

Differences in Uptake, Metabolism and Clearance of
Atrazine and Tamoxifen in a Fish and a Rat Species

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Atrazine and tamoxifen are known endocrine-disrupting chemicals (EDCs) that have metabolites exhibiting biological activities that are equally or more potent than the parent compound. To evaluate if uptake, metabolism and clearance of such EDCs is a concern in interspecies extrapolation, plasma concentrations of these chemicals and major metabolites were compared over time in fish and rats treated with a single oral dose of atrazine (50 mg/kg) or tamoxifen (25 mg/kg). For atrazine, plasma samples were collected 0.25, 0.5, 1, 3, 24, 72, and 120 hours after gavage. Atrazine and metabolites were quantified using GC/MS. Atrazine was detected in rat and fish plasma within minutes, indicating rapid uptake in both species. Rats metabolized atrazine quickly; metabolites were present at much higher concentrations than atrazine at all time points and concentration of the metabolite diaminochlorotriazine (DACT) in rat plasma was 30 times that in fish at 3 hours. In fish, atrazine was metabolized more slowly; at 3 hours, atrazine predominated in fish plasma at concentrations over 100 times that in rat plasma. By 120 hours, only DACT was still detectable in both rats and fish. For tamoxifen, animals were sampled 1, 4, 8, 16, 20, 24, 48 and 72 hours post-dosing. Tamoxifen and metabolites in plasma were quantified using HPLC. Peak plasma concentrations of tamoxifen (about 600 ng/ml) were observed at 1 hour in fish and at 4 hours in rats, indicating a slightly faster uptake in fish. From 4 hours forward, tamoxifen and metabolite 4-hydroxytamoxifen dominated in fish plasma, both at similar concentrations at each time point. In rat plasma, from 16 hours forward, tamoxifen and metabolite N-desmethyltamoxifen were prevalent, again at similar concentrations. These results indicate uptake and metabolism of environmental EDCs by different species can vary substantially and could be a significant issue when extrapolating effects across species.