

SSRIs in WWTP effluents and their disposition and effects in salmonids and marine flatfish

Irvin Schultz¹, Louisa Harding², Chris Monson², James West³, Sandra O'Neill³, Graham young², Penny Swanson¹

1. NOAA NWFSC; 2. UW; 3. WDFW TBiOS

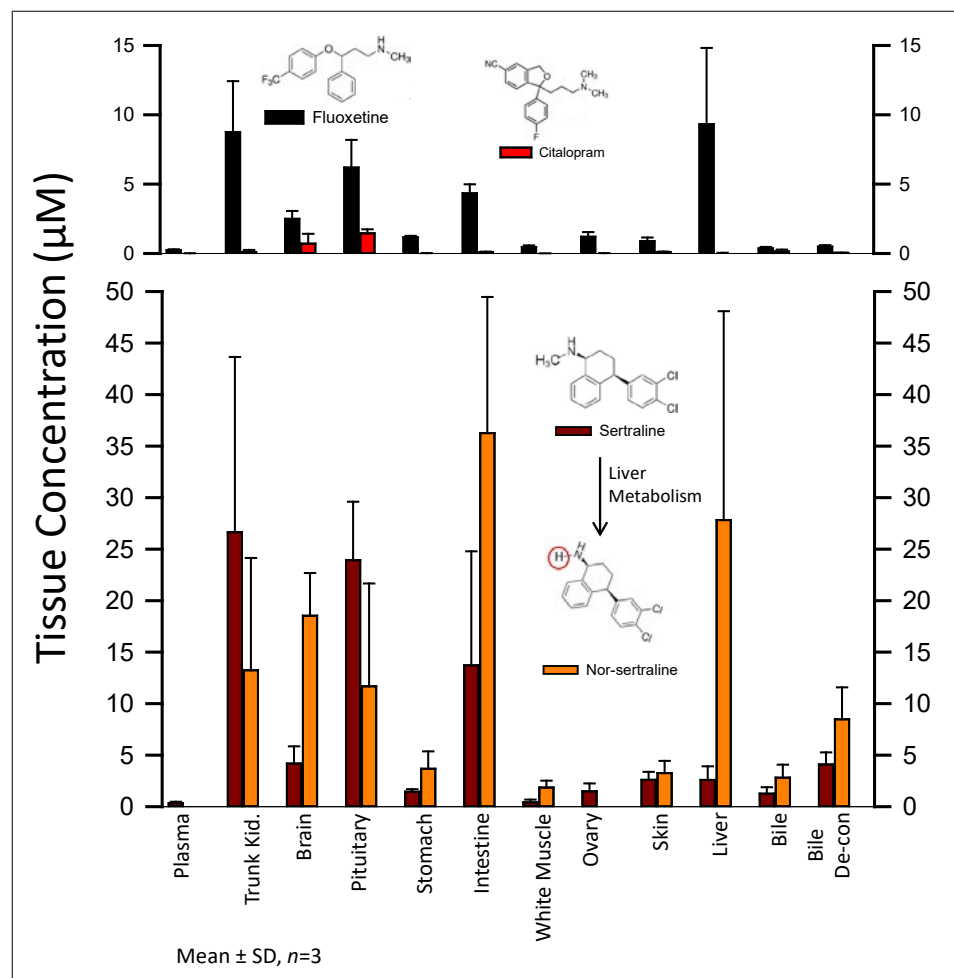
Contact: Irvin Schultz, Irvin.schultz@noaa.gov, 360-461-3746

- **Sertraline (Zoloft) is potentially the most harmful SSRI-type pharmaceutical to aquatic wildlife.**
- **Sertraline is extensively metabolized in fishes to nor-sertraline. Monitoring programs should include nor-sertraline.**

In the Puget Sound region, more than 90% of municipal wastewater treatment plant (WWTP) effluents are directly released into the marine environment. We surveyed eight WWTP effluents for six different selective serotonin reuptake inhibitors (SSRIs) and found total levels varied between 77 and 1,673 ng/L. The most abundant SSRIs (>90% of Σ SSRI) detected were citalopram >>> fluoxetine > sertraline. Other SSRIs monitored were paroxetine, venlafaxine, maprotiline, norfluoxetine, desmethylsertraline and were either not detected or a small fraction of the total SSRI content (norfluoxetine). We subsequently performed a series of in vivo and in vitro exposures to assess the uptake, metabolism and effects of these SSRIs both as a mixture (at ratios observed in WWTP effluents) and as individual chemicals in salmonids and English sole. Static water exposures to an SSRI mixture in rainbow trout revealed sertraline was the most rapidly absorbed SSRI with an uptake clearance of approximately 35 ml/hr/g, nearly 10x more rapid than fluoxetine. Citalopram was the least absorbed SSRI. Subsequent continuous exposures of trout and English sole to a similar SSRI mixture indicated the kidney >> liver > brain were the tissues that accumulated the highest concentrations of SSRIs (Figure 1). Substantial formation of the sertraline metabolite norsertraline was observed in both trout and English sole. Concentrations of norsertraline were similar to, or higher than sertraline in some tissues such as the liver and brain.

High levels of sertraline and norsertraline were found in bile. Subsequent tests using enzymatic deconjugation of bile samples indicated that only 25% of total sertraline and norsertraline is in free (un-conjugated) form. In vitro metabolism studies using hepatocytes or liver homogenates confirmed sertraline is the most rapidly metabolized SSRI. Additional in vitro effects studies using primary pituitary cells and isolated ovarian follicles, found the most sensitive

effect of SSRI exposure was antagonism of the estrogen induced expression of the beta subunit for luteinizing hormone, indicating that SSRI exposure might affect the reproductive cycle. Overall, these results suggest sertraline is the SSRI most likely to bioaccumulate and become biotransformed by fishes, resulting in tissue levels near the threshold for biological effects. Supported by EPA-STAR grant R835167, WA Dept. of Ecology G1400206.



Tissue concentrations of various SSRI-type pharmaceuticals in adult female rainbow trout. The trout were exposed for 72 hrs in a static water exposure system that contained a mixture of fluoxetine, sertraline and citalopram at an initial concentration of 20 µM / SSRI. Sertraline was the most rapidly absorbed SSRI and extensively converted to its de-methylated product nor-sertraline, as indicated on the graph.

RECOMMENDED CITATION

Schultz, I., Harding, L., Monson, C., West, J.E., O'Neill, S.M., Young, G., and Swanson, P. (2019) SSRIs in WWTP effluents and their disposition and effects in salmonids and marine flatfish. p. 52 in 2018 Salish Sea Toxics Monitoring Synthesis: A Selection of Research. Edited by C.A. James, R. Jordan, M. Langness, J. Lanksbury, D. Lester, S. O'Neill, K. Song, and C. Sullivan. Puget Sound Ecosystem Monitoring Program. Tacoma, WA. 88 pp: <https://www.eopugetsound.org/articles/2018-salish-sea-toxics-monitoring-synthesis>