Abstract Title:
Effects of a Short-term Exposure to the Aromatase Inhibitor Fadrozole on Steroid Production and Gene Expression in the Ovary of Female Fathead Minnows (*Pimephales promelas*)

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Cytochrome P450 aromatase is a steriodogenic enzyme that converts C19 androgens to C18 estrogens and is critical for normal reproduction in females. Fadrozole is a well-studied aromatase inhibitor that has been shown to suppress estrogen production in the ovaries of fish. However, little is known about the early impacts of aromatase inhibition on steroid production and gene expression in fish. Adult female fathead minnows (*Pimephales promelas*) were exposed to 0, 5, or 50 µg/L fadrozole for a time-course of 0, 0.5, 1, 2, 4, and 6 hours or exposed to 0 or 50 µg/L fadrozole for a time-course of 6, 12, and 24 h. We examined *ex vivo* 17β-estradiol (E2) and testosterone (T) production and plasma E2 and T concentrations from each study. Expression profiles of genes known to be impacted by fadrozole including aromatase (*Cyp19a1a*), steriodogenic acute regulatory protein (*StAR*), *Cyp11*, *Cyp17*, and follicle stimulating hormone receptor (*Fshr*) were measured in the ovaries by quantitative real-time polymerase chain reaction (QPCR). In addition, ovarian gene expression profiles were examined using a 15k fathead minnow microarray. *Ex vivo* E2 production was significantly reduced by the 5 µg/L exposures after 6h. In the 50 µg/L exposures ex vivo E2 was significantly reduced after just 2 hours of exposure and remained depressed at all time-points examined through 24 h. Plasma E2 was significantly reduced as early as 4 hours for both fadrozole concentrations and remained depressed throughout the 24h for the 50 µg/L exposure. *Ex vivo* and plasma T remained unchanged by either fadrozole concentrations throughout the time-course. Transcripts examined by QPCR showed an initial significant increase in expression followed by a significant decrease in expression by 6h. *Star*, *Cyp17*, and *Fshr* showed a significant increase in expression again by 12h and *Cyp191a1* showed a significant increase in expression by 24h. Microarray results showed concentration- and time-dependent changes in gene expression profiles associated with the chemical exposure. These results provide an indication of the early effects of aromatase inhibition on steroid production and gene expression in the fathead minnow ovary. *The contents of this abstract neither constitute, nor necessarily reflect, official US EPA policy.*