

10123- INTERACTIONS OF ORGANOPHOSPHATE BINDING IN BLOOD AND BRAIN AFTER LOW LEVEL EXPOSURE

Interactions of organophosphate (OP) and pyrethroid compounds delivered orally at low level doses ($\mu\text{g}/\text{kg}$) were quantified indirectly via [^{14}C]-OP binding in plasma, erythrocytes (RBCs) and brain. CD2F1 male mice were fed (1.0 $\mu\text{g}/\text{g}/\text{day}$) parathion (PTN) alone, permethrin (PER) alone, PTN + PER, or control [no compound(s)] for 5 days preceding a dose of 1 $\mu\text{g}/\text{kg}$ of ^{14}C - diisopropyl-fluoro-phosphate (DFP) in food. In a second experiment, pyridostygmine bromide (PYB, 50 $\mu\text{g}/\text{kg}$) was added to all pre-doses and separately to food prior to DFP dosing. Doses were provided in 300 mg food pellets that were rapidly consumed by the fasted mice who were singly caged and otherwise unstressed. Blood and tissues obtained 48 hr after dosing were washed and aliquots (20-50 μl) analyzed for ^{14}C by accelerator mass spectrometry. ^{14}C -DFP levels (pg DFP/g tissue) in plasma and RBCs were equivalent and significantly greater than levels in the brain in both experiments. ^{14}C -DFP levels were not significantly different with the addition of PYB except for depression of DFP-RBC binding under PYB-only exposure. However, PYB decreased DFP binding in all measured tissues. Brain ^{14}C levels were significantly greater in mice pre-dosed with PTN, PER, and PTN+PER, and RBC ^{14}C levels pre-dosed with PYB were significantly lower than in control animals. Response to DFP was therefore additive in plasma but non-additive in the brain or RBC under these exposures. Work performed in part under the auspices of the U.S. Department of Energy by University of California Lawrence Livermore National Laboratory under Contract No. W-7405-Eng-48. with support by NIEHS R01-ES09690.