

Defining adverse outcome pathways for effects of the fungicide propiconazole on fish reproduction

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Adverse outcome pathways (AOPs) are used to describe the linkage of chemical interactions in terms of molecular initiating events to whole organism responses suitable for risk assessment. This study was conducted to develop AOPs for the model fungicide propiconazole relative to reproductive effects in fish. Conazoles are a class of chemicals that inhibit 14- α -demethylase (cytochrome P450 [CYP] 51) in fungal cell wall development. In higher organisms, other CYPs also become the targets for conazoles, inhibiting key processes such as steroidogenesis. The objective of the present study was to assess the physiological and reproductive impacts of propiconazole on adult fathead minnows (*Pimephales promelas*) using a range of endpoints reflective both of mechanistic responses and adverse apical outcomes. Fathead minnows were exposed to 0, 5, 50, 500, or 1000 μg propiconazole/L for 21 days. Cholesterol, triglyceride, vitellogenin, and sex steroid (testosterone, 17 β -estradiol) concentrations were determined in the plasma. Expression of a number of cholesterol metabolism-related genes in liver and steroidogenesis-related genes in the gonad was determined. Propiconazole significantly reduced cumulative egg production at concentrations greater than 50 μg /L. Ovarian expression of CYP19 (aromatase) and steroidogenic acute regulatory protein was significantly increased in fish from the two highest concentrations; whereas, hydroxymethyl-glutaryl-CoA reductase was significantly decreased in these treatments. The AOPs derived from this research with propiconazole will be useful for predicting the reproductive toxicity to fish from conazole pesticides as a class.