

NRP Endocrine Disruptors

Final Summary

Original project title
Developmental toxicity of UV filters in mammals
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Effect of estrogenic UV filters on the developing organism in mammals

Some UV filters used in cosmetics and for product protection exhibit estrogenic activity. When administered to rats during pre- and postnatal life, two of these filters, 4-MBC and 3-BC, were found to delay puberty in males and to affect development of reproductive organs and brain, gene expression, and female sexual behavior in adult offspring.

Research questions

1. Do the estrogenic UV filters 4-MBC and 3-BC affect development of reproductive organs, brain, reproductive functions and sexual behavior in a mammalian model, the rat?
2. What is the effect on estrogen-regulated genes in reproductive organs and brain? Is gene regulation by natural estrogens altered?
3. How do internal levels of UV filters in rat offspring at doses affecting development compare with internal exposure levels in humans (margin of safety)?

Results

We discovered that several UV filters exhibit estrogenic activity; they mimic effects of the female sex hormone estradiol in cell cultures and acute in vivo tests. Some also antagonize male hormones. UV filters are present in surface waters and biosphere. Humans may be exposed through skin or by oral uptake of cosmetics (lip sticks) or food (fish). The developing organism is particularly sensitive to chemicals interacting with sex hormones because sex hormones control the development of reproductive organs and brain. In order to assess effects on mammalian development, we studied developmental toxicity of two estrogenic UV filters, 4-methylbenzylidene camphor (4-MBC) and 3-benzylidene camphor (3-BC) in rats. When administered in chow to the parent generation during pregnancy and lactation, and to their off-

spring until adulthood, 4-MBC and 3-BC affected growth of reproductive organs such as prostate, testis and uterus. The expression of estrogen-regulated genes was altered at the level of messenger ribonucleic acid and proteins in uterus and prostate of adult offspring and in brain regions involved in the control of sexual functions, and the sensitivity of genes to natural estrogen changed. Puberty was delayed in males. Sexual functions were affected in offspring: Female sexual behavior was impaired by 4- MBC and 3-BC, and estrous cycles were disturbed by 3-BC. At the lowest dose affecting organ weights or functions, 4-MBC levels in rat milk were only 13 times the highest level detected in human breast milk in a parallel study.

Perspectives

Our data indicate that the role of hormonally active UV filters in consumer products and environment deserves attention. Filters devoid of hormonal activity should be developed, and consumers should be informed how to reduce exposure during sensitive life stages. The data should also contribute to improving tests for risk assessment.