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Spectral Reflectance Measurement of Evaporating Chemical Films: Initial Results and Application to Skin Permeation

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ABSTRACT

The present study has 2 aims. First, the method of spectral reflectance was used to measure evaporation rates of thin (~25-300 μm) films of neat liquid volatile organic chemicals exposed to a well-regulated wind speed *u*. Gas-phase evaporation mass transfer coefficient (k_{evap}) measurements of 10 chemicals, 9 of which were measured at similar u, are predicted (slope of log-log data = 1.01; intercept = 0.08; $R^2 = 0.996$) by a previously proposed mass transfer correlation. For one chemical, isoamyl alcohol, the dependence of k_{evap} on $u^{0.52}$ was measured, in support of the predicted exponent value of ½. Second, measured k_{evap} of nicotine was used as an input in analytical models based on diffusion theory to estimate the absorbed fraction (F_{abs}) of a small dose (5 μL/cm^2) applied to human epidermis *in vitro*. The measured F_{abs} was 0.062 ± 0.023. Model-estimated values are 0.066 and 0.115. Spectral reflectance is a precise method of measuring k_{evap} of liquid chemicals, and the data are well described by a simple gas-phase mass transfer coefficient. For nicotine under the single exposure condition measured herein, F_{abs} is well-predicted from a theoretical model that requires knowledge of k_{evap}, maximal dermal flux, and membrane lag time.

Introduction

Small quantities of chemicals come into contact with skin from both unintended exposures, such as splashes or contact with contaminated surfaces or even air, and intentional exposures such as the application of cosmetics, perfumes, and pharmaceutical formulations. Dermal risk assessment strategies require estimates of the uptake of such possibly harmful substances into the body. Uptake depends not only on mass loading and the area of contact but also on the interplay among kinetic variables including skin permeation rate, binding or chemical transformations within the skin, and evaporation from the skin surface. For neat liquids, evaporation reduces the amount that is absorbed, as some of the applied mass is lost to the surrounding environment. For volatile substances that do not undergo chemical transformations, current theory[1-4] provides sound theoretical estimates of the dermal uptake. For example, we have previously demonstrated[4] that knowledge of maximal steady-state dermal flux, lag time, and evaporation rate of the substance are sufficient to predict the eventual mass uptake from exposures to small or finite doses of a volatile chemical. While the first 2 variables are readily derived from *in vitro* experimental permeation experiments, knowledge of the evaporation rates of chemicals applicable to dermal exposures is limited.

Various experimental studies have reported measurements of evaporation rates of pools of volatile organic chemicals (VOCs), and mass transfer correlations have been derived and validated using these data[5-12]; (recently reviewed[13]). These correlations depend on physical properties of the liquid including vapor pressure and vapor diffusivity in air, as well as environmental factors such as wind velocity, temperature and pool size, and have found use, for example, in industrial processes and in the estimation of evaporation rates of environmental spills.

With notable exceptions, much less is known about the evaporation rates of thin films relevant to dermal exposures. Gajjar et al.[14] gravimetrically measured evaporation rates of 21 VOCs within walled *in vitro* diffusion cell caps. They tested the correlation of these data with several published mass transfer functions and proposed using one that was developed by the U.S. Environmental Protection Agency (EPA)[11] to estimate chemical spill evaporation rates. However, the general applicability of this or other mass transfer correlations to skin exposure settings has not been established. This knowledge gap constrains the rational application of quantitative dermal risk assessment strategies.

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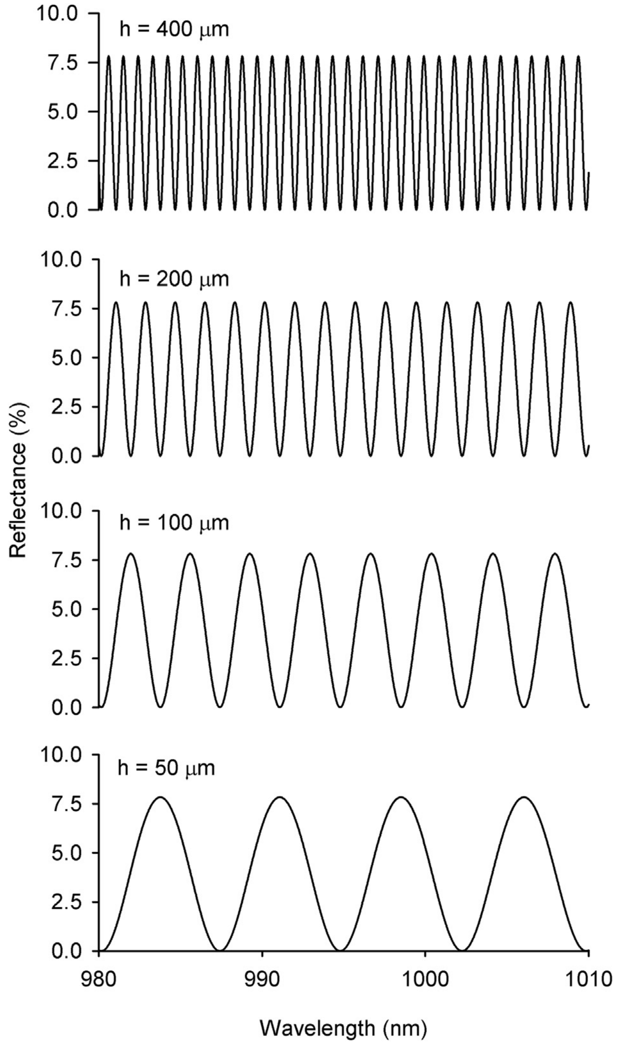

Figure 1. Theoretical optical reflectance of plane film of water surrounded by air, at listed thicknesses (h). Plots of Equation 2 with incident light angle = 0.

The aims of the current report are two-fold. First, we present the method of spectral reflectance as a tool to measure evaporation rates of thin (~25-300 μm) films of volatile neat organic chemicals. These data on 10 chemicals are compared with the predictions of a previously proposed[4] evaporative mass transfer coefficient. Second, we demonstrate an application of these data within an analytical framework to estimate the absorbed fraction of a semi-volatile neat chemical (nicotine) applied as a small dose on human skin *in vitro*.

Background and Theory

Spectral reflectance can quantify the thickness of a transparent liquid film. It measures reflected and/or transmitted light from a layered structure over a specified range of wavelengths and calculates the film thickness based on well-established optical theory. Consider the simple case of a plane parallel transparent film of thickness h and refractive index n_2, surrounded by a medium of refractive index n_1. A plane wave of monochromatic light, wavelength λ, is incident at an angle θ and is reflected off the inner surface of the film at angle θ'. It has been shown[15] that the phase difference δ between reflected waves from the inner and outer surfaces is related to the film thickness by:

$$\delta = \frac{4\pi}{\lambda} n_2 h \cos\theta' \tag{1}$$

and that the intensity of the reflected light I_r, normalized by incident intensity I_0, is given by

$$\frac{I_r}{I_0} = \frac{(2 - 2\cos\delta)R}{1 + R^2 - 2R\cos\delta} \tag{2}$$

where

$$R = \left(\frac{n_1 - n_2}{n_1 + n_2}\right)^2 \tag{3}$$

is the reflectivity of the film surface. Figure 1 displays Equation 2 for various thicknesses of water in air, with $\theta = \theta' = 0$. For films of these thicknesses, the curves appear near sinusoidal over a limited range of wavelengths, with multiple periods of very similar frequency. Thus, the fast Fourier transform (FFT) may be used to relate the fundamental frequency component to the film thickness. Similar theory applies to more complex layered structures, although analytical solutions such as Equation 2 may be elusive. The method has found broad applications in science and industry for coating and thin film analysis. It has been used to measure the thickness and sag of soap films,[16] but it has not, to our knowledge, been used to measure evaporation rates of VOCs.

The evaporation rate of a film within a constrained area can be determined from thickness measurements made over time. As outlined by Gajjar et al.,[14] the mass of an evaporating pool of pure liquid, initial mass M_0, on an impermeable surface is

$$m(t) = M_0 - m_{\mathrm{evap}}(t), \tag{4}$$

with the evaporated mass given by

$$m_{\mathrm{evap}}(t) = \int_0^t (k_{\mathrm{evap}}\rho A)\,dt. \tag{5}$$

Here, ρ is the liquid density, A is the surface area of the pool, and k_{evap} (length/time) is a liquid-phase evaporation mass transfer coefficient. If these are constant over time, then

$$m(t) = M_0 - k_{\mathrm{evap}}\rho A t, \tag{6}$$

and the area-normalized evaporative flux (mass/area/time) is:

$$J_{\mathrm{evap}} = k_{\mathrm{evap}}\rho. \tag{7}$$

Measurement of the thickness of the liquid film confined within a constant A over time represents a direct measurement of k_{evap}:

$$k_{\mathrm{evap}} = -\frac{\mathrm{d}h}{\mathrm{d}t}. \tag{8}$$

To the extent that k_{evap} is constant over time and the area, $m(t)$ is readily determined.

An important parameter in mass transfer phenomena is the gas-phase mass transfer coefficient, k_g. The following relationship holds:

$$k_{\mathrm{evap}}\rho = k_g \frac{p_{\mathrm{vap}} MW}{RT}, \tag{9}$$

where p_{vap} is vapor pressure at the temperature of the liquid, MW represents molecular weight, T is liquid temperature, and R the gas constant. Various correlations have been published to estimate k_g