A COMPARATIVE TOXICITY STUDY IN RATS AFTER *IN UTERO* AND LACTATIONAL EXPOSURE TO PURIFIED PCB180 OR TCDD

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In this study, the effects of *in utero* and lactational exposure of rats to highly purified PCB 180 (99.9999%) were compared to effects caused by the prototype dioxin like compound (DL), 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) on the same variables.

Pregnant Sprague Dawley rats were given PCB 180 (2,2',3,4,4',5,5'-heptachlorobiphenyl, DL impurities 2.7 ng TEQ_{WHO}/g PCB 180) at daily oral doses between gestational days 7 to 10; total doses 0, 10, 30, 100, 300 or 1000 mg/kg b.w.; or a single oral dose of TCDD at 0, 0.03, 0.1, 0.3 or 1.0 μg/kg b.w. on gestational day 11. One pup/sex/litter were sacrificed at PND7, 35 or 84 for PCB180 and at PND7, 35, or 70 for TCDD and evaluated for effects on body and organ weights, endpoints of sexual maturation and development, as well as profiles of hepatic retinoid and cytochrome P450 enzymes.

Dose-dependent decreases in body weight of offspring after TCDD exposure were observed until PND70, while inconsistent results were obtained for offspring exposed to PCB 180. Several organ weights were dose-dependently altered. The most sensitive and consistent effects following PCB 180 exposure were liver weight increase and prostate weight reduction with critical effect doses (CEDs) at different time-points in the range of 7.4 – 35.3 mg/kg b.w./day and 114 – 222 mg/kg b.w./day, respectively, and thymus and prostate weight reduction with CEDs at different time-points in the range of 0.102 – 0.252 μg/kg b.w. and 0.0518 – 0.0861 μg/kg b.w. following TCDD exposure. No effects were observed on endpoints of sexual maturation and development after PCB 180 exposure, which are typically affected after *in utero* and lactational exposure to TCDD. In offspring exposed to PCB 180, a dose-dependent decrease in hepatic retinol was observed, while in offspring exposed to TCDD, dose-dependent decreases in hepatic retinol and retinyl ester levels were observed. The EROD (CYP1A) activity of the PCB 180 treated offspring was 50 fold induced compared to the control group, but only at the highest dose of 1000 mg/kg b.w., whereas the PROD (CYP2B) activity was induced 2 – 10 fold in a dose dependent manner, starting from the dose of 10 mg/kg b.w. For comparison CYP1A1 mRNA data from TCDD treated rats showed dose and time dependent modulation of the CYP1A1 expression, which was induced from 13 – 2000 fold compared to control group, starting at a dose level of 0.03 μg/kg b.w. and declined over time.

In conclusion, the response to PCB 180 differed remarkably as compared to the response to TCDD, the prototype DL-compound for most endpoints studied.

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