MECHANISM OF TOXICITY OF A UNIQUE PESTICIDE: N-ETHYLPERFLUOROOCTANE SULFONAMIDE (NEPFOS), AND ITS METABOLITE PERFLUOROOCTANE SULFONAMIDE (PFOS) TO ISOLATED RABBIT RENAL CORTICAL MITOCHONDRIA (RCM).

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NEPFOS is currently being evaluated as a pesticide for the red imported fire ant. Previous studies from this laboratory showed that an early effect of NEPFOS and PFOS on rabbit renal proximal tubules was a concentration-dependent (5-200 uM) increase in ouabain-insensitive respiration (RESP). The goal of this study was to determine whether the increased RESP resulted from uncoupling of oxidative phosphorylation (OX PHOS). NEPFOS (5-100 uM) and PFOS (0.5-50 uM) increased state 4 RESP of RCM respiring on pyruvate/malate or succinate in the absence of a phosphate acceptor or in the presence of oligomycin, an inhibitor of FOF1-ATPase. The effect of NEPFOS (200 uM), PFOS (100 uM), and the known protonophore FCCP (1uM), on proton movement by RCM was examined. Immediately on addition, PFOS and FCCP, but not NEPFOS, dissipated the proton gradient. These results show that PFOS acts as a protonophore and uncouples OX PHOS by this mechanism. The lack of proton movement by NEPFOS suggests that NEPFOS may need to be metabolized to PFOS to produce cytotoxicity and uncoupling of OX PHOS. (Supported by VMES, Univ. Georgia).

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