1522 **THE DIFFERENTIAL EFFECTS OF THE HERBICIDE BANVEL (DICAMBA) ON PEROXISOMAL AND CYTOCHROME P-450 ACTIVITIES.** P Espandiari, V A Thomas, and L W Robertson. University of Kentucky, Lexington, KY.

The widely used broad leaf herbicide Banvel is similar in structure to xenobiotics which induce hepatic drug metabolism or proliferation of hepatic peroxisomes. The ability of xenobiotics to effect these hepatic changes often portends their positive outcomes in rodent chronic bioassays. Banvel's ability to induce hepatomegaly, peroxisome proliferation and drug metabolism was studied in male and female Sprague Dawley rats. Rats were placed on feed containing 0.001, 0.01, 0.1, and 1 % Banvel or 0.01% ciprofibrate for 3 weeks. Banvel had no effect on relative liver weight or feed efficiency in either female or male rats at all doses tested. Banvel caused a statistically significant increase in peroxisomal ß-oxidation in female rats only at 1% dietary level. Banvel significantly decreased ethoxyresorufin O-deethylase activity at several doses while benzyloxyresorufin O-debenzylase activity was increased at the highest dose of Banvel in both female and male rats. Lauric acid hydroxylase activity was increased in microsomes from male rats fed the highest level of Banvel.(Supported by NIOSH)

1523 **INHIBITION OF MOUSE HEPATIC MICROMSOMAL CATECHOLESTROGEN FORMATION *IN VITRO* BY THE ORGANOPHOSPHORUS INSECTICIDE PARATHION.** C W Berger, Jr and L G Sultatos. Univ. Med. and Dent. of NJ, Grad. Sch. Biomed. Sci., Newark, NJ.

Formation of 2-hydroxyestradiol (2-OH) and 4-hydroxyestradiol (4-OH) in mammals occurs by aromatic hydroxylation of ß-estradiol (E_2), a reaction catalyzed by cytochromes P450. In the present study, incubation of 50*u*M E_2 (containing 45nCi [6,7-^{3}H]estradiol) with mouse hepatic microsomes for 20 min @ 37^0 C resulted in NADPH-dependent production of 21.72 nmols/mg protein ± 2.89 (mean ± SD) 2-OH and 3.49 nmols/mg protein ± 0.46 4-OH, as determined by high performace liquid chromatography. Inclusion of the insecticide parathion (O,O-diethyl O-*p*-nitrophenyl phosphorothioate) (PS) (50*u*M) in the incubation eliminated formation of 4-OH and significantly reduced ($p < 0.05$) production of 2-OH to 5.12 nmols/mg protein ± 0.49. These data suggest that exposure to insecticides that undergo oxidative desulfuration by cytochromes P450 could interfere with metabolism of naturally-occuring steroids like estradiol, 2-OH, and 4-OH. (Supported by NIEHS Grant ES04355 and NIGMS Grant GM15150.)

1524 **ANTAGONISM OF THE ACUTE TOXICITY OF THE ORGANOPHOSPHORUS INSECTICIDE PARATHION BY ETHANOL.** J A O'Shaughnessy and L G Sultatos. Univ. Med. and Dent. of NJ, Grad. Sch. Biomed. Sci., Newark, NJ.

Ethanol exposure (15% ethanol in the drinking water for 6 days) antagonized the acute toxicity of a challenge dose of parathion (*O,O*-diethyl *O-p*-nitrophenyl phosphorothioate)(PS)(20 mg/kg, ip) in male Swiss Webster mice. This antagonism was not apparent 24h after the removal of ethanol or with a challenge dose of paraoxon (*O,O*-diethyl *O-p*-nitrophenyl phosphate)(PO)(3.25 mg/kg, ip). *In vitro* incubations of PS and ethanol with mouse hepatic microsomes from both control animals and ethanol treated animals resulted in greater production of *p*-nitrophenol (PNP) with no change in PO production compared to incubations without ethanol present. Furthermore, 4-nitrocatechol was detected after microsomal incubation of PS in the absence, but not presence of ethanol. Human P450 2B6, expressed from a transfected CYP2B6 cDNA in human ß-lymphoblastoid cells, does not hydroxylate PNP but oxidatively desulfurates PS. Incubation of human P450 2B6 in the presence or absence of ethanol did not result in a difference in the amount of PNP or PO produced. These data suggest that greater production of PNP from PS *in vitro* in the presence of ethanol resulted from inhibition of hydroxylation of PNP by P450 2E1. Therefore, the antagonism of PS toxicity after ethanol exposure does not result from a direct effect on oxidative desulfuration of this insecticide. (Supported by NIEHS Grant ES04335.)

1525 REDUCTION OF PARAQUAT-INDUCED TOXICITY IN VITRO USING HUMAN AND MOUSE CELLS. R Gorantla, R Ratnasabapathy and R Raje. Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY.

Paraquat is a widely used bipyridyl herbicide. Several hundred cases of accidental or suicidal fatalities from paraquat ingestion have been reported in the past decade. The toxicity is associated with renal damage followed by pulmonary damage resulting in respiratory failure and death. The biochemical mechanism of paraquat toxicity has been reported to be due to the generation of superoxide anion radical. In this study, Hela and NIH 3T3 cells were grown in presence of paraquat or paraquat and a free radical scavenger such as propylthiouracil or aminosalicylate (4-aminosalicylate and 5-aminosalicylate). Cell viability was determined using standard procedures. Paraquat induced toxicity in these cell lines was significantly reduced by propylthiouracil and to a lesser extent by 5-aminosalicylate. 4-Aminosalicylate, however, was found to potentiate the toxicity of paraquat.

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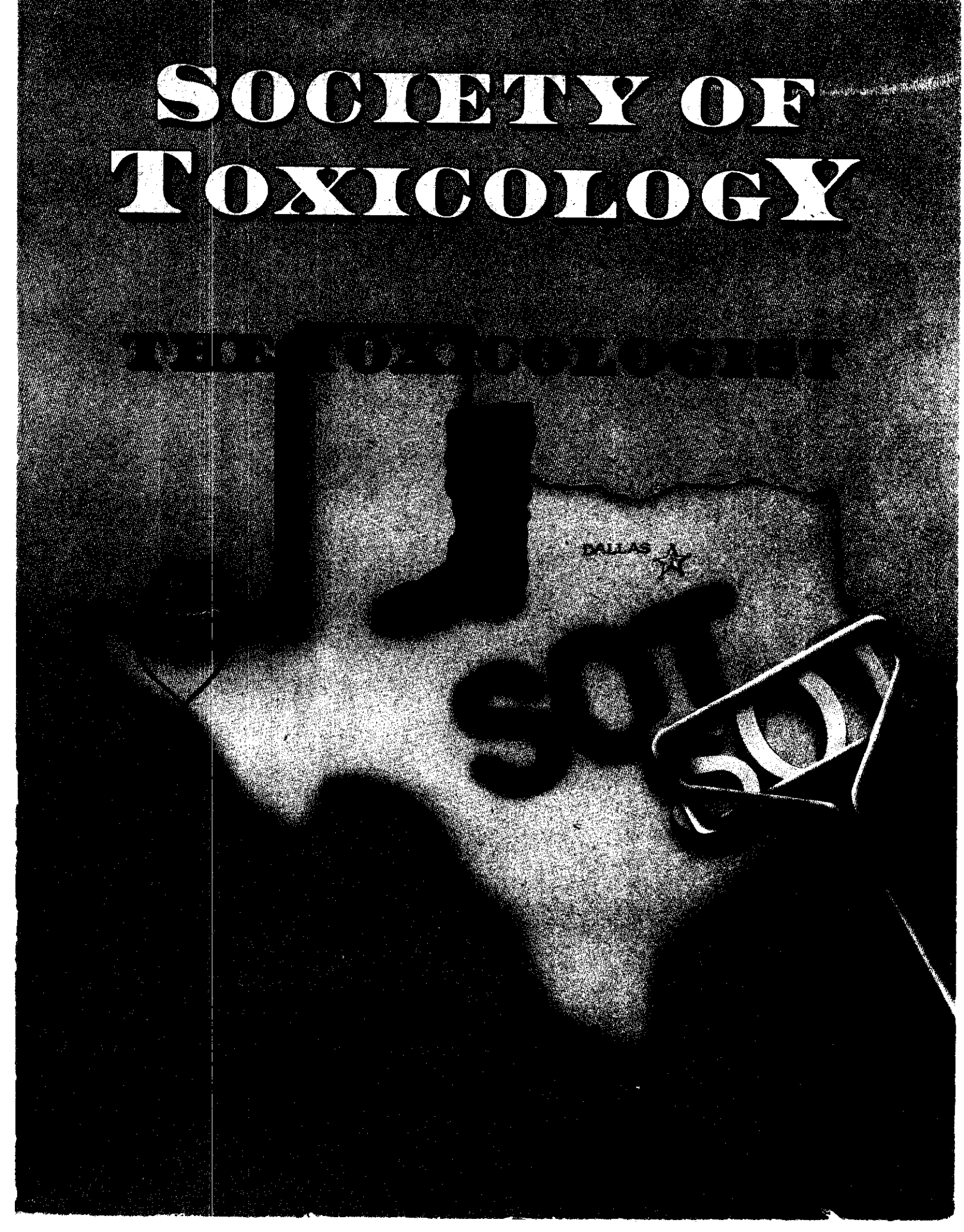

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster/discussion, and poster sessions of the 33rd Annual Meeting of the Society of Toxicology, held at the Loews Anatole Hotel, Dallas, Texas, March 13-17, 1994.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 439.

The issue also contains a Keyword Index (by subject or chemical) to the titles of all the presentations, beginning on page 467.

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