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Evaluation of the Dermal Absorption of Common Solvents

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Exposure assessment is an important component in estimating health risk for individuals exposed to chemicals. Regulatory agencies have established standards for allowable occupational exposures, primarily via the inhalation pathway. In contrast, very little data is available to provide agencies sufficient guidance to establish permissible dermal exposure levels. Part of this shortfall lies in the fact that measurement of the amount of chemical absorbed through the skin is both experimentally difficult and time consuming. In the research described here an innovative methodology was utilized to non-invasively evaluate dermal absorption by continually analyzing exhaled breath. Because breath concentrations can be used to reflect blood concentrations, constant analysis of exhaled breath provides an opportunity to evaluate differences in the rapidly changing blood compartment that occurs immediately following peak exposure. Animal studies were conducted to collect time-course data on the dermal absorption of two common solvents - toluene and xylene. Both of these solvents are components of various paint and adhesive products, and may be frequently encountered in the occupational setting and by the consumer. Studies were conducted to expose animals to these compounds as both aqueous material and as vapors in order to provide an understanding of the impact of exposure matrix on dermal absorption. The exhaled breath kinetic data collected from each exposed animal was subsequently evaluated using an established mathematical model to determine the rate of dermal absorption. The studies conducted to date indicate that the aqueous compounds are rapidly absorbed through the skin of a rat with permeability coefficients of 0.074 +/- 0.005 and 0.058 +/- 0.009 cm/hr for toluene and xylene, respectively. In comparison, the rat in vivo permeability coefficient was significantly higher for toluene and xylene vapor exposures, at 0.91 +/- 0.05 and 0.65 +/- 0.08 cm/hr, respectively. However, numerous investigators have shown that the dermal absorption of a variety of compounds is greater in rats than in humans. Therefore, focused human studies were conducted to evaluate the dermal absorption of aqueous toluene and xylene in a realistic exposure scenario to mimic bathing. Volunteers were exposed at initial water concentrations of approximately 500 µg/L toluene or xylene, and exhaled breath collected and analyzed as described for the animal studies. The human dermal permeability coefficients estimated from the exhaled breath data using the PBPK model were 0.012 +/- 0.007 cm/hr for toluene and 0.005 +/- 0.001 cm/hr for xylene. Although a comparative human value for xylene was not located in the literature, the U.S. EPA estimate for toluene absorption in the human of 1 cm/hr is in sharp contrast to the data determined here and suggests that a reevaluation of human dermal absorption may be warranted. Furthermore, although these studies were conducted using vapor and aqueous exposures, the resulting permeability estimates form the basis for comparing relative dermal bioavailability of these common solvents in the organic matrices of occupational and consumer products (Supported by NIOSH 5-RO1-OH03658-02 and NIEHS 1-P42-ES10338-01).

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