DEVELOPMENT OF A COMPUTATIONAL MODEL FOR FEMALE FATHEAD MINNOWS EXPOSED TO 17α-ETHYNYLESTRADIOL AND 17β-TRENBOLONE

Li Z[1]*, Kroll KJ[2], Jensen K[3], Villeneuve D[3], Ankley GT[3], Ekman D[4], Collette T[4], Brian J[5], Sepulveda MS[6], Orlando EF[7], Denslow ND[2], Watanabe KH[1]; [1]Oregon Health & Science University, Beaverton, OR, [2]University of Florida, Gainesville, FL, [3]U.S. EPA, Duluth, MN, [4]U.S. EPA, Athens, GA, [5]Brunel University, Uxbridge, Middlesex, UK, [6]Purdue University, West Lafayette, IN, [7]University of Maryland, College Park, MD,

Endocrine disrupting chemicals (e.g., estrogens, androgens and their mimics) are known to affect reproduction in fish. A synthetic estrogen used in birth control pills, 17α-ethynylestradiol (EE_2), is discharged from wastewater treatment plants into water bodies throughout the United States. 17β-trenbolone (TB) is a relatively stable metabolite of trenbolone acetate, a synthetic androgen used as a growth promoter for cattle. TB enters the environment mainly through runoff from cattle feedlots. In this study, we developed a physiologically based computational model of female fathead minnows (FHM, *Pimephales promelas*) to simulate how EE_2 or TB affects reproductive parameters, such as plasma concentrations of steroid hormones (17β-estradiol (E_2), and testosterone (T)) and vitellogenin (Vtg, a precursor to egg yolk proteins). The model contains six tissue compartments, and mass balances are used to formulate a set of differential equations describing the dynamics of T, E_2, Vtg, EE_2, and TB, and their reaction kinetics in each compartment. The model is being calibrated with data from 75 unexposed FHMs, 59 FHMs exposed to 0.005, 0.05, 0.5, 5, and 50 ug TB/L for 21 days, and 61 FHMs exposed to 10 and 100 ng EE_2/L for 8 days followed by 8-day depuration. Thus far, 10,000 iterations of the model calibration are done, but one model parameter has not converged. To check the model's ability to fit the data, we performed an intermediate simulation of the data used in model calibration with the non-converged last 1000 iterations of the calibrated parameter sets. The results show that our model captures the non-monotonic, U-shaped dose-response relationships between the nominal water concentrations of TB and plasma concentrations of E_2, T, and Vtg observed in female FHMs exposed for 21 days. Once calibrated, the model will be evaluated with independent, published experimental data from 23 FHMs exposed to 0.005, 0.05, and 0.5 ug TB/L for 2 days, 30 FHMs exposed to 0.005, 0.05, and 0.5 ug TB/L for 14 and 28 days, and 4 FHMs exposed to 1.5 ng EE_2/L for 21 days. The model will be useful to estimate how EE_2 or TB affects the plasma concentrations of steroid hormones and Vtg, which are important variables for population dynamics, to generate hypotheses for experimental tests, and to help us understand biochemical processes related to steroidogenesis in female FHMs.

Contact Author: Zhenhong Li, Oregon Health & Science University
Division of Environmental and Biomolecular Systems
20000 NW Walker Rd., Beaverton, OR 97006
Phone: (503) 748-4075, Fax: (503) 748-1464, liz@ebs.ogi.edu

Presenter: Z Li, Oregon Health & Science University
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