Perinatal exposure to mixtures of anti-androgenic chemicals causes proliferative lesions in rat prostate

BACKGROUND:
Elevated levels of endogenous or exogenous estrogens during fetal life can induce permanent disturbances in prostate growth and predispose to precancerous lesions. Recent studies have indicated that also early anti-androgen exposure may affect prostate cancer risk.

METHODS:
We examined the influence of perinatal exposure to mixtures of anti-androgenic and estrogenic chemicals on prostate development. Wistar rats were exposed from gestation day 7 to postnatal day 22 to a mixture of 8 anti-androgenic compounds (AAMix), a mixture of four estrogenic compounds (EMix), or paracetamol or a mixture of all 13 compounds (TotalMix) in mixture ratios reflecting human exposure levels.

RESULTS:
Ventral prostate weights were reduced by the TotalMix and AAMix in pre-pubertal rats. Histological changes in prostate appeared with increasing age and indicated a shift from the normal age-dependent epithelial atrophy towards hyperplasia. These lesions showed similarities to pre-cancerous lesions in humans. Increased proliferation was observed already in pre-puberty and it was hypothesized that this could be associated with reduced ERβ signaling, but no clear conclusions could be made from gene expression studies on ERβ-related pathways. The influences of the estrogenic chemicals and paracetamol on prostate morphology were minor, but in young adulthood the estrogen mixture reduced ventral prostate mRNA levels of Igf1 and paracetamol reduced the mRNA level ofPbpc3.

CONCLUSIONS:
Mixtures of endocrine disrupters relevant for human exposure was found to elicit persistent effects on the rat prostate following perinatal exposure, suggesting that human perinatal exposure to environmental chemicals may increase the risk of prostate cancer later in life. Prostate.
Effects of perinatal ethinyl estradiol exposure in male and female Wistar rats

Perinatal exposure to endocrine disrupting chemicals with estrogenic activity can adversely affect reproductive development, but few studies evaluating estrogen-sensitive endpoints have been performed in Wistar rats. Therefore, time-mated Wistar rats (n=10) were gavaged during gestation and lactation with 0, 5, 15 or 50μg/kg bw/day of ethinyl estradiol. This potent estrogen was found to induce an increased number of nipples and reduced ovary weight in female offspring. Malformations of female genitalia were found in young as well as adult offspring, as an increased AGD was seen at birth and a deeper urethral slit length was seen in adulthood. In prepubertal male offspring, estrogen-regulated gene
expression in ventral prostate was increased dose-dependently and a decreased ventral prostate weight was seen at 15μg/kg. Female external sexual characteristics and prostate development were found to be targets for exposure to estrogenic compounds and may be of interest in studies on estrogenic environmental compounds.
Predictive value of cell assays for developmental toxicity and embryotoxicity of conazole fungicides.

This paper evaluates in vivo predictability of a battery of in vitro tests covering developmental toxicity and embryotoxicity of five widely used conazole fungicides. The conazoles were investigated in the embryonic stem cell test, and data were compared to in vivo embryotoxicity data. The same conazoles were evaluated on the basis of data from a battery of cell assays for endocrine activity, including assays for AR, ER, AhR, and sex hormone synthesis, and data were compared to in vivo developmental toxicity data. Overall, the ranking of the five conazole fungicides based on in vitro data were in reasonably good agreement with available in vivo effects. Ketoconazole and epoxiconazole are the most potent embryotoxic compounds, whereas prochloraz belongs to the most potent developmental toxicants. In conclusion, a rough prediction of the ranking of these conazole fungicides for in vivo toxicity data was possible by a holistic evaluation of data from a panel of cell-based assays.

General information
State: Published
Organisations: Division of Toxicology and Risk Assessment, National Food Institute
Pages: 319-330
Publication date: 2013
Peer-reviewed: Yes

Publication information
Journal: A L T E X. Alternatives to Animal Experimentation
Volume: 30
Issue number: 3
ISSN (Print): 1868-596x
Ratings:
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.47 SJR 1.001 SNIP 1.167
Web of Science (2017): Impact factor 5.232
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Differential effects of environmental chemicals and food contaminants on adipogenesis, biomarker release and PPARγ activation

Eleven environmental relevant chemicals were investigated for their ability to affect adipogenesis in vitro, biomarker release from adipocytes and PPARα and γ activation. We found that butylparaben stimulated adipogenesis in 3T3-L1 adipocytes and increased release of leptin, adiponectin and resistin from the cells. Butylparaben activated PPARγ as well, which may be a mediator of the adipogenic effect. Polychlorinated biphenyl (PCB153) also stimulate adipogenesis and biomarker release, but did not affect PPARs. The data indicates that PPARγ activating chemicals often stimulate adipocyte differentiation although PPARγ activation is neither a requirement nor a guarantee for stimulation. Four out of the eleven chemicals (bisphenol A, mono-ethylhexyl phthalate, butylparaben, PCB 153) caused increased adipogenesis. The release of adipocyte-secreted hormones was sometimes but not always correlated with the effect on adipocyte
differentiation. Eight chemicals were able to cause increased leptin release. These findings strengthen the hypothesis that chemicals can interfere with pathways related to obesity development.

**General information**

State: Published
Organisations: National Food Institute, Division of Toxicology and Risk Assessment, Technical University of Denmark, University of Southern Denmark
Contributors: Taxvig, C., Sørensen, K. D., Boberg, J., Nellemann, C. L., Schelde, A. B., Pedersen, D., Boergesen, M., Mandrup, S., Vinggaard, A. M.
Pages: 106-115
Publication date: 2012
Peer-reviewed: Yes

**Publication information**

Journal: Molecular and Cellular Endocrinology
Volume: 361
Issue number: 1-2
ISSN (Print): 0303-7207
Ratings:
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.76 SJR 1.629 SNIP 1.103
Web of Science (2017): Impact factor 3.563
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.82 SJR 1.779 SNIP 1.077
Web of Science (2016): Impact factor 3.754
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 4.22 SJR 2.14 SNIP 1.242
Web of Science (2015): Impact factor 3.859
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 4.02 SJR 1.963 SNIP 1.273
Web of Science (2014): Impact factor 4.405
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 4.48 SJR 2.085 SNIP 1.424
Web of Science (2013): Impact factor 4.241
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 4.13 SJR 1.668 SNIP 1.248
Web of Science (2012): Impact factor 4.039
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 4.03 SJR 1.794 SNIP 1.191
Web of Science (2011): Impact factor 4.192
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.648 SNIP 1.073
Web of Science (2010): Impact factor 4.119
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.603 SNIP 1.167
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.556 SNIP 1.016
Scopus rating (2007): SJR 1.425 SNIP 0.941
Scopus rating (2006): SJR 1.418 SNIP 0.884
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 2.52 SJR 0.846 SNIP 0.761
Web of Science (2017): Impact factor 2.58
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.92 SJR 1.078 SNIP 1.001
Web of Science (2016): Impact factor 2.341
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 3.36 SJR 1.229 SNIP 1.102
Web of Science (2015): Impact factor 2.85
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 3.28 SJR 1.274 SNIP 1.101
Web of Science (2014): Impact factor 3.227
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 2.91 SJR 1.036 SNIP 1.061
Web of Science (2013): Impact factor 2.771
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 3.28 SJR 1.198 SNIP 1.088
Web of Science (2012): Impact factor 3.141
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 3.15 SJR 1.138 SNIP 1.231
Web of Science (2011): Impact factor 3.226
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.334 SNIP 1.391
Web of Science (2010): Impact factor 3.137
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 0.937 SNIP 1.125
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.048 SNIP 1.071
Scopus rating (2007): SJR 0.656 SNIP 0.825
Scopus rating (2006): SJR 0.769 SNIP 1.055
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.623 SNIP 0.911
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.658 SNIP 0.966
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.598 SNIP 0.992
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.565 SNIP 0.757
Scopus rating (2001): SJR 0.532 SNIP 1
Web of Science (2001): Indexed yes