-vehicle partition coefficient, C_i's are chemical concentrations in the region surrounding the membrane, and $u(t-\tau_i)$ is the unit step function, delayed by $t = \tau_i$. In words, the concentration at the surface of the membrane is a series of square pulses of magnitudes $K_{mv}C_i$ with durations t_i, beginning at times τ_i. Sink conditions exist at the inner surface of the membrane $(x = h)$:

$$C(h,t) = 0 \tag{5}$$

Laplace domain solution

The Laplace transforms of eq. (4) and eq. (5) are:

$$\hat{C}(0) = K_{mv}\sum_{i=1}^{n}\frac{C_i e^{-s\tau_i}(1-e^{-st_i})}{s} \tag{6}$$

$$\hat{C}(h) = 0 \tag{7}$$

(Eq. (6) reduces to the single transient dermal dose (Frasch and Barbero, 2005) for the special case of $n = 1$ and $\tau_1 = 0$.) Inserting eq. (6) and eq. (7) into eq. (3) gives:

$$b = \hat{C}(0) \qquad (8)$$

$$a = -\frac{\hat{C}(0)\cosh(\lambda h)}{\sinh(\lambda h)} \qquad (9)$$

Substituting these into eq. (3) gives:

$$\hat{C}(x) = \hat{C}(0)\left(-\frac{\cosh(\lambda h)\sinh(\lambda x)}{\sinh(\lambda h)} + \cosh(\lambda x)\right) \qquad (10)$$

Eq. (10) can be simplified by using the identity

$$\sinh(A \pm B) = \sinh(A)\cosh(b) \pm \cosh(A)\sinh(B) \qquad (11)$$

to give:

$$\hat{C}(x) = \hat{C}(0)\frac{\sinh\left[\lambda(h-x)\right]}{\sinh(\lambda h)} = \frac{K_{mv}}{s}\frac{\sinh\left[\lambda(h-x)\right]}{\sinh(\lambda h)}\sum_{i=1}^{n}C_i e^{-s c_i}(1-e^{-s t_i}) \qquad (12)$$

Flux is given by:

$$\hat{F}(x) = -D\frac{d\hat{C}}{dx} = \frac{K_{mv}D\lambda\cosh\left[\lambda(h-x)\right]}{s\sinh(\lambda h)}\sum_{i=1}^{n}C_i e^{-s c_i}(1-e^{-s t_i}) \qquad (13)$$

The total mass accumulation of permeant per unit area on the underside of the membrane, is given by:

$$\hat{M} = \frac{\hat{F}(h)}{s} = \hat{C}(0)\frac{D\lambda}{s\sinh(\lambda h)} = \frac{K_{mv}D\lambda}{s^2\sinh(\lambda h)}\sum_{i=1}^{n}C_i e^{-s c_i}(1-e^{-s t_i}) \qquad (14)$$

Final value calculation

The steady-state solution, or the solution for the total amount of chemical per unit area that penetrates the membrane after a "long" time, can be determined by using the final value theorem of Laplace transform theory:

$$\lim_{t\to\infty} m(t) = \lim_{s\to 0} s\hat{M} = \lim_{s\to 0} \left[\frac{K_{mv}D\lambda}{s\sinh(\lambda h)} \sum_{i=1}^{n} C_i e^{-s\tau_i}(1-e^{-st_i}) \right] \tag{15}$$

To evaluate this limit, the functions $e^{-s\tau_i}$, e^{-st_i} and $\sinh(\lambda h)$ are expanded into infinite series. For $s \approx 0$,

$$e^{-s\tau_i} \approx 1 - s\tau_i \tag{16}$$

$$e^{-st_i} \approx 1 - st_i \tag{17}$$

$$\sinh(\lambda h) \approx \lambda h \tag{18}$$

Substituting these into eq. (15) gives:

$$\lim_{t\to\infty} m(t) = \lim_{s\to 0} \frac{K_{mv}D\lambda}{s\lambda h} \sum_{i=1}^{n} C_i(1-s\tau_i)(st_i) = \frac{K_{mv}D}{h} \sum_{i=1}^{n} C_i t_i = k_p \sum_{i=1}^{n} C_i t_i \tag{19}$$

where k_p is the steady-state permeability coefficient.

For more realistic occupational exposures, in which intermittent dermal contacts exist over different areas of skin (A_i), the total amount of chemical that penetrates the skin is:

$$M = k_p \sum_{i=1}^{n} A_i C_i t_i \tag{20}$$

In words, the total penetration is given by the products of cross sectional area, concentration, and time interval, summed over all exposures, times the permeability coefficient.

Time domain solutions

Time domain solutions of eqs. (6), (12), (13) and (14) are obtained by numerical inversion, using the software package Scientist 2.0 (MicroMath Scientific Software, Salt Lake City, UT.

Results

Figure 1 displays a simulation of flux (eq. (13)) and mass accumulation (eq. (14)) for a typical simulated exposure (top panel). Results are for a stratum corneum membrane with $h = 20$ μm and $D = 1.33 \times 10^{-6}$ cm^2/hr (time lag = 0.5 hr). Note that there is no requirement that flux must reach steady-state prior to the subsequent changes in input concentration.

The total accumulated amount after 10 hr from this simulation (1.266×10^{-3} μg/cm^2) precisely equals the amount predicted by the final value theorem eq. (19)).
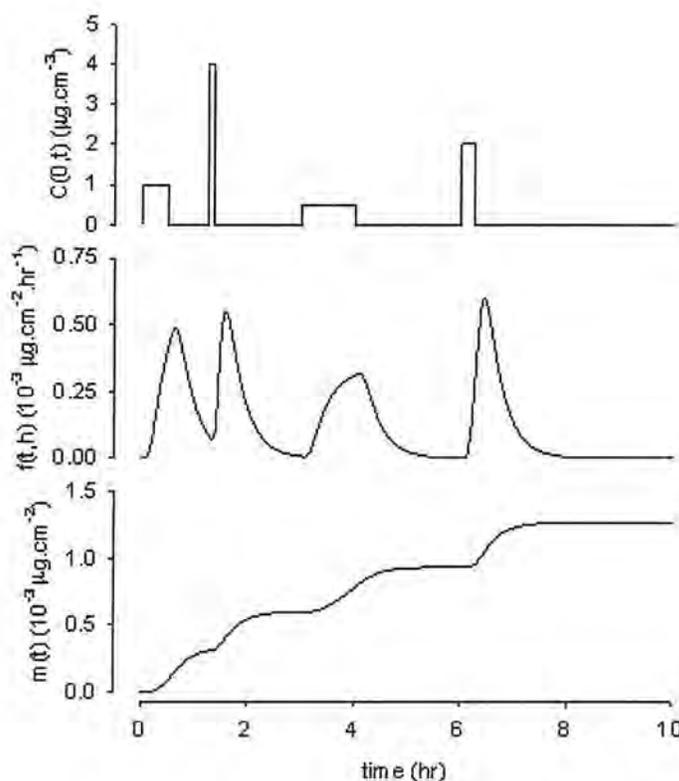

Figure 1. Simulated flux (middle panel) and mass accumulation (bottom panel) for a multiple transient dermal exposure (top panel).

Discussion and Conclusions

The equations derived here may be appropriate for application to the modelling and prediction of total systemic uptake from workplace dermal exposures. Even though these individual exposures may not achieve steady-state, the total uptake can be predicted using eq. (20), with knowledge only of the steady-state permeability coefficient and the skin exposures.

The proposed model provides a link between finite dose and infinite dose experiments. If only the steady-state permeability coefficient is known, than the total accumulation of

mass in these finite dose experiments can be determined. Conversely, steady-state permeability can be obtained from these finite dose experiments. If both permeability coefficient and time lag are known, than the entire time course of mass accumulation can be predicted (Frasch and Barbero, 2005).

The model considers the skin to be a single homogeneous membrane. While this may be a gross oversimplification from an anatomical perspective, it has been demonstrated repeatedly that skin exhibits the characteristics of a homogeneous membrane from the standpoint of diffusion. The key is to apply appropriate values for effective diffusivity and effective thickness (Frasch and Barbero, 2003).

These equations apply to the case where no significant depletion of chemical occurs during the time of dermal contact. These exposures are finite in the exposure time, but not in the amount of chemical during that exposure time. Also, the specified boundary condition between intermittent exposures (zero concentration at surface) applies to volatile compounds. For non volatile compounds, a different boundary condition (zero flux at surface) would be applicable.

Acknowledgement

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References

Frasch HF and AM Barbero, 2003. Steady-state flux and lag time in the stratum corneum lipid pathway: results from finite element models. J. Pharm. Sci. 92: 2196-2207.

Frasch HF and AM Barbero, 2005. The transient dermal dose problem. Companion poster, this conference.

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