

## SUMMARY

---

**Background:** *Usnea* lichens are a genus of lichens and a source of usnic acid that has been used in traditional medicines. The use of usnic acid in weight-loss supplements has come under scrutiny by the U.S. Food and Drug Administration due to concerns regarding hepatotoxicity (liver-related toxicity). In two companion NTP studies, the effects of 3-month dietary exposures to (+)-usnic acid ([TOX-104](#)) or *Usnea* lichens (the current report) were evaluated in male and female rats and mice to identify potential toxicity in humans.



**Methods:** Groups of 10 male and 10 female rats and mice were fed rodent feed containing ground *Usnea* lichens for 3 months. The concentrations of *Usnea* lichens in the feed were selected to obtain final (+/-)-usnic acid concentrations of 30, 60, 120, 360, or 720 parts per million (ppm) in the feed for rats and 15, 30, 60, 180, or 360 ppm for mice. Other groups were not exposed to the chemical and served as control animals (0 ppm). At the end of the study, tissues from more than 40 sites were examined for signs of disease. Systemic evaluations of body weight, survival, and female estrus cyclicity were also conducted.

**Results:** All rats in the highest exposure groups (720 ppm) exhibited drastic weight loss and died before the end of the study. However, no reductions in survival were observed in rats from any of the other groups. In contrast to the rats, most mice did not lose weight and survived until the end of the study. For both sexes, mice from the highest exposure group failed to steadily gain weight over time; these mice ultimately weighed less at the end of the study than at the start.

Of all observed tissues in rats and mice, the liver was the most adversely affected at the lowest exposure concentrations. In rats, hepatocellular (liver) degeneration was observed in each sex, and males were more sensitive than females. Similarly, the liver was adversely affected in mice from the highest exposure group. Elevated alanine aminotransferase, an indicator of liver toxicity, was observed in male and female rats from the highest exposure groups, but not in mice. Other organs and tissues were adversely affected in rats fed the highest concentrations of *Usnea* lichens, including the thymus, bone marrow, and adrenal cortex in each sex and the seminiferous tubule in males. These effects were not observed in mice. Estrus stage length was prolonged in female rats and mice fed the highest concentrations of *Usnea* lichens. Damage to DNA was evident in male and female mice from a 2-week exposure to 600 ppm.

---

**Conclusions:** Under the conditions of this 3-month feed study, dietary exposure to *Usnea* lichens resulted in hepatotoxicity in male rats and influenced estrus cycle length in female rats and mice. *Usnea* lichens appear to be more toxic than equivalent concentrations of pure usnic acid that were used in the companion NTP study.

---