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

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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 25 mg/kg body weight/day PFHxS, EDmix-only, 0.05, 5 or 25 mg 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 5 mg/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.

General information
Publication status: Published
Organisations: National Food Institute, Research group for Molecular and Reproductive Toxicology, University of Southern Denmark, Brunel University
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Pages: 579-591
Publication date: 2018
Peer-reviewed: Yes

Publication information
Journal: Toxicological Sciences
Volume: 163
Issue number: 2
ISSN (Print): 1096-6080
Ratings:
BFI (2018): BFI-level 2
Scopus rating (2018): CiteScore 3.73 SJR 1.28 SNIP 1.043
Web of Science (2018): Impact factor 3.564
Web of Science (2018): Indexed yes
Original language: English
Electronic versions:
kfy055.pdf. Embargo ended: 06/03/2019
DOIs:
10.1093/toxsci/kfy055
Source: FindIt
Source ID: 2396997204
Research output: Contribution to journal › Journal article – Annual report year: 2018 › Research › peer-review