Effects of cholesterol-altering pharmaceuticals on cholesterol metabolism, steroidogenesis, and gene expression in the fathead minnow (*Pimephales promelas*)

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Pharmaceuticals that target cholesterol biosynthesis and uptake are among the most widely prescribed drugs and have been detected in the aquatic environment. Fibrates are a class of pharmaceuticals that indirectly modulate cholesterol biosynthesis through effects on peroxisome proliferator-activated receptors. Statins are prescribed to lower endogenous cholesterol production by inhibiting 3-hydroxy-3-methylglutaryl coenzyme A reductase, the rate limiting step in cholesterol synthesis. The objective of the present study was to assess the potential physiological and reproductive impacts of a fibrate, gemfibrozil, and a statin, rosuvastatin, on adult fathead minnows (*Pimephales promelas*). Fathead minnows were exposed to gemfibrozil or rosuvastatin in three different studies. Cholesterol, triglyceride, vitellogenin, and sex steroid (testosterone (T), 17β-estradiol (E2)) concentrations were determined in the plasma. The gene expression of a number of cholesterol metabolism-related genes in liver and steroidogenesis-related genes in the gonad were determined. *Ex vivo* production of T and E2 by gonad tissue was also determined. Two short-term 8 day exploratory tests with each chemical were completed. Gemfibrozil significantly lowered plasma cholesterol concentrations in the males exposed to 600 μg/L for 8 d. 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. In addition to the short-term exploratory test with gemfibrozil, 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 common pharmaceutical pollutants on fish.