Relative chemical binding affinities for trout and human estrogen receptor using different competitive binding assays.

Denny, J[1], Hornung, M[1], Tapper, M[1], Schmieder, P[1], Pregenzer, J[2], McKim IV, J[2], Blakeman, D[2]

[1]US EPA, ORD, NHEERL, Mid-Continent Ecology Division, Duluth, MN.

[2]CeeTox, Kalamazoo, MI

Rainbow trout-based assays for estrogenicity are currently being used for development of predictive models based upon quantitative structure activity relationships. A predictive model based on a single species raises the question of whether this information is valid for other species. To partially address this question, relative binding affinities (RBA) for six alkylphenols, seven alkylanilines, and three mono-hydroxy parabens were compared among three separate ER binding assays. The ERs used were from rainbow trout hepatic cytosol, a recombinant rainbow trout ERα, and a recombinant human ERα. The two trout-based assays used displacement of 3H-estradiol from the ER, and the human ERα-based assay used displacement of a flourescent ligand as the measure of ER binding. RBAs determined using the trout hepatic cytosol were lower than those determined using the recombinant trout or recombinant human ERα. RBAs determined using the two recombinant ERs (trout and human) were more similar to each other, than either was to RBAs determined with the trout cytosolic ER. This suggests that interspecies differences in receptors may contribute less to differences in RBAs than the differences between other parameters of the binding assays. Matrix differences such as higher protein concentration in the cytosolic preparation in comparison to that in purified recombinant receptor assays, may lead to differences in the bioavailability of a test chemical to interact with the receptor. Thus, knowledge of chemical parameters such as the free fraction of test chemical may be critical for accurately comparing the same endpoint among different assays. This abstract does not necessarily reflect EPA policy.

Key words: QSAR, estrogenicity, estrogen, receptor

Jeff Denny
Mid-Continent Ecology Division
US EPA
6201 Congdon Blvd
Duluth, MN 55804
T: 218-529-5124
F: 218-529-5003
Email:denny.jeff@epa.gov

I prefer poster presentation