PS 115 EVALUATION OF THE SENSITIZING POTENTIAL OF DIPHOTERINE® IN ADULT VOLUNTEERS WITH NORMAL SKIN.

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Diphoterine®, a decontamination solution for chemical splashes, contains an amphoteric compound. It is non-irritating, non-cytotoxic, non-mutagenic and non-toxic by dermal and oral routes in rodents. Its sensitizing capacity has been previously evaluated in the Guinea pig without any observed reaction. The objective was to assess the allergenic potential of Diphoterine® in humans when applied pure under an occlusive patch with dermatological control following the Marzulli-Maibach method. 164 normal volunteers were divided into 3 groups. A sample of 25 µL (on a paper filter disk) was applied on the homological (induction phase) and contralateral scapular area under an occlusive dressing. Another dressing without Diphoterine® was applied in the same conditions as a blank application. During the induction phase, the application of the product was renewed 3 times per week for 48H each time. There were 8 or 9 applications. The induction, latency and elicitation phases ended after 3 weeks, 2 weeks, and 1 week respectively. Neither the homolateral area during the Induction Phase nor the contralateral area during the revelation phase were wetted. 161 volunteers completed the study. Clinical examinations during the induction phase allowed continuing Diphoterine® and blank applications throughout this period and during the relevation phase. During the elicitation phase, no reaction was observed. An index of average irritation (I.I.M) was calculated at each examination. The I.M.M at day 22, for the 111 normal volunteers who had 9 successive Diphoterine® applications, was 0.09. Diphoterine® remains non-irritating during the first 5 applications, then becomes lightly irritating (I.M.M = 0.25) during the 3 following applications. Thus, among 111 normal volunteers, who received 9 successive dermal applications, Diphoterine® was not a skin irritant. To conclude, the risks of skin sensitization from dermal contact with Diphoterine are negligible. Thus Diphoterine® may be classified as hypoallergenic.

PS 116 CYTOKINES IN RAT SKIN AFTER A ONE-HOUR EXPOSURE OF JET PROPULSION FUEL-8.

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Jet Propulsion fuel-8 (JP-8) may cause inflammation upon skin contact. To develop therapeutic or prophylactic measures, we have to understand the trigger of inflammation induced by JP-8. One of the early events in inflammation is the expression of inflammatory cytokines. In this study, we have investigated the expression of inflammatory cytokines, interleukin (IL) -1 alpha, IL-1 beta, IL-6, macrophage inflammatory protein-2 (CXCL2) and tumor necrosis factor (TNF) alpha, at different times after a 1-h exposure of rat skin to JP-8. A patch containing five hundred microliters of JP-8 or an empty patch was placed on the fur-clipped back of male Fisher rats. At 0, 1, 2, 3, 4, and 8h post exposure, we humanely killed the rats using CO2 and excised the skin. We isolated protein, to quantify cytokines, by pulverizing and homogenizing the skin in extraction buffer with protease inhibitors. The cytokines were estimated using a sandwich ELISA utilizing capture and detection antibodies from R & D systems (Minneapolis, MN). IL-1 alpha decreased at 3h and CXCL2 increased at 1h post exposure. IL-1 beta, IL-6 and TNF alpha did not significantly change at any time point up to 8h. IL-1 alpha is thought to be preformed and stored in skin. The reduction in the level of IL-1 alpha may be due to its release in response to JP-8 exposure. Released cytokine binds to the receptor and may be internalized for degradation. CXCL2, a chemokine involved in the attraction of polymorphonuclear granulocytes, was detected in low amounts compared to the other cytokines. We expected to see a significant change in the signaling protein levels based on mRNA expression studies in our lab. In this study, we show that only two cytokines among the five studied have a change in protein levels. The decrease in IL-1 alpha and increase in CXCL2 levels may be some of the earliest protein events in the inflammatory cascade induced by JP-8. (Sponsored by Air Force Office of Scientific Research)

PS 117 UV EFFECTS AND CHEMICALS SKIN TOLERANCE ASSESSMENT USING THE *IN VITRO* RECONSTRUCTED HUMAN FULL THICKNESS SKIN MODEL REALSKIN.

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In vitro Reconstructed human skin models are of growing interest for regulatory purposes in the framework of alternatives to animal testing, and for safety or efficacy studies.

The reconstructed human full thickness skin model RealSkin is an organotypic culture composed of a living dermal equivalent (human fibroblast-contracted collagen gel) and a well-stratified and fully differentiated epidermis (human keratinocytes). In the present study, we investigated dermis and epidermis compartments responses after exposure to different stress agents. Thus, tissues were subjected to UVs exposure as well as topical treatment with known potentially cytotoxic and non cytotoxic chemicals with available historical in vivo skin tolerance data.
For UV effects, skin tissues were exposed to increasing doses of UVA or UVSSR (UVA+B) from 0 to 55 J.cm-2. For skin tolerance studies, chemical were topically applied onto the skin. Following UV or product treatments, tissues were incubated overnight at 37°C, 5% CO2 with fresh maintenance medium. Cell viability assessment (MTT conversion test), pro-inflammatory mediator measurements and histological studies were performed. Our results showed that 1- UVA-induced damage predominantly affected the dermal compartment whereas UVA+B exposure simultaneously induced damages in both dermal and epidermal compartments, 2- The skin model with adapted protocols was able to discriminate between cytotoxic and non cytotoxic chemicals in relation with their irritant potency, 3- damages depth can be documented.
These preliminary results suggested that RealSkin is a promising tool for understanding in vitro skin tolerance effects of products and for studies involving UV effects. They may serve as a basis for further larger scale experiments.

PS 118 EFFECT OF METAL WORKING FORMULATIONS ON BIOCIDE ABSORPTION IN A PDMS MEMBRANE COATED FIBER.

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Biocides and preservatives are commonly used in metal working industry applications as additives to extend the shelf life of commercially manufactured aqueous metal working fluid (MWF) formulations. While little is known of the dermal absorption and disposition of these and other MWF formulation components, 5 major classes of these biocides have been associated with occupational contact dermatitis (OCD) in metal machine workers exposed to these mixtures. A PDMS membrane coated fiber (MCF) was exposed to three industrial generic aqueous cutting fluid formulations; soluble oil (SO), semi-synthetic oil (SSYN), and synthetic oil (SYN), as well as surrogate formulations of PEG-200 (PEG) and mineral oil (MO) (to mimic synthetic and soluble oil formulations respectively) at three different concentrations (0.05%, 0.5%, and 5%) to determine the absorption of 37 solutes, including representatives from each of the 5 classes of biocides known to cause OCD. Log K_{mcf} values were used to quantify dermal absorption and to determine differences between the formulation and/or concentrations. Initial trends indicate that highest absorption occurs at the lowest concentration (absorption at 0.05%> 0.5%>5.0%) across formulations. This trend is best demonstrated in soluble oil (SO) formulation, and Log $K_{o/w}$ values best correlated with the 0.05% concentration (R^2 = 0.77). Changes in absorption of solutes with low log $K_{o/w}$ values were less likely to be influenced by changes in MWF concentrations, while changes in absorption were magnified at higher Log $K_{o/w}$ values. The biocide 4-tertiary amylphenol showed its most pronounced absorption difference between the 3 concentrations in the MO formulation, followed by SO, SYN, and then PEG; the later with little or no difference in absorption between the concentrations. These phenomena suggest that there is not only a chemical but also concentration dependent influence on absorption of individual solutes in the presence of more complex formulations or mixtures. This work was supported by NIOSH grant R01-01-03669.

PS 119 CUTANEOUS RADIATION INJURY: LIPOSOMAL GLUTATHIONE TREATMENT AND MONITORING BY OPTICAL REFLECTANCE SPECTROSCOPY.

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Exposure to ionizing radiation from radiological or nuclear weapons and terrorist devices will likely cause life threatening radiation cutaneous injuries. To date, mechanistic and health effects of cutaneous radiation injury have been investigated only to a limited extent, and no specific countermeasures are available for treatment. Radiation has been shown to deplete the function of glutathione reductase and a decrease in glutathione can occur systemically or locally in affected tissues. Thus it is hypothesized that the combined administration of topical and systemic glutathione will reduce the severity of cutaneous radiation injury and accelerate healing. A stable liposomal encapsulation of glutathione that can be orally and topically administered has recently become available and has been evaluated for efficacy in mitigating cutaneous radiation injuries using F344 rats exposed thigh only. Visually, glutathione reduced cutaneous injury and increased healing compared to

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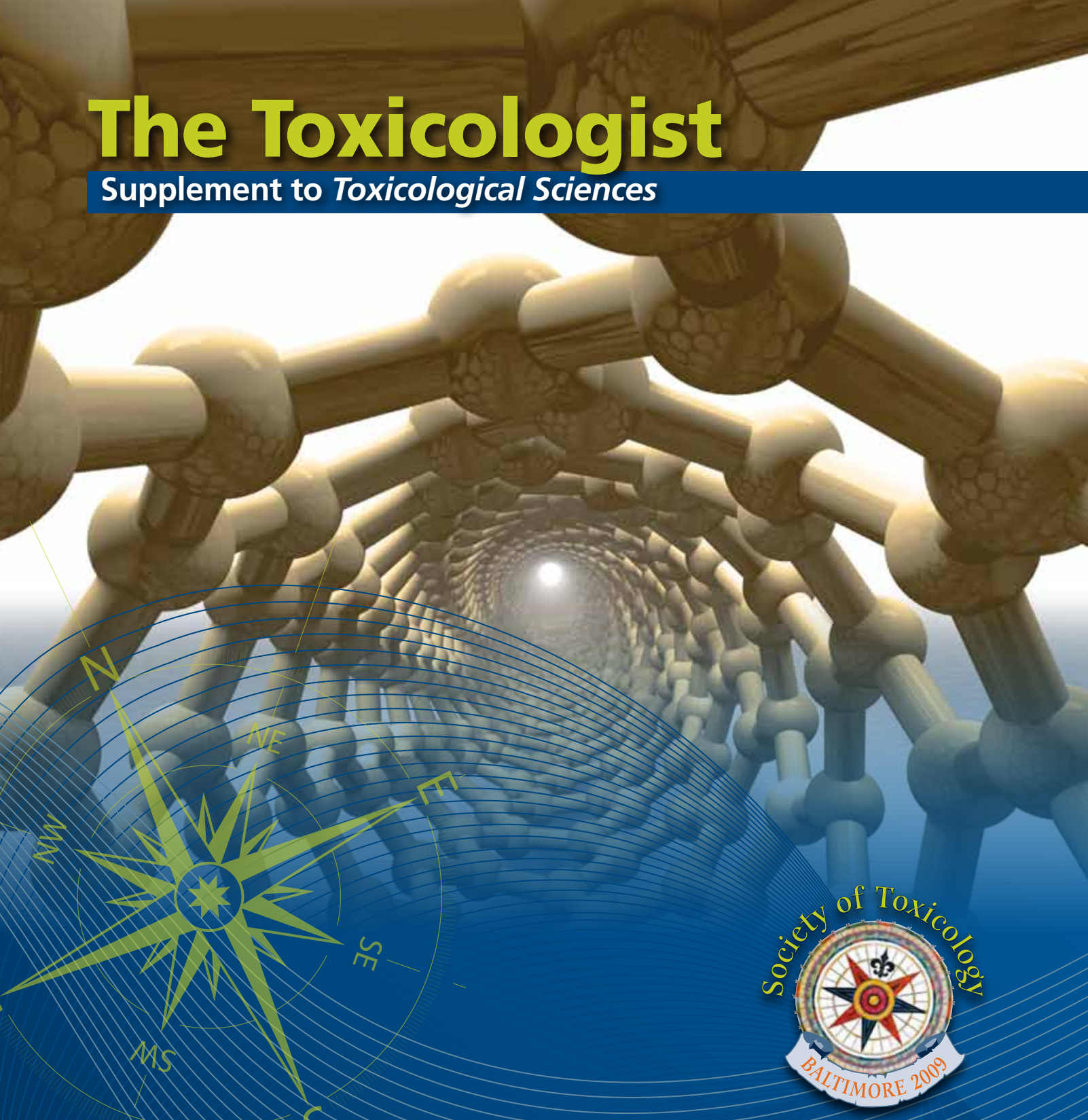

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