

## Effects of gemfibrozil on cholesterol metabolism and steroidogenesis 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 both 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 for two or eight days at water concentrations of 0, 15, and 600 µg/L. Plasma, liver, and gonads were collected. Cholesterol and triglyceride levels were determined in the plasma. Quantitative real-time PCR examined the expression of a number of cholesterol metabolism-related genes in liver and steroidogenesis-related genes in the gonad. Testosterone (T) and 17β-estradiol (E2) concentrations in the plasma and *ex vivo* production of T and E2 by gonad tissue was determined. Gemfibrozil significantly lowered plasma cholesterol concentrations in the males exposed to 600 µg gemfibrozil/L for 8 d. There were no significant effects on plasma triglycerides or cholesterol concentrations in females, suggesting that effects of gemfibrozil exposure may be sex-dependent. PPAR-alpha expression was significantly up-regulated in the liver of males exposed to 600 µg gemfibrozil/L for 8 d. 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. This study adds to our knowledge of possible effects of a common pharmaceutical pollutant on fish.

Key words: gemfibrozil, fathead minnow, steroidogenesis