physico-chemical descriptors. All Kp values were experimentally determined and obtained from literature sources, while the values for the selected molecular descriptors were experimentally measurable and can be calculated readily. The analyzed descriptors included calculated octanol-water partition coefficient (Kow), octanol-water partition coefficient of all species (unionized and ionized) at pH 5 and 7.4 (D), molecular weight (MW), molecular volume, polar surface area, water solubility (Sw), topological polar surface area, melting point (m.p.) and hydrogen donors/acceptors. Using the CAChe program's (Fujitsu America Inc., Portland, OR) stepwise regression analysis, five out of the ten molecular descriptors in the data set were determined to have significant statistical correlation: log P, log DpH 7.4, molecular weight (MW), solubility (SW), and Melting Point (m.p.). LogKp = -0.005530X(MW) + 0.6205X(log Kow) + 3.030e-07X(Sw) + 0.08239X(log DpH7.4) - 0.001483*(m.p.) - 2.759 In conclusion, an algorithm to estimate human skin absorption is derived based on physical properties of over three hundred compounds. Compared to other skin absorption QSAR models in the literature, our model has incorporated more physical properties like Sw, log DpH7.4 and m.p. in addition to the commonly used MW and log Kow with good correlation coefficient. An independent test data set will be generated to test the reliability of this model.

1579 DERMAL TOXICITY OF SUPER VASMOL 33 WITH AYURPRASH, SUPER VASMOL 33, COMBINED EXTRACT AND TWO SOLUTION DYE SAMPLES.

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Hair dye containing hydrogen peroxide and para-phenylenediamine is popularly used for cosmetic purpose. Ayurprash, a combination of Embilica officinalis, Trigonella foenum graecum, Eclipta alba, Hibiscus rosasinensis in definite proportion imparts glow and smoothens hair. Toxicity reports of Ayurprash in combination with hair dye/hydrogen peroxide are not available. The objective was to compare and investigate acute dermal toxicity of the following formulations in rabbits 1) Super Vasmol 33 with Ayurprash (SVA), 2) Super Vasmol 33 without Ayurprash (SVWA), 3) Combined extract (CE) of the plant material used as Ayurprash. Two marketed hair dye samples containing hydrogen peroxide viz., 4) Sample A(SA) and 5)Sample B(SB) were also used for the study.New Zealand white rabbits of either sex weighing 1.54 to 2.0 kg with its back shaved in 4 round patches of equal diameter, 2 on each side were used. After application of 1ml/kg of formulations to the shaved patches on the dorsal side of rabbits hair growth and color, skin color, its texture and toxicity (inflammation) were noted weekly for 10 weeks. SA group showed slight rough texture of skin till 10th week. SVA, CE groups showed slow hair growth on days 7 and 14 and rapid hair growth subsequently. SVWA, Control, SA, SB groups showed no hair growth upto day 21. SA showed roughness of skin and SB showed deposition of black dye leading to darkening of skin. SVA, SVWA, SA and SB showed brownish black color and CE and control groups showed white hair colour. Hydrogen peroxide formulations showed more dermal toxicity than SVA. These studies indicate that SVA is safer than hair dyes containing hydrogen peroxide. Ayurprash was beneficial for rapid hair growth and is non toxic to skin.

1580 THE PIG AS AN EXPERIMENTAL MODEL IN WOUND HEALING RESEARCH.

P. Glerup, M. Skydsgaard, J. T. Jensen and S. Klastrup. *General toxicology and pharmacology, Scantox A/S, Lille Skendsved, Denmark.* Sponsor: R. Harling.

The use of pigs in studies of wound repair is known to provide results of high reproducibility and reliability for the efficacy and safety evaluation of new pharmaceuticals or medical device products. The skin of pigs has been shown to be anatomically, biochemically and immonulogically similar to human skin. The poster gives an overview of some methods and practical procedures, in the context of the investigations currently performed at Scantox. They are based on extensive experience with pigs and minipigs as animal models. Studies are performed using Gottingen minipigs or Landrace pigs. The wounds, excisional split-thickness or full-thickness wounds, are surgically prepared under general anaesthesia. A number of variations in the nature of wound models are possible, for example wound shape and size, eschar induction (for evaluation of debriding agents) or determination of infectious burden. Dressings can be changed on a daily basis until complete healing. During the recovery phase wounds are evaluated macroscopically in detail, including planimetric measurement of wound areas. In addition, bacteria in the wound site can be determined, or blood samples may be taken in order to assess systemic exposure to test article(s). After harvesting, histopathological analysis of the wound tissues is performed, including special stainings to estimate angiogenesis and collagen formation. The generation of collagen may also be evaluated indirectly by HPLC assay of hydroxyproline concentration. A full necropsy evaluating possible adverse systemic effects of test compound may be performed. Data from wound observations and planimetric measurements will be presented in the poster as well as histopathological results.

1581 SIMULATED SOLAR UV LIGHT (SSL) INDUCES INFLAMMATION AND OXIDATIVE STRESS IN THE SKIN OF SKH-1 HAIRLESS MICE.

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The skin is continuously exposed to a variety of hazardous environmental insults, such as ultraviolet light, ozone, and ionizing radiation. These exposures result in the production of free radicals and reactive oxygen species, which may play a role in the development of inflammatory skin disorders, skin cancer, cutaneous autoimmune disorders, phototoxicity, and premature ageing. A variety of antioxidant defense mechanisms are present to prevent oxidative stress; however, UV irradiation has been shown to overwhelm these mechanisms. We hypothesized that UV-light exposure results in the formation of free radicals, which causes antioxidant depletion, lipid peroxidation and DNA damage. To experimentally evaluate the effects of simulated solar light (SSL) on SKH-1 hairless mice, animals were exposed to SSL (13.7 mJ (CIE)/cm^2) for 1 hour, 5 days a week for 3 weeks. Twenty-four hours following the last exposure, mice were sacrificed. The skin was evaluated for changes in several parameters of oxidative stress. A significant amount of GSH oxidation as well as decreases in the levels of protein thiols, total antioxidant reserves, and vitamin E were seen as a result of exposure to SSL. A significant increase in lipid peroxidation and myeloperoxidase activity (MPO), indicating infiltration of neutrophils into the skin, was observed following SSL irradiation. The production of pyrimidine dimers seen after exposure is indicative of DNA damage occurring as a result of the direct action of SSL on DNA. Histological evaluation of the skin following exposure to SSL irradiation showed increased skin thickness and inflammatory cell infiltration. These data indicate that SSL exposure induces the production of pyrimidine dimers and free radicals in the skin, which result in the development of oxidative stress and inflammatory cell infiltration.

1582 MOLECULAR CHANGES IN RAT SKIN RELATED TO IRRITATION BY JP-8 JET FUEL.

J. N. McDougal, C. M. Garrett and C. M. Amato. *Pharmacology/Toxicology, Wright State University, Dayton, OH.*

Dermal irritation due to occupational exposure of Air Force personnel to jet fuels can be an important occupational health issue. Irritant contact dermatitis from a wide variety of chemicals is the most common occupational skin disease. It costs the US government millions of dollars each year. Having a mechanistic understanding of the early process of skin irritation provides the potential for prophylactic and therapeutic intervention. We have previously studied the changes in gene and protein expression in rat skin for up to four hours after one-hour cutaneous exposures to JP-8. These studies in male, Fisher 344 rats address molecular changes in the skin induced by longer *in vivo* exposures; 4, 8 and 24 hours. Five hundred microliters of JP-8 was placed in a modified Hill Top Chamber and held in place on the clipped back with a modified Lomir rodent jacket. Sham-treated controls with an empty chamber to control for the effect of hydration were used for comparisons at each time point. At the end of the exposures, skin was excised, flash frozen and pulverized for the isolation of total RNA and proteins. Affymetrix gene array (RG-U34A) was used to determine changes in gene expression. Real time PCR was used to quantify changes in mRNA levels and sandwich enzyme linked immunosorbent assay (ELISA) was used to quantify changes in specific protein levels. Gene array studies showed that the JP-8 treatment caused up regulation of genes involved in the process of inflammation and protein synthesis. Genes down regulated were related to metabolism and support functions of the skin. Real time PCR confirmed up and down regulation in some but not all genes investigated. ELISA measurements of some of the inflammatory and regulatory proteins related to the gene changes showed that protein levels in whole skin are affected by the JP-8 treatment especially at later time points. The results of this study increase our understanding of the JP-8-induced inflammatory process and may allow us to build quantitative mathematical models of the irritant process. (supported by the Air Force Office of Scientific research)

1583 ASSESSMENT OF SKIN BARRIER CREAMS TO LOWER PENETRATION OF JP-8 JET FUEL.

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Skin irritation as well as skin and systemic toxicity from accidental JP-8 jet fuel exposure is a concern for the USAF and their fuel handling personnel. Personal protection equipment and clothing (PPEC) is a necessity under normal operations; but

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, workshop, roundtable, platform and poster sessions of the 43rd Annual Meeting of the Society of Toxicology, held at the Baltimore Convention Center, Baltimore, Maryland, March 21-25, 2004.

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