Tittlemier, S.A., Kennedy, S.W., Hahn, M.E., Reddy, C.M. and Norstrom, R.J., *Naturally-produced halogenated dimethyl bipyrroles bind to the aryl hydrocarbon receptor and induce cytochrome P4501A and porphyrin accumulation in chicken embryo hepatocytes*, Env. Tox. Chem., 2003; v22, 1622-1631

Halogenated di-Me bipyrroles (HDBPs) recently have been identified as a group of environmentally persistent naturally produced bioaccumulative organohalogens. The ability of these compds. to activate the aryl hydrocarbon receptor (AhR) signaling pathway in vitro was examd. Induction of cytochrome P 4501A (CYP1A), measured as ethoxyresorufin-O-deethylase (EROD) activity, and porphyrin accumulation were monitored after exposure of chick embryo hepatocytes to three individual HDBP congeners and two HDBP mixts. All HDBP congeners and mixts. tested caused induction of EROD activity. Induction equivalency factors, calcd. as the ratio of the effective concn. of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) to induce 10 and 50% of the maximal EROD induction to that of the HDBP congener or mixt. ranged from 0.0004 to 0.05. Halogenated di-Me bipyrroles also caused porphyrin accumulation, which increased with exposure time of the hepatocytes and molar bromine content of the HDBP congener or mixt. Heptacarboxylporphyrin III and corproporphyrinogen III were the most abundant porphyrins obsd. after an exposure period of 48 h. The individual HDBP congeners and mixts. also inhibited binding of [3H]TCDD to chicken and mouse AhR. Binding of [3H]TCDD to chicken AhR was inhibited approx. 20% by tetra- to hexabrominated congeners at concns. of 20 to 40 mM; binding to mouse AhR was inhibited 40 to 50% by tri- and tetrabrominated di-Me bipyrroles (DBPs) at 10 mM. The relative affinity of the hexabrominated DBP congener (vs. TCDD) for binding to chicken AhR was estd. to be 0.000017. The results of this work illustrate that HDBPs act as agonist ligands for the AhR in the same manner as many anthropogenic organohalogens.