tancy evaluation and ranking of bath and body wash products based on ET_{50} values showed a good correlation with the expected irritation potential of individual ingredients. Histology analysis confirmed the overall MTT viability results and provided additional information regarding the effect of the tested products on the tissues integrity. However, IL-1α release did not appear to be as sensitive a marker as the MTT viability assessment at the short exposure times used (20 minutes, 1, 2, and 4 hours). This *in vitro* safety screening approach shows promise for predicting the vaginal irritancy of tested products and in meeting the typical needs of product development groups charged with developing increasingly milder products.

PS 492 DEVELOPMENT AND CHARACTERIZATION OF HUMAN AND MOUSE PRIMARY EPITHELIAL CELL CULTURES FOR ASSESSING ARSENIC TOXICITY.

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Inorganic arsenic exposure can induce skin, lung, and bladder cancer in humans; however, it has typically not produced tumors in standard animal bioassays. To better understand the mechanisms of arsenic induced bladder cancer and the reasons for species differences in sensitivity, *in vitro* tissue and species specific models are needed. The purpose of this study was to develop human and mouse primary uroepithelial cell culture models to investigate arsenic toxicity of the bladder. Human ureter sections from transplant patients were received in refrigerated Custodial® solution. Epithelial cells were isolated by gently scraping the interior to release the cells. Cells were passed through a 100 micron nylon filter, centrifuged, and washed with keratinocyte-SFM to remove debris. Cell viability was >80%. Cell yield varied depending on the size and quality of donor tissue, but average yield was 3.7 x 10^6 viable cells. Human cells were seeded at 50K/well in collagen-coated 96-well plates and grown to confluency for ~3 weeks. RT-PCR analysis confirmed PPAR-gamma, Keratin 10 and UPK2 expression, indicating cell differentiation and proliferation. Mouse uroepithelial (UE) cells were isolated using the same protocol as human ureter cells. Total cell yield was approximately 0.5 x 10^6 cells per bladder and cells were seeded at 100-200K per well into collagen-coated, 96-well plates. Unlike human cells, mouse cells did not adhere to the culture plates and did not express key markers of growth and differentiation. Cell viability decreased rapidly over time. Several variations in media and plate coatings did not improve mouse cell viability or growth properties. This work demonstrates that human ureter epithelial cells may be useful for assessing arsenic toxicity and improving risk assessment models, while the use of mouse UE cells requires additional work.

PS 493 DERMAL ABSORPTION IN RATS EXPOSED BODY-ONLY AND NOSE-ONLY TO CHEMICAL VAPORS.

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Groups of 6 rats each were exposed body-only or nose-only for 4 hours to vapor atmospheres of 4 chemicals: toluene, isopropanol, dioxane, or methyl ethyl ketone (MEK). Blood samples were collected from each rat at 0, 1, 4, and 18-hour timepoints and analyzed for concentration of the primary chemical and its metabolites. The mean blood concentration of toluene in rats exposed to 8,000 ppm toluene ranged from 12-13 μg/ml and 210-240 μg/ml for rats exposed body-only and nose-only, respectively. The mean blood concentration of isopropanol/acetone in rats exposed to 10,000 ppm isopropanol ranged from 2-4/15-32 μg/ml and 410-1200/240-980 μg/ml for rats exposed body-only and nose-only, respectively. The mean blood concentration of dioxane in rats exposed to 5,000 ppm dioxane ranged from 8-33 μg/ml and 430-1700 μg/ml for rats exposed body-only and nose-only, respectively. The mean blood concentration of MEK/2,3-butanediol in rats exposed to 5,000 ppm MEK ranged from 5-20/3-5 μg/ml and 320-860/12-90 μg/ml for rats exposed body-only and nose-only, respectively. The concentration of chemical/metabolite in the blood of rats was consistently higher for nose-only exposures compared to body-only exposures for each of the four chemicals tested. The nose-only / body-only blood concentrations ratios were 19 (toluene), 52 (dioxane), 61 (MEK), and 188 (isopropanol). The data from this study suggests that prediction of the body-only to nose-only blood ratios may be possible utilizing specific properties for a chemical (e.g., molecular weight, Kow). Testing with additional chemicals should clarify whether the blood concentration ratios between the two exposure modes and the resulting data could be used in determining dermal protection factors for individual chemicals that could be applied to existing health based occupational exposure criteria.

PS 494 FROM TOPICAL ANTIDOTE AGAINST SKIN IRRITANTS TO A NOVEL COUNTER-IRRITATING AND ANTI-INFLAMMATORY PEPTIDE.

U. Wormser[1], M. Aschner[2], Y. Schussheim[1], A. Rosengarten[1], E. Proscura[1], E. Shapira[1] and B. Brodsky[1]. *[1]The Hebrew University, Jerusalem, Israel and [2]Vanderbilt University Medical Center, Nashville, TN.*

The primary purpose of the present study was to investigate the mechanism of the counter-irritating activity of topical iodine against skin lesions induced by chemical and thermal stimuli. The hypothesis that iodine exerts its activity by inducing an endogenous anti-inflammatory factor was confirmed by exposing guinea pig skin to heat stimulus followed by topical iodine treatment and skin extraction. Injection of the extract into naïve guinea pigs reduced heat-induced irritation by 62%. The protective factor, identified as a new nonapeptide (histone H2A 36-44, H-Lys-Gly-Asn-Tyr-Ala-Glu-Arg-Ileu-Ala-OH), caused reduction of 40% in irritation score in heat-exposed guinea pigs. The murine analog (H-Lys-Gly-His-Tyr-Ala-Glu-Arg-Val-Gly-OH, termed IIIM1) reduced sulfur mustard (SM)-induced ear swelling at a dose-dependent bell shape manner reaching peak activity at 1mg/kg. Cultured keratinocytes transfected with the peptide were more resistant towards SM than the control cells. The peptide suppressed oxidative burst in activated neutrophils in a concentration-depended manner. In addition, the peptide reduced glucose oxidase- and carrageenan-induced skin edema in mice. Apart from thermal and chemical-induced skin irritation, this novel peptide might be of potential use in chronic dermal disorders, such as psoriasis and pemphigus, as well as non-dermal inflammatory diseases like multiple sclerosis, arthritis and colitis. (Supported by the US-Israel Binational Science Foundation 0378320)

PS 495 PREDICTING SKIN PERMEABILITY: INCORPORATION OF CHEMICAL MIXTURE EFFECTS INTO SIMPLE QUANTITATIVE STRUCTURE PERMEATION RELATIONSHIPS (QSPER).

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Predicting the degree of dermal absorption of topically exposed chemicals is an important issue in both environmental and occupational risk assessment. Most risk assessment approaches and QSPeR models are based on data obtained from dosing chemicals neat or in simple aqueous vehicles, yet most exposures are to complex mixtures. We have previously demonstrated that a simple QSPeR model based on 12 penetrants in 24 mixtures could be constructed if the physical chemical properties of the mixture components and vehicle were also incorporated. The present study significantly expands on this analysis by increasing the number of penetrants studied using in vitro porcine skin diffusion cells to 16 for a total of 384 treatment combinations. In addition, we applied the model to 31 penetrants dosed in a total of 189 treatment combinations using an isolated perfused porcine skin model previously shown to be predictive of in vivo human absorption. These studies demonstrated that mixture chemical descriptors including topical polar surface area/or ovality significantly improve prediction of dermal absorption using different base QSPeR models (e.g. Abraham 5-term or Potts and Guy 2-term models). These studies suggest that such information could be incorporated into dermal risk assessment protocols to improve prediction of chemical absorption based on more realistic exposure scenarios (Supported by NIOSH OH-07555)

PS 496 DEVELOPMENT OF QUANTITATIVE METHODS FOR ASSESSING SOLAR UV-INDUCED GENOTOXICITY ON RECONSTRUCTED SKIN: DNA DAMAGE, P53 STATUS, AND APOPTOSIS.

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Even if normal human keratinocytes in culture constitute a relevant and a validated model for photogenotoxicity studies, complementary information on 3D tissues in conditions closer to human skin is necessary. In this regard, industrial reconstructed skin models such as Episkin model are very convenient. The aim of this study was to provide quantitative methodologies in order to precisely assess the genotoxic impact of sunlight. Such methods should be faster and better adapted for screening purpose than classical immuno-histochemistry approaches. Here, a full thickness reconstructed skin model (including dermis with fibroblasts embedded in collagen) was exposed to simulated solar UV radiation similar to zenithal sunlight in terms of spectral power distribution. Biological endpoints related to genotoxicity were then

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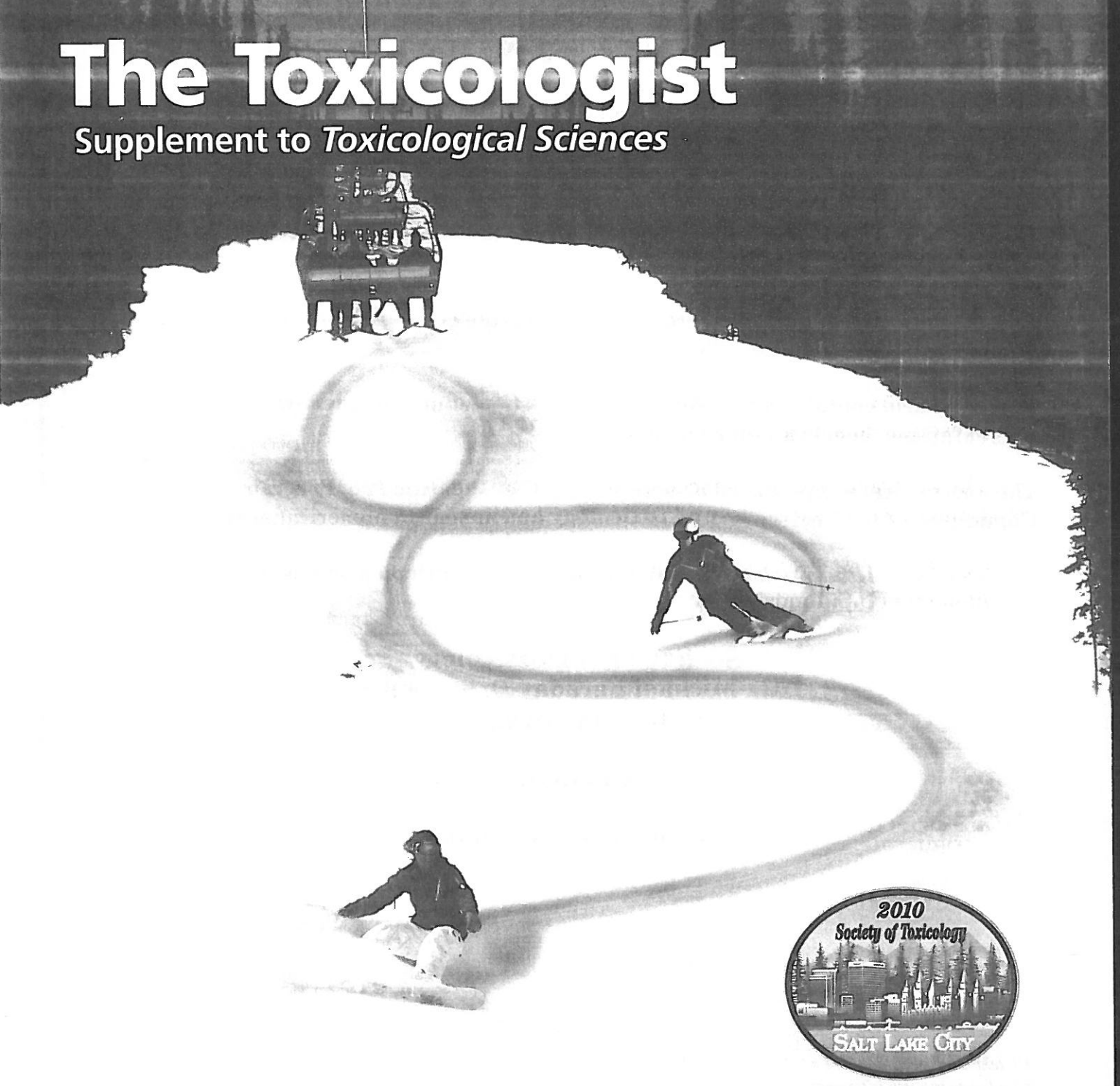

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 49th Annual Meeting of the Society of Toxicology, held at the Salt Palace Convention Center, March 7–11, 2010.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 473.

The issue also contains a Key Word Index (by subject or chemical) of all the presentations, beginning on page 496.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence.

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