

and irradiated with UV light at 20 J/cm², were negative for phototoxic response by the local lymph node assay. Hairless mice dosed daily at 300 mg/kg × 1 or 100 mg/kg × 7d with BAY 12-8039 and exposed to UV A/B irradiation exhibited no phototoxicity; lomefloxacin control animals had a phototoxic response at 10 mg/kg. Dermal exposure during the irradiation period in these studies was confirmed by separate radiolabelled skin distribution studies. In separate studies BAY 12-8039 is reported to be negative in photogenotoxic assays, and has recently been shown to be negative in blinded, controlled clinical phototoxicity studies. The results of these studies with BAY 12-8039 show an absence of evidence for photoactivation or phototoxicity consistent with the molecular design of this molecule.

1914 EVALUATION OF THE SKIN'S ROLE IN NATURAL RUBBER LATEX SENSITIZATION.

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Over the past decade, Type I immediate hypersensitivity to natural rubber latex (NRL) has become a significant health problem in the United States. The IgE-mediated cascade is initiated by cytoplasmic proteins produced by the rubber tree *Hevea brasiliensis*. The major protein allergens found in NRL products range in size from 5–100+ kDa. Health care worker (HCW) exposure and sensitization to latex proteins are thought to occur mainly via inhalation and dermal exposure. Major efforts to reduce inhalation exposures are being implemented worldwide which would lessen the role of respiratory sensitization. The other route of latex sensitization is via percutaneous absorption, but it has been postulated that molecules greater than 1 kDa in size are unable to penetrate an intact skin barrier. Therefore, the purpose of these studies was to evaluate the skin's role in NRL sensitization. Initial studies investigated the sensitization potential of NRL in the murine LLNA and a draining lymph node phenotyping assay. Groups of female B6C3F1 mice were typically exposed to NRL for 3 consecutive days (days 1–3) and radioassayed on day 5 and phenotyped on day 10. In these intact skin models, no sensitization occurred following exposure to NRL as evidenced by a lack of increase in lymph node proliferation (as compared to controls) or alterations in CD3+, CD4+, CD8+, IgE+, or B220+ cells. However, most conditions for NRL exposure for HCW involve abraded skin under occluded conditions. Therefore, subsequent studies will evaluate the potential for latex proteins to penetrate through different skin conditions. Using *in vitro* diffusion models for intact, abraded, irritated, and occluded skin, human and animal skin preparations will be put in flow-through cells to determine the penetration of non-ammoniated protein mixtures, ammoniated protein mixtures, and purified latex proteins. Penetrating proteins will be characterized by Western immunoblotting techniques.

1915 HUMAN CADAVER SKIN VIABILITY FOR IN VITRO PERCUTANEOUS ABSORPTION: STORAGE AND DETRIMENTAL EFFECTS OF HEAT-SEPARATION AND FREEZING.

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Research laboratories use cadaver skin to study the percutaneous absorption of drugs and hazardous chemicals of environmental concern. Procedures such as heat treatment to separate epidermis from dermis are performed as part of the skin preparation for these studies. Human cadaver skin is not an easily obtained commodity, and storage for use becomes necessary. Refrigeration of, and freezing, skin are commonly done. With treatment and storage, skin viability has become a concern. This study determined human cadaver skin viability from point of death through time of storage, and the effect of heat and freezing treatment.

Our system uses dermatomed human cadaver skin immediately placed in Eagles MEM-BSS and refrigerated after donor death, then transferred to the laboratory and placed in Eagles MEM-BSS with 50 µg/ml gentamicin at 4°C for storage. Skin viability, determined by anaerobic metabolism, where glucose is converted to lactose, was highest (p<0.000) during the 18 hours of the first day after donor death, decreased some three-fold by day 2 (p<0.000), but then maintained steady-state viability through day 8. Viability then decreased by approximately one-half by day 13. Thus, using the above criteria, human skin will sustain viability for 8 days following donor death, in this system. Heat-treated (60°C water for one minute) and heat-separated epidermis and dermis lose viability. Human skin viability thus can be main-

tained for absorption studies. It is recommended that this system be used, and that heat-separation and skin freezing not be used, in absorption studies where skin viability and metabolism might be contributing factors.

1916 IN VIVO PERCUTANEOUS ABSORPTION OF BORIC ACID, BORAX AND DISODIUM OCTABORATE TETRAHYDRATE IN HUMANS.

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Cases of morbidity and mortality have been reported from topical use of boric acid. Studies of absorption through intact skin were impaired by lack of analytical sensitivity for boron in biological fluids. Inductively coupled plasma mass spectrometry allowed quantitation of percutaneous absorption of ¹⁰B in ¹⁰B-enriched boric acid, borax and disodium octaborate tetrahydrate (DOT) in biological matrices in the presence of natural dietary boron intakes. Human volunteers (8 per group) were dosed on the back with 10³ enriched boric acid, 5.0%, borax, 5.0% or disodium octaborate tetrahydrate, 10%, in aqueous solutions. The residual dose was removed by 24 hr washing. Urinalysis for boron changes in boron isotope ratios were used to measure absorption. Boric acid percent dose absorbed was 0.226 ± 0.125, with flux and permeability constant (Kp) at 0.0094 µg/cm²/hr and 1.9 × 10⁻⁷ cm/hr. Borax percent dose absorbed was 0.210 ± 0.194, with flux and Kp at 0.00875 µg/cm²/hr and 1.8 × 10⁻⁷ cm/hr, respectively. DOT percent dose absorbed was 0.122 ± 0.108, with flux and Kp at 0.010 µg/cm²/hr and 1.0 × 10⁻⁷ cm/hr, respectively. Approximately one-half of the administered topical dose was recovered after 24 hours in a t-shirt covering the dosed skin area and in the dose-terminating skin washes. Pre-treatment with the potential skin irritant 2% sodium lauryl sulfate had no effect on boron skin absorption. No skin irritation was observed for any of the dosage forms. These *in vivo* percutaneous absorption parameters, percent dose absorbed, flux and Kp for boron as boric acid, borax or DOT are low, when compared to other chemicals.

1917 IN VITRO PERCUTANEOUS ABSORPTION OF BORIC ACID, BORAX AND DISODIUM OCTABORATE TETRAHYDRATE IN HUMAN SKIN FROM INFINITE AND FINITE DOSING.

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In vitro percutaneous absorption of boric acid, borax and disodium octaborate tetrahydrate (DOT) was done with infinite and finite doses for comparison to *in vivo* absorption. Inductively coupled plasma mass spectrometry made it possible to quantify *in vitro* percutaneous absorption of ¹⁰B present in ¹⁰B-enriched chemicals, using human cadaver skin mounted on Teflon flow-through diffusion cells over a 24 hour period. Percent boric acid absorbed was 1.2 for a 0.05% solution, 0.28 for a 0.5% solution and 0.70 for a 5.0% solution. Skin surface soap and water washes removed, respectively, 72.4%, 86.0% and 81.9% of the applied doses at the end of the dosing period. Flux values were, respectively, 0.25, 0.58 and 14.58 µg/cm²/hr and permeability constants (Kp) of 5.0 × 10⁻⁴, 1.2 × 10⁻⁴, and 2.9 × 10⁻¹ cm/hr for the 0.05%, 0.5% and 5.0% solutions. The above *in vitro* doses were at "infinite," 1000 µl/cm², dosing volumes. When 5% boric acid solution was applied at a 2 µl/cm² volume (the *in vivo* dosing volume), flux decreased significantly to 0.07 µg/cm²/hr with a Kp of 1.4 × 10⁻⁶ cm/hr. Borax dosed at 5.0%/1000 µl/cm² had a 0.41 percent absorbed. Flux was 8.5 µg/cm²/hr, and Kp was 1.7 × 10⁻⁴ cm/hr. DOT dosed at 10%/1000 µl/cm² was 0.19 percent absorbed. Flux was 7.9 µg/cm²/hr, and Kp was 0.8 × 10⁻⁴ cm/hr. These *in vitro* results from "infinite" doses (1000 µl/cm²) were a thousand-fold higher than those obtained in the *in vivo* study. The results from the finite (2 µl/cm²) *in vitro* dose were closer to the *in vivo* (2 µl/cm²) results.

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshop, roundtable, and poster sessions of the 37th Annual Meeting of the Society of Toxicology, held at the Washington State Convention Center, Seattle, Washington, March 1-5, 1998.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 407.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 433.

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