

## Short-term effects of propiconazole on hypothalamic-pituitary-gonadal function in the fathead minnows (*Pimephales promelas*)

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Propiconazole is an ergosterol inhibitor commonly used in agriculture and has been detected in aquatic environments. Ergosterol inhibitors decrease fungal growth through effects on 14 $\alpha$ -demethylase, a cytochrome P450 (CYP), isoform important for ergosterol biosynthesis. In higher organisms, other CYPs are targets for ergosterol inhibiting compounds, such as CYPs involved in sex steroid synthesis or those responsible for Phase I xenobiotic metabolism. To determine the short-term effects of propiconazole on endpoints related to function of the hypothalamic-pituitary-gonadal axis, adult female fathead minnows (*Pimephales promelas*) were exposed to 0 or 1000  $\mu\text{g/L}$  of the fungicide via the water. The fish were treated for up to 24 hours, with sampling at 6, 12, and 24 hours when plasma, liver and ovary were collected. Ovarian *ex vivo* production of testosterone and 17 $\beta$ -estradiol (E2) and plasma E2 were determined by radioimmunoassay. Additionally, quantitative real-time PCR was used to examine expression of a number of genes in ovary and liver. Propiconazole rapidly reduced circulating E2 concentrations and *ex vivo* E2 production, but had no effect on the ovarian expression of genes coding for proteins related to steroidogenesis, including steroidogenic acute regulatory protein and CYP19 aromatase. Hepatic expression of *cyp11a1*, which is involved in metabolism of xenobiotics, was significantly up-regulated at all time-points. This study will aid in understanding the short-term responses of the liver-ovary axis to endocrine disrupting chemicals.

<b>STICs Field</b>	<b>Entry</b>
1 – Influence/profile	Not applicable
2 – Clearance tracking no.	Assigned automatically
3 – Principal Investigator / Project Officer	Gerald Ankley
4- Product title	Copy and paste from abstract
5 - Authors	See abstract
6a- Product type	Presentations and technical summaries
6b-Product subtype	Abstract
6c – Records schedule	Not a senior official
7a – Impact statement	n/a
7b- Product description	Paste in abstract
8 – Bibliographic citation	SETAC North America 33rd Annual Meeting, 11-15 November, Long Beach, CA, USA.
9 - Access	Public
10 – Tracking and Planning Task	2.1.1 2.1.1: Adverse outcome pathway (AOP) discovery and definition
10 – Tracking and Planning Product	(2) AOP descriptions comparing linkages (e.g., causal) between specific pathway perturbations and reproductive or developmental outcomes in multiple species (e.g., rodents, fish, invertebrates) (reports). These will provide data that support the development of tools and guidance cross-species extrapolation of effects and hazard.
11 – Copyright permission	No
12 - QA	not applicable
13 – Policy implications	No
14 - Keywords	pesticide steroidogenesis gene expression aquatic toxicology