sorbed DBP in vivo was found excreted in urine. In vitro DBP absorption over 24 hr found 28.9 ± 2.1 %ADA in receptor fluid with approximately 21.8 % remaining in skin. Extended absorption studies for 72 hr found receptor fluid levels of 55.9 ± 3.9 %ADA with 17.3 %ADA remaining in skin. Charcoal impregnated filter paper attached (for 1 hr) to the top of the diffusion cell or to the top of the in vivo dosing chamber improved recovery by trapping the volatile DBP. These studies indicate there is considerable DBP absorption in skin. In conclusion, DBP tends to form a skin reservoir in vitro as shown by the increased receptor fluid levels found after 72 hr when compared to 24 hr. The 72 hr in vitro absorption values correlated most closely with the 24 hr in vivo results. These studies help determine the importance of including DBP remaining in the skin at the end of an in vitro study as potentially available for systemic absorption.

2096 ASSESSMENT OF DERMAL ABSORPTION BY THERMAL GRAVIMETRIC ANALYSIS – DEVELOPMENT OF A 2-COMPARTMENT DIFFUSION MODEL.

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Recent work in our laboratory shows that it is possible to register the dermal uptake of chemicals *in vitro* by thermal gravimetric analysis (TGA), i.e. by exposing a piece of skin to chemical vapour of known concentration while recording its weight in a high-precision scale during carefully controlled temperature and humidity conditions.
We have previously studied several organic solvents with the TGA technique using trypsinated porcine skin. The data indicate that the shape of the weight curve is related to the skin:air partition (P) and diffusion (D) coefficients of the chemical. To define the relations more precisely, a solution to Fick's second law of diffusion was derived, for the special case of recording total weight over time in the TGA setup. A good fit to observed data was obtained using a 2-compartment diffusion model. The parameters P and D were obtained by best fit to observed weight curves of butyl acetate, methanol, 2-propanol and toluene using the Berkeley Madonna software.
The same chemicals were also studied using conventional Franz' diffusion cells and dermatomed porcine skin. A good correlation was obtained between the diffusion coefficients derived from the Franz' cell experiments and those derived from the faster of the two compartments in the TGA diffusion model.
In conclusion, experiments with a limited number of chemicals indicate that skin:air partition and diffusion coefficients can be obtained by fitting a TGA-specific solution to Fick's second law to TGA weight curves and that the numerical values correlate well to the those obtained in conventional diffusion cell experiments. Further studies on several different types of chemicals are needed to confirm the usefulness of the method.
This study was supported by the Swedish Council for Working Life and Social Research (FAS).

2097 MARKOV CHAIN MODEL FOR QUANTITATING DERMAL ABSORPTION FROM COMPLEX MIXTURES.

C. S. Pitts[1, 2], C. E. Smith[2], R. E. Baynes[1], J. D. Brooks[1] and J. E. Riviere[1, 2]. *[1]Center for Chemical Toxicology Research and Pharmacokinetics, North Carolina State University, Raleigh, NC and [2]Biomathematics Program, North Carolina State University, Raleigh, NC.*

Exposure to pesticides dosed in complex chemical mixtures is a common environmental and occupational health concern. Risk assessors need to know the rate at which a pesticide is absorbed in to the skin in order to predict the toxicity of exposure to the pesticide. However, experimentally obtaining the absorption rates for even a small number of possible pesticide mixtures are expensive and time consuming. The objective of this study is to create a Markov chain model to predict pesticide absorption rates through the skin. The model parameters were fit to absorption data collected in the isolated perfused porcine skin flap (IPPSF) for a mixture of ethyl-parathion in ethanol. The model was investigated both analytically and through simulations using Gillespie's algorithm and was fit to the data using least squares methods. A model with three internal states, two absorbing states plus a delay appears to describe these data adequately. The structure of this model was compared to classical modeling approaches commonly used in dermal absorption studies (e.g. compartmental models and their reduction, PBPK models). Future work will expand the number of pesticide mixtures analyzed as well as search for correlations between absorption parameters and the physical and chemical properties of the pesticides and the mixture components into which they are exposed. These correlations may enable risk assessors to predict absorption profiles after chemical exposures in complex mixtures or formulations based on mixture component physical and chemical properties. (Supported by NIOSH R01 OH 07555).

2098 INCORPORATION OF COMPLEX CHEMICAL MIXTURE EFFECTS INTO A QSAR MODEL OF DERMAL ABSORPTION.

J. E. Riviere[1, 2] and J. D. Brooks[1]. *[1]Center for Chemical Toxicology Research and Pharmacokinetics, North Carolina State University, Raleigh, NC and [2]Biomathematics Program, North Carolina State University, Raleigh, NC.*

Significant progress has been made on predicting dermal absorption/penetration of topically applied compounds by developing quantitative structure activity relationship (QSAR) models based on linear free energy relations (LFER). However, all of these efforts have employed compounds applied to the skin in aqueous or single solvent systems, a dosing scenario that does not mimic occupational, environmental nor pharmaceutical exposure. We have explored using hybrid QSAR equations describing individual compound penetration based on the molecular descriptors for the compound modified by a mixture factor (MF) which accounts for the physiochemical properties of the vehicle/mixture components. The MF is calculated based on percentage composition of the vehicle/mixture components and physical chemical properties selected using principal components analysis. This model has previously been applied to 12 different compounds in 24 mixtures for a total of 288 treatment combinations obtained from flow-through porcine skin diffusion cells (Toxicol. Appl. Pharmacol. 208:99-110, 2005). The data reported here includes using three fundamentally different LFER models (Abraham, Potts and Guy, Hostynek and Magee) on this diffusion cell dataset as well as applying them to a new experimental dataset in the ex vivo isolated perfused porcine skin flap model consisting of 10 of the same compounds in 5 mixtures for a total of 50 treatment combinations. The use of the MF in combination with classic LFERs based on penetrant properties significantly improved the ability to predict dermal absorption of compounds dosed in complex chemical mixtures across three different LFER models and two biological systems. (Supported by NIOSH R01 OH 07555).

2099 CUSTOM MADE PANI FIBER TO ASSESS DERMAL PARTITIONING AND ABSORPTION OF BIOCIDES.

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A custom-made polyaniline (PANI) coated metal alloy fiber was evaluated for its use in assessing dermal partitioning and absorption of certain biocides. This PANI coating provides a unique functionality compared to three commercially available fibers polyacrylate (PA), polydimethylsiloxane (PDMS), and Carbowax/templated resin. The production of this custom-made fiber is a relatively simple process that can be controlled by utilizing cyclic voltammetry (CV). The CV program for coating the metal alloy fiber consisted of one initial scan from –0.2V to +1.1V followed by several sets of scans from –0.2V to +0.8V with a 15 second equilibration time at –0.2V between scan sets and scan rate of 50 mV/sec. The electrolyte solution was 0.1M aniline in 1.0M sulfuric acid. The bare metal alloy fiber SPME assembly, commercially donated, served as the working electrode. In our experiments, cyclic voltammetry appeared to give more consistent results and control in coating the metal alloy fiber with PANI as opposed to using a constant deposition potential. To assess the PANI fiber, solid-phase microextraction (SPME) was performed by direct immersion into water solutions containing either a single component or a mixture of biocides at 37°C and stir rate of 400 R.P.M. The PANI fiber was desorbed directly in the GC-MS injector port for 5 minutes at 200°C following immersion. This PANI coated fiber exhibited good reproducibility and durability. The RSD's averaged 6 to 9% over a period of three days for the first 46 injections of a single component (5ppm 2-phenylphenol) in water with only three outliers. Time profile experiments revealed that both p-chloro-o-cresol and o-phenylphenol reached equilibrium before 10 minutes while the equilibrium time for o-benzyl-p-chlorophenol was greater than 90 minutes. This research was supported by NIH OH003669-06.

2100 PREDICTING SKIN PERMEABILITY OF MOLECULES FROM CHEMICAL MIXTURES USING AN INERT MEMBRANE-COATED FIBER ARRAY.

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Predicting skin permeability of compounds from chemical mixtures is required for transdermal drug delivery, safety evaluation of cosmetics and risk assessment of chemicals, where most exposure occurs in complicated chemical mixtures, not individual chemicals. We have developed a membrane-coated fiber technique that can be used to measure the partition coefficients of molecules from chemical mixtures with high precision and throughput. This novel approach predicts skin permeability based on its correlation with the partition coefficients from chemical mixtures determined in a fiber array. Each of the membrane-coated fibers represents a pattern of molecular interactions: polydimethylsiloxane (PDMS, lipophilic), polyacrylate (PA, polarizable) and CarboWax (Wax, polar). Molecular interactions occurring during percutaneous absorption can be simulated by the multiple fibers:

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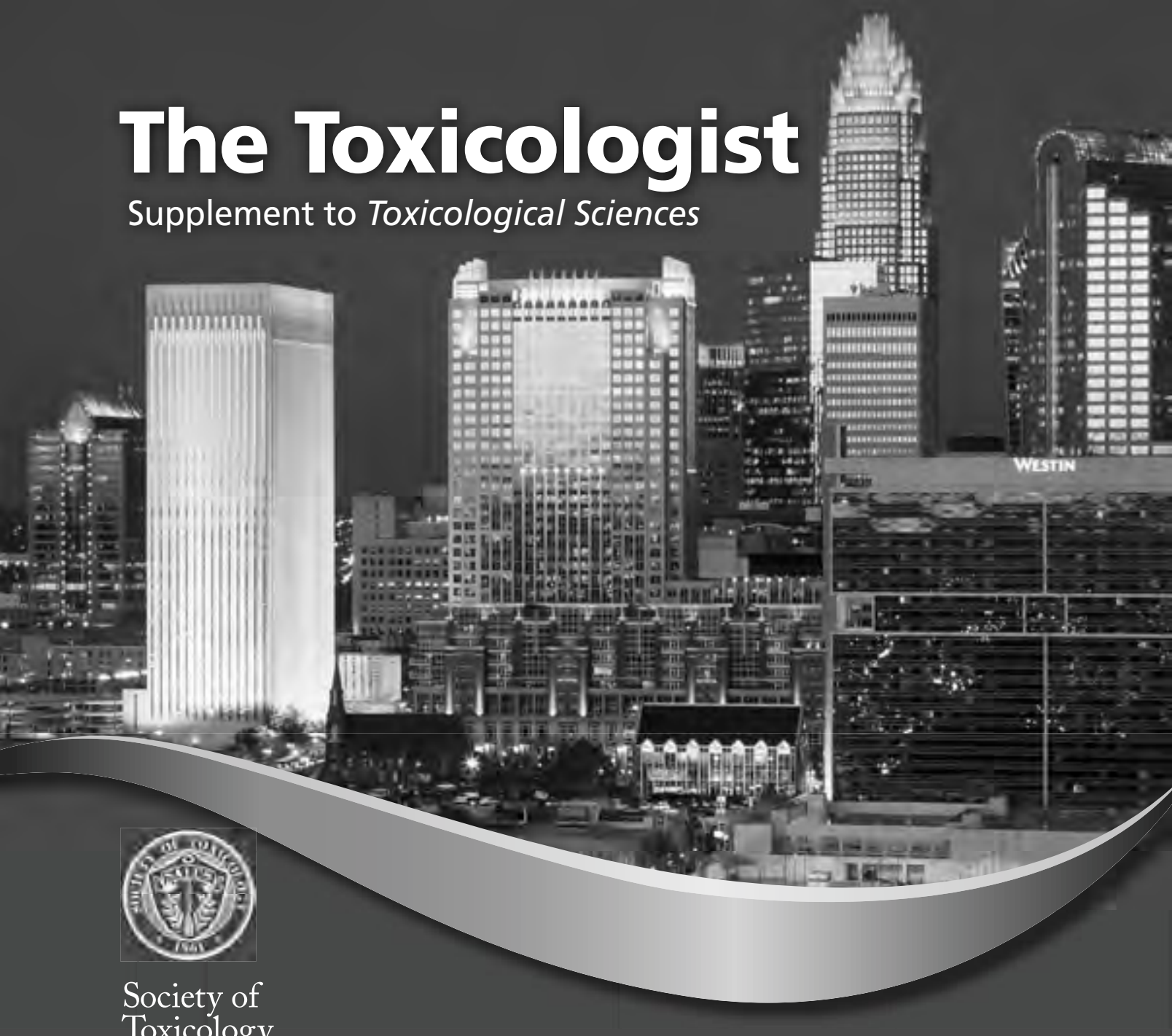

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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

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