

**Abstract for Midwest SETAC meeting**

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A time-course analysis of effects of the steroidogenesis inhibitor ketoconazole on components of the hypothalamic-pituitary-gonadal axis of fathead minnows

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**Abstract:**

The objective of this study was to evaluate temporal effects of the model steroidogenesis inhibitor ketoconazole (KTC) on aspects of reproductive endocrine function controlled by the hypothalamic-pituitary-gonadal (HPG) axis in the fathead minnow (*Pimephales promelas*). Ketoconazole inhibits the activity of two cytochrome P450s (CYPs) key to sex steroid production in vertebrates, CYP11a and CYP17. Sexually-mature fish were exposed to KTC (30 or 300 µg/L) for up to 8 d, following which animals were allowed to recover in clean water. Samples were collected after 1, 4 and 8 d of exposure, and after 1, 8 and 16 d of recovery. A shorter-term time-course experiment was conducted in which females were sampled on seven occasions during a 12-h KTC exposure. Ketoconazole depressed *ex vivo* gonadal synthesis of testosterone (T) in both sexes, and 17β-estradiol (E2) in females during exposure and recovery phases of the studies. Early in exposures plasma concentrations of T in males and E2 in females also were depressed by KTC exposure. The discrepancy between the *ex vivo* and *in vivo* data at later stages in the test is consistent with some type of compensatory response to KTC in fish. Although a number of genes related to steroid synthesis were up-regulated in male and female gonads during the exposure and early recovery phases of the experiment, this did not seem to account for the ability of KTC-exposed animals to maintain plasma steroid concentrations comparable to controls. Overall, our results demonstrate the complex, temporally-dynamic nature of the vertebrate HPG system in response to chemical stressors.

**Keywords:** Steroid Synthesis, Fungicide, Toxicity, Fish

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