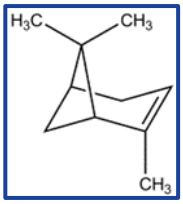
SUMMARY

Background: α-Pinene is a naturally occurring compound produced by some plants that is used as a fragrance or flavor ingredient, in addition to being the main constituent of turpentine. Humans can be exposed to α-pinene via inhalation in occupational settings (e.g., lumber and cleaning industries) and through consumer product use (e.g., air fresheners). The effects of inhalation exposure to α-pinene in male and female rats and mice were studied to identify potential toxicity or cancer-related outcomes.



Methods: Groups of 50 male and 50 female rats and mice were exposed to air containing 50, 100, or 200 parts per million (ppm) (rats) or 100, 200, or 400 ppm (mice) α-pinene via whole-body inhalation for 6 hours per day, 5 days per week for 2 years. Additional 3-month studies were conducted to assess toxicity in the urinary bladder (10 male mice at 100, 200, or 400 ppm α-pinene), to evaluate reproductive performance (25 male rats and 25 male mice at 100, 200, or 400 ppm α-pinene), and to evaluate early predictors of carcinogenicity in the mammary glands, as well as measure internal concentrations of α-pinene and its metabolite, α-pinene oxide (10 male and 10 female rats at 50, 100, or 200 ppm α-pinene). Control animals (rats and mice) for all studies were exposed to air alone with no chemical added (0 ppm α-pinene). At the end of the 2-year study, tissues from more than 35 sites from every animal were examined for signs of disease.

Results: Exposure of male rats to α-pinene for 2 years had no overt effect on their health and survival; whereas in female rats, exposure to α-pinene resulted in increased mortality. Neoplasms (which can include benign or malignant growths) were observed in the urinary bladder of male rats and in the mammary gland and uterus of female rats. Exposure of mice to α-pinene for 2 years had no effect on their survival; however, male mice had decreased body weights. Neoplasms were observed in the Harderian gland (a gland in the eye), liver, lung, and forestomach (an organ that stores undigested food) of male and female mice, in the mammary gland and ovary of female mice, and in the urinary bladder of male mice. Other effects observed in the 2-year studies included lesions in the testis, epididymis (a tube behind the testes), adrenal gland (glands on top of the kidneys), and liver of male rats; uterus, bone marrow, and spleen of female rats; liver, lung, urinary bladder, testis, and epididymis of male mice; and lung, urinary bladder, ovary, and forestomach of female mice. In the 3-month studies, exposure to α-pinene resulted in lesions in the urinary bladder of male mice. Male reproductive endpoints were also affected, with decreased testis and epididymis weights in rats and decreased testis weight in mice. Other effects observed in the 3-month studies included lesions in the testis of male rats and disruptions in the estrous cycle of female rats.

Conclusions: *The NTP four-point scale rates the level of evidence that a substance has the ability to cause cancer in laboratory animals. Under the conditions of these 2-year inhalation studies, there was clear evidence that α-pinene exposure has the ability to cause cancer in female rats based on mammary gland neoplasms; in male mice based on Harderian gland, liver, and lung neoplasms; and in female mice based on Harderian gland, liver, lung, and mammary gland neoplasms. There was some evidence that α-pinene has the ability to cause cancer based on urinary bladder neoplasms in male rats. Uterine neoplasms in female rats, urinary bladder and forestomach neoplasms in male mice, and ovarian and forestomach neoplasms in female mice were also related to exposure. In addition, α-pinene exposure increased the incidence of lesions in the testis, epididymis, adrenal gland, and liver of male rats; uterus, bone marrow, and spleen of female rats; liver, lung, urinary bladder, testis, and epididymis of male mice; and lung, urinary bladder, ovary, and forestomach of female mice.*