

and freshly prepared rat liver sections incubated at 42°C for 2 to 3 hours *in vitro*. Hsp72 expressing cells were heterogeneously distributed in both cell line and tissue cultures, indicating differential responsiveness or susceptibility to hyperthermia. Analysis of Hsp72 expression by ISH and ICC was used to study the *in vivo* effect of an NMDA receptor antagonist, MK 801, on cingulate neurones in the rat brain. Data produced showed a close temporal association between Hsp72 expression and neuronal morphology. It is concluded that Hsp72 is a useful and sensitive monitor of intracellular stress with utility for both *in vitro* and *in vivo* studies.

#### 1440 DETECTION OF METHADONE, LAAM AND THEIR METABOLITES BY METHADONE IMMUNOASSAYS.

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*l*-alpha-Acetylmethadol (LAAM) is a recently approved substitute for methadone. Both LAAM, methadone and their common metabolite, methadol (M) are extensively N-demethylated. The structural similarities between LAAM and its metabolites with methadone suggests they may cross-react in methadone immunoassays. To test this hypothesis, drug-free urine was fortified with: LAAM, nor-LAAM, dinorLAAM, M, norM, dinorM, methadone, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), or 2-ethyl-5-methyl-3,3-diphenylpyrrolidine (EMDP) at 12 concentrations (30 to 100,000 ng/mL). Samples were then analyzed using: 2 enzyme immunoassays (Behring Diagnostics, EIA-b; Diagnostic Reagents, EIA-d); a fluorescent polarization immunoassay (Abbott, FPIA); 2 enzyme-linked immunosorbent immunoassays (Diagnostic ELISA-d; STC Technologies, ELISA-s) and a radioimmunoassay (Diagnostic Products, RIA). In summary: LAAM had high cross-reactivity with ELISA-d (318.3%), RIA (249.5%), EIA-d (100.8%), and ELISA-s (75.3%). M also displayed relatively high cross-reactivity as follows: EIA-d (97.8%), ELISA-d (70.3%), and FPIA (37.7%). Successive N-demethylations of LAAM and M were associated with loss of cross-reactivity. EDDP and EMDP were barely detectable. These findings suggest that LAAM use could result in positive immunoassay results for many of the commercially available methadone immunoassay kits. Confirmation for LAAM may need to be considered. (The authors gratefully acknowledge donation of all immunoassay reagents by the vendors).

#### 1441 DEVELOPMENT OF A NOVEL SYSTEM TO GENERATE AND CHARACTERIZE ADVANCED COMPOSITE MATERIAL COMBUSTION PRODUCTS DURING AN ANIMAL EXPOSURE.

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Due to the increasing use of advanced composite materials (ACM) in weapons systems and their potential for human exposures in a combustion scenario, we have previously developed and fabricated a system containing a modified UPITT II mini-cone calorimeter to produce and characterize combustion products from ACM. However, the need to concomitantly characterize the combustion products and expose experimental animals to that specific atmosphere has necessitated the development of more appropriate systems. We modified our existing system to include real-time FTIR sampling, real-time gas analysis for CO, CO<sub>2</sub>, O<sub>2</sub>, HCN, impinger collection for ion chromatography and employment of typical gravimetric collection methods for particulate materials (i.e. multistage, multijet impactors, closed faced filters, etc.). Several of the subsystems were coupled to a master data acquisition system allowing for increased sampling efficiency and rapid manipulation of collected data. In addition to the generation of a combustion atmosphere, extreme thermal activity was observed during preliminary operation and necessitated cooling of the combustion slipstream prior to introduction into the mini-nose only exposure chamber. These advances have produced a system which can assess evolving combustion atmospheres during an animal exposure.

#### 1442 USE OF AN AUTOMATED SOLID PHASE EXTRACTION PROCESS FOR MEASURING EXCISED DNA-METHYL ADDUCTS IN HUMAN URINE BY GAS CHROMATOGRAPHY-MASS SPECTROMETRY.

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An automated method was developed to measure excised methyl adenine (mA) and methyl guanine (mG) DNA adducts in urine obtained from workers exposed to nitrosamines, such as nitrosodimethylamine. Workers were categorized into 5 groups, I through V, with category I working in closest proximity as described in a recent NIOSH Health Hazard Evaluation Report (HETA 94-0072-2648). First void urine taken on the morning after exposure was frozen. A Benchmate<sup>®</sup> robotic workstation was used for Solid Phase Extraction (SPE) processing of urine. Deuterated 3-mA ([<sup>13</sup>C-d<sub>3</sub>]-N3mA), for use as an internal standard, and radiolabeled [<sup>14</sup>C]-N3mA for use as a tracer, were synthesized. Urine was filtered to remove exfoliated cells, adjusted to pH 8, and refiltered. The Benchmate<sup>®</sup> workstation was programmed to tare sample tubes, add internal standards (2.5 ng [<sup>13</sup>C-d<sub>3</sub>]-N3mA or 1 ng 9-mG) to 3-mL urine, mix and determine sample density. Bond Elute<sup>®</sup> 500 mg C8 SPE columns were conditioned with 3 mL MeOH:NH<sub>4</sub>OH (10:0.1 conc.) and 3 mL H<sub>2</sub>O pH 8. Urine was loaded onto the SPE columns, rinsed sequentially with 1 mL H<sub>2</sub>O pH 8 and 1 mL HCl 0.1 N, and >97% of mA and mG adducts were eluted in a 1-mL fraction of 20% MeOH in HCl 0.1 N. Samples dried under vacuum were derivatized in 100 µL pyridine and N-(tert-butylidimethylsilyl)-N-methyltrifluoroacetamide. Gas Chromatographic-Mass Spectrometric (GC-MS) analysis using a 25 meter × 0.2 mm I.D. Hewlett-Packard Ultra 2 column was accomplished using a Hewlett-Packard quadrupole GC-MS system in the selected ion mode (SIM). Limits of quantitation (LOQ) for mA adducts ranged from 10–100 ng/mL and from 10–250 ng/mL for mG adducts. Levels of 2-, 3-, 6-, and 7-mA and 2-, 6-, and 7-mG were detected for workers tested, but intra-category variation was high. When only exposure category was considered, no significant difference was noted for the adducts tested. The results of the study showed that mA or mG urinary adducts can be rapidly quantified in a single assay using an automated system, but additional sample numbers may be required for further evaluation.

#### 1443 A CLINICAL STUDY TO ASSESS THE NEUROSENSORY IRRITATION POTENTIAL OF FACIAL MOISTURIZERS AMONG A DEFINED SENSITIVE SKIN GROUP AND A DEFINED NORMAL GROUP OF SUBJECTS.

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A clinical study of 4 moisturizers was conducted to evaluate the potential change in facial skin neurosensory responsiveness under normal product use conditions. Test subjects were pre-screened and classified as "sensitive" or "normal" based on their subjective responses to two facial neurosensory challenges, one with 10% aqueous lactic acid, the other with 10:90 chloroform/methanol. Subjects were then randomly assigned one of 4 products with varying irritancy potential to use twice daily for 2 weeks. Subjects' responsiveness to neurosensory challenge was then reevaluated on study days 1, 2, 3, 4, 7 and 14 of the product use period. Additionally, the objective skin irritation (edema/erythema/dryness) responses to the facial moisturizers were evaluated by clinical grading of the facial skin during the use period (2 weeks) and by repeated patch application under occlusive conditions for one week. While the "sensitive" and "normal" subjects remained distinct with respect to the magnitude of their responsiveness to lactic acid and chloroform/methanol, there was no change from their respective baseline responsiveness during the 2-week facial product use period. Correlation of these results with the objective irritation potential of the products will also be discussed.

#### 1444 INCREASED SENSITIVITY IN THE DETERMINATION OF VALINE-BUTADIENE MONOXIDE ADDUCTS BY SILYLATION OF THE PPTH-VALINE ADDUCT DERIVATIVES.

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Occupational exposure to 1,3-butadiene (BD) has been monitored by measuring hemoglobin adduct formation with its primary reactive metabolite, butadi-

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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 37<sup>th</sup> 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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