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### Aquatic Toxicology

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## Mechanistic basis for estrogenic effects in fathead minnow (*Pimephales promelas*) following exposure to the androgen 17 $\alpha$ - methyltestosterone: conversion of 17 $\alpha$ -methyltestosterone to 17 $\alpha$ - methyleneestradiol

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### Abstract

Exposure of adult fathead minnows (*Pimephales promelas*) to the androgen 17 $\alpha$ -methyltestosterone (MT) produces both androgenic and estrogenic effects, manifested as nuptial tubercle formation in females, and vitellogenin production in males and females, respectively. The present study was conducted to determine if the unanticipated estrogenic effects are produced by conversion of MT via aromatase activity to 17 $\alpha$ -methyleneestradiol (ME2). Aromatase activity at the end of a 7-day waterborne MT exposure (20, 200  $\mu$ g/l) was significantly decreased in ovarian microsomes and brain homogenates from exposed fish, to about 30–50% of control activity. Although aromatase activity was decreased by 7 days, it is possible that the conversion of MT to ME2 occurred soon after initial exposure. In support of this, ME2 was detected in plasma samples of the fish following the 7-day exposure, confirming their ability convert the androgen MT to the estrogen ME2. The concentration of ME2 in plasma was within the range of plasma 17 $\beta$ -estradiol (E2) found in control female fathead minnows (4–5 ng/ml). These results, in conjunction with competitive binding assays that indicate ME2 binds to the fathead minnow estrogen receptor with a relative binding affinity of 68.3% of E2, support the hypothesis that aromatization of MT to ME2 contributes to the estrogenic effects in fathead minnows following exposure to this androgen.

**Author Keywords:** Methyltestosterone; Aromatase; Endocrine disruption; Fish; Vitellogenin; Estrogen receptor

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