ENDOCRINE-ACTIVE PHARMACEUTICALS: AN ENVIRONMENTAL CONCERN?

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Recently, there has been growing interest in pharmaceuticals that are specifically designed to have endocrine activity, such as the estrogens used in birth control pills, exerting unintended effects on fish and other aquatic organisms. These pharmaceuticals may not be persistent in water, nor present in large quantities, but they are constantly entering the environment in wastewater effluent and are specifically designed to have physiological effects at minute concentrations. For example, tamoxifen, a widely-used treatment for breast cancer and an estrogen receptor ligand, has been detected in high ng/ml concentrations in British waters. Another class of pharmaceuticals used to supplement or replace tamoxifen treatment for breast cancer is aromatase inhibitors. The prospect of aromatase inhibitors entering aquatic environments in wastewater effluent is of concern because aromatase is the enzyme responsible for estrogen biosynthesis in all vertebrates, and is critical to normal reproductive processes. Laboratory experiments were conducted with the marine fish cunner, (*Tautogolabrus adspersus*), to evaluate whether these pharmaceuticals have an impact on reproduction or aromatase activity in spawning adults. Cunner were treated with tamoxifen (0, 0.5 or 5 mg/kg) or one of the three aromatase inhibitors (0, 0.075 or 0.75 mg/kg) administered by oral gavage on days 0, 4, 8, 12 and 16 of each experiment. Egg production, viability and fertility were determined daily. On day 17, fish were sacrificed, and brain and ovary tissues were flash-frozen for later analysis of aromatase activity. In tamoxifen-treated fish, downward trends in the rate of egg production and the percentage of fertile or viable eggs were not significantly different from controls. Of the aromatase inhibitors, anastrozole and exemestane significantly decreased the rate of egg production in fish treated with the high concentration (750 µg/kg), while letrozole had no effect, although there was a significant decrease in the percentage of fertile and viable eggs in fish treated with letrozole. Female GSI was significantly reduced in anastrozole treatments, significantly increased in 75 µg/kg letrozole treatment, and unaffected by tamoxifen or exemestane treatment. Effects on aromatase activity were variable depending on treatment and tissue (brain or ovary). In fish treated with anastrozole or exemestane, aromatase activity was significantly decreased in brains. Tamoxifen, anastrozole and letrozole treatments significantly increased ovarian aromatase activity. Overall, results indicate that these pharmaceuticals can modulate aromatase activity in fish on a chemical and tissue specific basis, and have the potential to adversely impact fish reproduction.