gene and the MCF-7 E3 estrogen responsive proliferation assays. The extracts from Olay Quench Lotion and CeraVe Daily Moisturizing Lotion induced estrogen agonist activity in the MCF-7 proliferation assay. The extract from the Cortizon-10 Lotion did not induce significant estrogen activity. The product ingredients of each OTC topical medications tested listed ethyl and propyl parabens while the Olay Quench Lotion also contained the least estrogenic paraben methylparaben. We propose that the estrogenic potential of OTC topical medications can be estimated with LC-MS analysis determination of paraben content and concentration. This study illustrates that measurable estrogen activity from OTC topical medications requires the presence of estrogenic parabens (ethyl and propyl) at total concentrations that exceed a threshold. Thus, estrogen activity depends on the type and concentration of paraben present in the OTC topical products. While the capacity for these OTC topical medications to induce estrogen activity in individuals using the products is unclear, consumers may benefit from more information about the paraben type and concentration present.

Endocrine Disruption

ENDOCRINE DISRUPTING COMPOUNDS: MECHANISMS OF ACTION AND CLINICAL IMPLICATIONS

Exposure to Iodoacetic Acid, a Water Disinfection Byproduct, Leads to Abnormal Expression of Key Reproductive Axis Genes in the Hypothalamus and Pituitary

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Iodoacetic acid (IAA) – a water disinfection byproduct (DBP) formed from the reaction between an oxidizing disinfectant, i.e. chlorine, and iodide – is an understudied, yet potentially dangerous environmental toxicant. DBPs have been epidemiologically associated with reproductive dysfunction. *In vitro* studies have indicated that IAA is one of the most cyto- and genotoxic DBPs. Further, murine ovarian research has shown that IAA exposure significantly inhibits antral follicle growth and reduces estradiol levels. Despite this evidence, little is known about the other components of the reproductive axis: the hypothalamus and pituitary. To address this, we tested the hypothesis that IAA exposure would lead to disrupted expression of key hypothalamic and pituitary genes related to reproductive function. We exposed adult female CD1 mice to 0.5, 10, 100, or 500 mg/L IAA in their drinking water from postnatal day 40 (P40) to their first day in diestrus after P75. From this experiment, we collected whole pituitaries and hypothalamic punches containing the arcuate nucleus (ARC), anteroventral periventricular zone (AVPV), and medial preoptic nucleus (mPOA), and processed them for mRNA analysis. We also exposed pituitary explant cultures to IAA to observe direct effects on gene expression. *In vivo,* we found that mRNA levels of kisspeptin (*Kiss1)* are significantly increased in the ARC, the region that controls pulsatile GnRH release, at 0.5 and 10 mg/L IAA concentrations. *Kiss1* is unchanged in the AVPV, the neuron population responsible for generating the LH surge. We also measured ARC expression of neurokinin B (*Tac2*) and dynorphin (*Pdyn*), neuropeptides secreted by kisspeptin co-expressing neurons to autosynaptically stimulate *Kiss1* release. We saw no difference in either. GnRH (*Gnrh1*) expression was also unchanged. Both *in vivo* at 10 mg/L IAA and in culture, we found IAA exposure significantly reduced *Fshb* mRNA. Preliminary immunohistochemistry (IHC) data suggests it also leads to an apparent reduction in FSH-positive cells *in vitro* (N=2). *Lhb* and the α-subunit (*Cga*) were unaltered *in vivo*, though were significantly reduced with *in vitro* exposure. In neither context was mRNA expression of the GnRH receptor (*Gnrhr*) changed. Noting apparent direct effects of IAA on the pituitary, we assessed expression of the cell-cycle inhibitor p21 (*Cdkn1a*), which has been shown to increase with toxicant exposure. We found *Cdkn1a* increased *in vivo* at 500 mg/L IAA, trending at 100 mg/L (p=.070), and *in vitro*. IHC data *in vitro* suggests a marked increase in P21-positivity following IAA exposure. These data, together with prior ovarian findings, implicate IAA as a potential reproductive axis disruptor at each major level – through ARC *Kiss1* expression, *Fshb* expression *in vivo* and *in vitro*, FSH expression *in vitro*, and *Lhb* and *Cga in vitro*. Further, *Cdkn1a*/P21 induction indicates IAA toxicity at the level of the pituitary.

Endocrine Disruption

ENDOCRINE DISRUPTING COMPOUNDS: MECHANISMS OF ACTION AND CLINICAL IMPLICATIONS

Exposure to the Endocrine Disruptor, Propylparaben, During Pregnancy and Lactation, Alters Typical Parity-Induced Reorganization of the Mouse Mammary Gland

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The mammary gland is a hormone sensitive organ that is susceptible to endocrine disrupting chemicals (EDCs) during several vulnerable periods, including pregnancy and lactation. Mammary gland reorganization during pregnancy and lactation is hormone driven and provides long-term protection against breast cancer risk. It is unknown if EDC exposures during these sensitive windows can alter mammary reorganization to either enhance or offset parity-induced protection against breast cancer. Here, we examined effects of propylparaben (PP), a common preservative used in personal care products and foods with estrogen receptor (ER) agonist properties, on the parous mouse mammary gland. Pregnant BALB/c mice were treated with 0, 20, 100, or 10,000 μg/kg/day PP throughout pregnancy and lactation. These doses were selected for their relevance to human exposures. We also included an unexposed nulliparous female group to evaluate the typical changes associated with parity. Five weeks post-involution (and five weeks after the last PP exposure), mammary glands were collected and