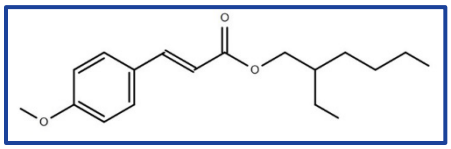
SUMMARY

Background: 2-Ethylhexyl p-methoxycinnamate (EHMC) is a common chemical used in sunscreens and other personal care products to protect users from sunburn. EHMC was selected for evaluation due to concerns about its potential endocrine and reproductive effects. EHMC exposure via diet was selected for this study to ensure a consistent level of exposure to the animal because rodent grooming habits lead to inconsistent exposure for compounds applied to the skin. The effects of EHMC exposure in male and female rats were studied to identify potential developmental and/or reproductive toxicity that could be relevant to humans.



Methods: Groups of 26 pregnant female rats (F_0 generation) were fed diets containing 1,000, 3,000, or 6,000 parts per million (ppm) of EHMC throughout pregnancy and while nursing their offspring (F_1 generation). Control animals were fed diets with no chemical added (0 ppm EHMC). Offspring (F_1 generation) from each exposure group were randomly assigned to one of four cohorts (prenatal, reproductive performance, subchronic, or biological sample collection) and continued to receive feed containing the same dietary concentration of EHMC as their respective mothers. In the F_1 prenatal cohort, fetal development of the offspring of F_1 rats (the F_2 generation) was assessed on gestation day 21. In the reproductive performance cohort, the F_2 generation's viability and growth were assessed until postnatal day 28. In the subchronic cohort, the general toxicity of F_1 rats was assessed on postnatal days 110–113. At the end of the subchronic and reproductive cohort studies, tissues from organ systems from the control group and the 6,000 ppm group were examined for signs of disease.

Results: F_0 female rats exposed via feed to EHMC during gestation had no significant differences in body weights or feed consumption compared to control rats. EHMC had no effect on markers of pregnancy such as viable litters, gestation length, or litter size. F_0 females had slightly decreased body weight and feed consumption during lactation. There were no signs of estrogenic or androgenic effects on reproduction in the F_1 generation. The male and female F_1 generation had lower body weights, indicating an apparent effect on growth rate, which showed some recovery by the end of the study. No toxicologically relevant changes in organ weights were observed in the F_1 cohort. In males, markers of reproductive ability, including testicular descent, sperm motility (the ability of sperm to move, a requirement to reach the egg), testis spermatid head counts, sperm counts, and sperm concentrations, were not affected by EHMC, but there was a significant 2-day delay in puberty onset in the highest exposure group. F_1 females in the two highest exposure groups showed significant delays in puberty onset and longer estrus cycles. The delayed onset of puberty for male and female rats may be the result of lower body weights.

Conclusions: *The NTP four-point scale rates the level of evidence that a substance has the ability to cause reproductive and/or developmental toxicity in laboratory animals. Under the conditions of this study, there was no evidence that EHMC exposure has the ability to cause reproductive toxicity in rats and equivocal (uncertain) evidence, based on the apparent effects on growth, that EHMC exposure has the ability to cause developmental toxicity in rats.*