

## Effects of gemfibrozil on cholesterol metabolism, steroidogenesis, and reproduction in the fathead minnow (*Pimephales promelas*)

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Fibrates are a class of pharmaceuticals that indirectly modulate cholesterol biosynthesis through effects on peroxisome proliferator-activated receptors (PPAR), which are transcriptional cofactors that regulate expression of genes related to lipid metabolism. Gemfibrozil is a fibrate that has been detected in wastewater treatment plant effluents and drinking water. The objective of the present study was to assess the potential physiological and reproductive impacts of gemfibrozil on adult fathead minnows (*Pimephales promelas*). Fathead minnows were exposed to gemfibrozil in two different studies. The first was a short-term 8 day exploratory test with water concentrations of 0, 15, and 600 µg/L. Cholesterol, triglyceride, vitellogenin, and sex steroids (testosterone (T), 17β-estradiol (E2)) concentrations were determined in the plasma. Quantitative real-time PCR was used to examine the expression of a number of cholesterol metabolism-related genes in liver and steroidogenesis-related genes in the gonad. *Ex vivo* production of T and E2 by gonad tissue was also determined. Gemfibrozil significantly lowered plasma cholesterol concentrations in the males exposed to 600 µg/L for 8 d. There were no significant effects on plasma triglycerides or cholesterol concentrations in females, suggesting that effects of gemfibrozil may be sex-dependent. The expression of several genes important to lipid metabolism was significantly altered suggesting that gemfibrozil does affect lipid metabolism in fish. There was a significant reduction in male *ex vivo* T production after 2 d of exposure to gemfibrozil; however, after 8 d of exposure this effect was not seen. In addition to the short-term exploratory test, a definitive 21 day reproduction study was completed to further investigate the effects observed in the male fathead minnows and their potential implications for fish reproduction. This study adds to our knowledge of possible effects of a common pharmaceutical pollutant on fish.