during dermal permeation of 4 phenolic biocides in 4 different formulations using a LSER approach, with a calibrated flow through diffusion cell system. Infinite doses of 4 biocides and 25 probe chemicals in water, 17% methanol and 2 commercial removal fluids namely Astrocut–C® and Tapfree 2® were applied to porcine skin flow through diffusion cells. The strength coefficients for the 25 probe compounds for each system were determined from multiple linear regression analysis and plugged into the Abraham's LSER equation to predict permeability values for biocides. Biocide permeability significantly decreased in methanol, Astrocut–C® and Tapfree 2® when compared to water. The strength coefficients revealed that hydrophobicity played an important role in explaining the reduced permeability in vehicles when compared to water. This finding is important for selection of biocides and cutting fluid formulations. The R^2 between experimental and predicted log Kp of probe solutes for water, methanol, Astrocut–C® and Tapfree 2® were 0.70, 0.78, 0.89 and 0.84 respectively. In conclusion, the LSER approach in part explained several chemical interactions resulting in reduced permeability and also predicted the dermal permeability of 4 biocides in commercial cutting fluids. Further dermal permeability of biocides will be determined in individual and combinations of different components of commercial cutting fluids to ascertain which component has prominent influence in dermal permeability. (Supported by NIOSH OH 03669)

1558 *IN VITRO* STUDIES OF PERCUTANEOUS ABSORPTION AND SURFACE-TO-SKIN TRANSFER OF D-METHAMPHETAMINE HYDROCHLORIDE USING HUMAN SKIN.

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Studies were designed to evaluate the percutaneous absorption and surface-to-skin transfer efficiency of [14C] d-methamphetamine hydrochloride (d-meth HCl) from contaminated materials to human cadaver skin, in vitro, using the finite dose technique and flow through diffusion cells.

The studies were performed on a minimum of three sections from three different cadaver skin donors. Two materials, vinyl tile and fabric, were used to measure the efficiency of d-meth HCl transfer from the material surface to skin. At pre-selected times during material-skin contact, the treated vinyl tile or fabric disks were removed from the upper surface of the skin, and skin incubation and receptor fluid collection were continued for up to 24 hours. In addition, the effect of wetting the fabric was evaluated to examine the potential influence of moist environmental conditions on transfer efficiency and skin absorption. All samples were analyzed for recovery of radioactivity using a liquid scintillation analyzer.

The results showed that d-meth HCl is very sensitive to changes in environmental pH. When the pH was greater than 4, the hydrochloride salt converted to its free base form, thereby increasing its volatility. d-Meth HCl penetrated into and through human cadaver skin quickly when skin was exposed to contaminated materials; transfer efficiency was directly related to contact duration. Moist conditions during the material surface-skin transfer accelerated transfer efficiency and subsequent percutaneous absorption. The smoothness and porosity of the contact surface also altered the efficiency of transfer. d-Meth HCl retained in the skin layer continued to be released into the receptor fluid even after the contact material had been removed. For future study, we recommend exploring the skin retention/penetration and skin surface decontamination/penetration relationships of d-meth HCl.

1559 COMPARATIVE EFFECTS OF SURFACTANTS (SLS AND LAS) ON THE DERMAL ABSORPTION OF A SERIES OF COMPOUNDS IN ISOLATED PERFUSED SKIN.

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Surfactants are a common constituent of many complex chemical mixtures encountered in occupational and environmental waste exposure scenarios. This study focused on assessing the effect of the surfactants sodium lauryl sulfate (SLS) or linear alkylbenzene sulfonate (LAS) on the dermal penetration and absorption on aqueous solutions of six chemicals (fenthion, parathion, ρ-nitrophenol, phenol, propazine and triazine) dosed topically on the isolated perfused porcine skin flap (IPPSF) model. SLS and LAS were selected because of their widespread applicability to practical dermal exposure scenarios, and their molecular similarity differing only in the absence or presence, respectively, of an aromatic ring in their polar head region. IPPSF absorption was assessed into perfusate, stratum corneum, and skin using radioassay of ^{14}C labeled compounds, with absorption parameters for individually-dosed compounds in SLS and LAS compared to aqueous controls without surfactant. Across all penetrants, absorptive flux and skin penetration was greater with SLS compared to LAS. The relationship of absorption from water varied, with surfactant treatments less than water for ρ-nitrophenol, parathion, fenthion and propazine, while absorption from water was intermediate between SLS and LAS for phenol and triazine. Surfactants also had variable effects of maximum flux. This work begins to establish a relationship between the physical chemical properties of penetrants and properties of the surfactant, an important phenomenon to understand when predicting chemical absorption from common mixtures. (Supported by NIOSH OH-07555)

1560 DERMAL EXPOSURE INDUCES KERATIN ADDUCTS IN THE SKIN.

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Polyaromatic hydrocarbons such as naphthalene are ubiquitous in the environment. Significant potential exists for naphthalene toxicity through dermal and inhalation exposure. Dosimetry and possible mechanisms of action through contact with respiratory epithelium and skin are poorly understood. Using 3-D reconstructed human skin exposed to naphthalene we observed that epoxide metabolites of naphthalene are generated by specific cytochrome P450 isoforms (e.g., CYP 2E1) in viable epidermis and form adducts with skin proteins such as keratin 1 (K1) and keratin 10 (K10). We then developed and tested enzyme-linked immunosorbent assays (ELISA) for dermal samples collected by tape stripping from workers exposed to naphthalene-containing jet fuel to quantitate naphthyl-keratin adducts as biomarkers of exposure to naphthalene. The four naphthyl-keratin adducts were detected at 0.170 ± 0.159, 0.127 ± 0.120, 0.495 ± 0.342, and 1.852 ± 1.067 pmole adduct/μg keratin for 1-naphthyl-K1, 2-naphthyl-K1, 1-naphthyl-K10, and 2-naphthyl-K10, respectively. Quantitation of keratin adducts obtained from the stratum corneum of exposed individuals will allow us to investigate the importance of dermal penetration, metabolism, and adduction of keratin as well as to make accurate prediction of the contribution of dermal exposure to the systemic dose for inclusion in exposure- and risk-assessment models.

1561 EFFECT OF BLOCKING THE IL-1 RECEPTOR ON JP-8-INDUCED GENE EXPRESSION IN RAT SKIN.

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Jet Propulsion fuel-8 (JP-8) may cause inflammation as a result of skin contact. Interleukin-1 alpha (IL-1 alpha), a proinflammatory cytokine, is preformed and stored in the epidermis. We hypothesize that the release of the preformed IL-1 alpha plays an important role in the inflammatory cascade induced by JP-8. To test this hypothesis, we applied JP-8 on rat skin after blocking the IL-1 alpha receptor using the IL-1 receptor antagonist (IL-1 ra) (Kineret, Amgen, Thousand Oaks, CA) and studied the changes in gene expression. After anesthetizing the rats, 100 micro liters of IL-1 ra or phosphate buffered saline (control), was injected into the skin without disrupting the barrier layer at the region of exposure. One hour after the injection, 500 micro liters of JP-8, in a gauze-filled, occlusive, plastic patch (3.14 cm2), was applied to the clipped back of male Fischer 344 rats for one hour. The rats were humanely killed using CO2. Injected and exposed skin was removed, placed in ice-cold RNAlater (Ambion, TX), and stored at 20 ○C overnight. Total RNA was isolated from the skin and labeled using Affy Target Labeling Kit. Biotinylated RNA was hybridized to rat genome 230 2.0 GeneChip arrays (Affymetrix) containing 31,099 genes. The chips were then scanned and the digitalized image data was processed using GCOS software (Affymetrix) and analyzed with GeneSpring GX 7.3 (Agilent Technologies, CA). The analysis showed two-fold changes in only 170 genes out of 31,099 probe sets. Up-regulated genes downstream of IL-1 were Lef1, Wnt 5a, and orosomucoid 1. The change in gene expression with IL-1 blockade suggests that JP-8 irritation may involve the release of preformed IL-1 alpha. (Sponsored by AF Office of Scientific Research)

1562 COMPARISON OF GENE EXPRESSION IN THE EPIDERMIS AFTER BRIEF EXPOSURES TO JP-8 IN HUMAN VOLUNTEERS AND RATS.

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Various groups have studied the irritation of the jet fuel, JP-8, in a wide variety models and have shown that inflammatory and growth pathways are activated by JP-8. We have investigated the time course of gene expression in rat epidermis after 1 h exposures to JP-8 (Tox Sci, 95(2): 495, 2007). The purpose of this investigation was to determine if an identical exposure to the skin of human volunteers would re-

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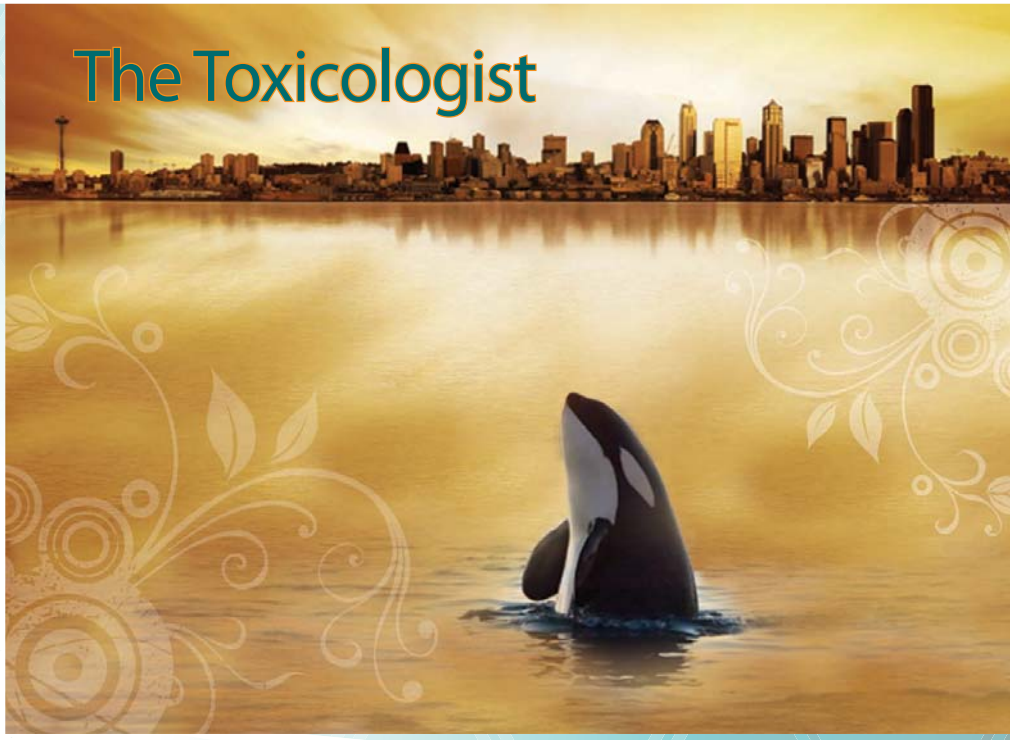

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