Dynamic Nature of Alterations in the Endocrine System of Fathead Minnows Exposed to Prochloraz

Kahl, MD[1], Cavallin, JE[1], Jensen, KM[1], Makynen, EA[1], Martinovic, D[2], Mueller, ND[1], Villeneuve, DL[1], Wehmas, LC[1], Ankley, GT[1]

[1] US EPA Mid-Continent Ecology Division, Duluth, MN;
[2] University of St. Thomas, St. Paul, MN.

The vertebrate hypothalamic-pituitary-gonadal (HPG) axis is controlled through various feedback mechanisms, ideally maintaining dynamic homeostasis in the face of changing environmental conditions, including exposure to chemical stressors. These studies assessed the effects of the fungicide prochloraz on HPG axis function in adult fathead minnows (*Pimephales promelas*), with multiple sampling times during an 8-day exposure and 8-day recovery phase. Consistent with one anticipated mechanism of action of prochloraz, cytochrome P450 aromatase (CYP19A) inhibition, exposure to prochloraz depressed *ex vivo* ovarian production and plasma concentrations of 17β-estradiol (E2) in females. At 30 µg prochloraz/L, inhibitory effects on E2 production were transitory, and did not persist during the 8-day exposure phase. At 300 µg prochloraz/L, inhibition of E2 production was evident throughout the 8-day exposure, but steroid titers recovered within one day of chemical exposure cessation. Compensation and/or recovery of steroid production in the prochloraz-exposed females were accompanied by up-regulation of several ovarian genes associated with steroidogenesis, including CYP19A, CYP17 (lyase), CYP11A (cholesterol side-chain cleavage), and follicle-stimulating hormone receptor. In male fish, the 8-day prochloraz exposure decreased testosterone (T) production, possibly through inhibition of CYP17. However, *ex vivo* testicular production and plasma concentrations of T recovered within one day after stopping the chemical exposure. Testicular genes involved in steroidogenesis up-regulated by prochloraz included CYP17 and CYP11A. Overall, these studies demonstrate the adaptability of the HPG axis to chemical stress, and highlight the need to consider the dynamic nature of the system when developing empirical or predictive approaches to assess potential risks of endocrine-active chemicals.

Author Contact Information:
Jenna Cavallin
US EPA, Mid-Continent Ecology Division
6201 Congdon Boulevard
Duluth, MN 55804
T: 218-529-5246
Email: cavallin.jenna@epa.gov

I prefer a poster presentation.