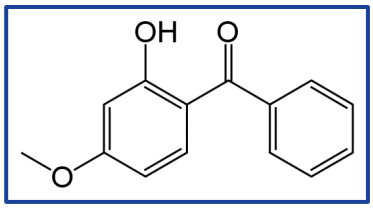
SUMMARY

Background: 2-Hydroxy-4-methoxybenzophenone (2H4MBP) is a common chemical used in sunscreens and other personal care products to protect users from sunburn. 2H4MBP was selected for evaluation due to concerns about its potential endocrine and reproductive effects. 2H4MBP 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 2H4MBP 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 25 pregnant female rats (F_0 generation) were fed diets containing 3,000, 10,000, or 30,000 parts per million (ppm) of 2H4MBP throughout pregnancy and while nursing their offspring (F_1 generation). Vehicle control animals were fed diets with no chemical added (0 ppm 2H4MBP), and positive control animals were fed diets containing 0.05 ppm ethinyl estradiol (EE), a synthetic form of estrogen. Offspring (F_1 generation) from each exposure group were randomly assigned to one of three cohorts (prenatal, reproductive performance, or biological sample collection) and continued to receive feed containing the same dietary concentration of 2H4MBP or EE 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. At the end of the reproductive cohort study, tissues from organ systems from every animal were examined for signs of disease.

Results: Exposure to 2H4MBP via feed showed no effects on mating or pregnancy in F_0 female rats. A small, but significant, decrease in litter size occurred in both the prenatal and reproductive performance cohorts. There were no signs of estrogenic or androgenic effects on reproduction in the F_1 generation. Maternal and offspring F_1 and F_2 rats exposed to 2H4MBP had lower body weights relative to vehicle control animals. In the 30,000 ppm dose groups, body weights decreased over time, but those decreases were not associated with lower feed consumption. Male reproductive organ weights in the 30,000 ppm group were slightly lower than those of vehicle control animals. Low incidences of diaphragmatic hernias (a birth defect in the diaphragm, the muscle that separates the chest cavity from the abdomen) were observed in dosed F_1 and F_2 animals but not in vehicle control animals. Because low incidences of diaphragmatic hernias in vehicle control animals have been reported in similar studies, it is not clear whether those observed in this study were related to 2H4MBP exposure. Noncancerous kidney abnormalities, including swelling and discoloration, occurred in F_0, F_1, and F_2 rats.

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 equivocal (uncertain) evidence that 2H4MBP exposure has the ability to cause reproductive toxicity in rats and some evidence that 2H4MBP exposure has the ability to cause developmental toxicity in rats.*