Proceedings of the International Conference on Occupational & Environmental Exposures of Skin to Chemicals: Science & Policy

Hilton Crystal City September 8-11, 2002

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Electrospray Ionization Tandem Mass Spectrometry (ESI-MS/MS) Analysis Of 1-Bromopropane Mercapturic Acid Metabolites In Urin

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1-Bromopropane (1-BP, CAS 106-95-5), used as an alternative solvent t chlorofluorocarbons and 1,1,1-trichloroethane, has been reported to cau reproductive and neurotoxicity in male rats. The related 2-bromopropane has been shown to cause similar toxicity in rats as well as amenorrhea, oligozoospermia, and anemia induction in workers. Although the mechanism of action of 1-BP has yet to be explained, it is thought that metabolic activation to reactive intermediates may be important. Metabol of 1-BP is complex and is reported to occur by pathways which include debromination, oxidation by CYP2E1 and glutathione S-conjugation. 3-Bromopropionic acid and n-propanol are reported urinary metabolites of BP whereas the glutathione conjugate, S-n-propyl-glutathione is further cleaved to S-n-propyl-L-cysteine and further to mercapturic acids N-acet S-(n-propyl)-L-cysteine (M1), N-acetyl-S-(n-propyl)-L-cysteine-S-oxide (M N-acetyl-S-(2-carboxyethyl)-L-cysteine (M3), and N-acetyl-S-(3-hydroxy-n propyl)-L-cysteine (M4). A potential biomonitoring method was developed measure urinary levels of (M1), (M2), (M3) and (M4). The mercapturic ac standards as well as the stable isotope-labeled analog of (M1) internal standard were synthesized using the general procedure of van Bladern e al. (1980). A BenchMate® II robotic workstation was used to automate sample preparation. Bond Elute® 500 mg C18 SPE columns were conditioned with acetone, MeOH (5% HCl) and 5% MeOH in H2O pH 3. Samples were mixed with internal standard and loaded onto columns. A fraction containing >90% of 1-BP metabolites was collected in 3-mL acetone, reduced to dryness under N2 and dissolved in 1 mL MeOH for

HPLC-MS/MS (ThermoQuest Finnegan LCQ tandem mass spectrometer analysis on a 150 X 2 mm Phenomenex Aqua 3µm C18 300A column. Chromatographic standards were chromatographed using a 10-min linea gradient H2O 1% acetic acid to MeOH 1% acetic acid at 300 microliters/r to elute the compounds of interest within 10 min. During the chromatographic run the mass spectrometer was operated in multiple segments using ESI-MS/MS, in the positive ion mode for detection of protonated (M1), (M2), (M3) and (M4) and Selected Reaction Monitoring major transition products. Urine samples fortified with a mixture of standards were mixed with 10 micrograms/mL of internal standard and processed for evaluation of recovery, limits of detection (LOD) and limits quantitation (LOQ). Calibration of (M1), (M2), (M3) and (M4) was linear fr 30 - 10000 ng/mL (r^2>0.99). The sample preparation and analysis appeai to offer significant advantages over typical preconcentration and derivatization procedures that would be required for GC-MS analysis of these compounds. Thus, 1-BP internal exposure levels for various expos situations can be rapidly determined by analysis of these metabolites in a single assay using a selective automated sample preparation system.

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The National Institute for Occupational Safety and Health (NIOSH) co-sponsored this inaugural conference to bring together dermatologists, occupational hygienists, laboratory researchers, policy makers and other to focus on the science, knowledge gaps and policy opportunities related occupational and environmental exposures of the skin to chemicals.

The site was the Hilton Crystal City at Ronald Reagan National Airport hotel. The main conference was followed by a one-day workshop focusin on specific research and public health opportunities for decreasing the burden of skin exposures to chemicals in both workplaces and the gener environment.

Approximately 135 individuals attended. A second conference is expecte in 2004

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