Perfluorohexane Sulfonate (PFHxS) and a Mixture of Endocrine Disrupters Reduce Thyroxine Levels and Cause Anti-Androgenic Effects in Rats

The developmental toxicity of perfluorohexane sulfonate (PFHxS) is largely unknown despite widespread environmental contamination and presence in human serum, tissues and milk. To thoroughly investigate PFHxS toxicity in developing rats and to mimic a realistic human exposure situation, we examined a low dose close to human relevant PFHxS exposure, and combined the dose-response studies of PFHxS with a fixed dose of twelve environmentally relevant endocrine disrupting chemicals (EDmix). Two reproductive toxicity studies in time-mated Wistar rats exposed throughout gestation and lactation were performed. Study 1 included control, two doses of PFHxS and two doses of PFHxS+EDmix (n=5-7). Study 2 included control, 0.05, 5 or 25mg/kg body weight/day PFHxS, EDmix-only, 0.05, 5 or 25mg PFHxS/kg plus EDmix (n=13-20). PFHxS caused no overt toxicity in dams and offspring but decreased male pup birth weight and slightly increased liver weights at high doses and in combination with the EDmix. A marked effect on T4 levels was seen in both dams and offspring, with significant reductions from 5mg/kg/day. The EDmix caused anti-androgenic effects in male offspring, manifested as slight decreases in anogenital distance, increased nipple retention and reductions of the weight of epididymides, ventral prostrate and vesicular seminalis. PFHxS can induce developmental toxicity and in addition results of the co-exposure studies indicated that PFHxS and the EDmix potentiate the effect of each other on various endpoints, despite their different modes of action. Hence, risk assessment may underestimate toxicity when mixture toxicity and background exposures are not taken into account.
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