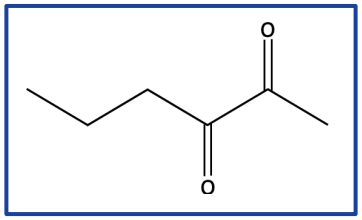
SUMMARY

Background: 2,3-Hexanedione occurs naturally in coffee and beer and is considered safe for consumption in these substances. It is also used as an artificial flavoring and fragrance agent. Limited toxicity data are available, however, for inhalation exposure to 2,3-hexanedione vapors that can occur from the use of electronic cigarettes and hookah pipes with flavored tobacco and in occupational settings without proper ventilation. 2,3-Hexanedione is chemically related to 2,3-butanedione, a compound that has been found to be associated through occupational exposure with obliterative bronchiolitis, an uncommon lung disease characterized by scarring and constriction of the small airways. The effects of 2,3-hexanedione vapor in mice were studied to characterize potential toxicity.



Methods: Groups of six male and six female mice were exposed to 100, 150, or 200 parts per million (ppm) 2,3-hexanedione in air by whole body inhalation 6 hours per day, 5 days per week for 2 weeks and 2 days (12 exposure days total). Mice exposed to clean air in the same type of inhalation chambers served as control groups. At the end of the study, respiratory tract tissues (nose, larynx, trachea, bronchi, and lung) from all mice were collected and examined.

Results: Body weights of female mice exposed to 150 or 200 ppm 2,3-hexanedione were significantly lower than those of the control mice. Exposure to 2,3-hexanedione resulted in a variety of lesions in the nose, larynx, and trachea of male and female mice. Squamous metaplasia (change in cell type), a common lesion caused by inhaled irritants, was present in the respiratory tract of almost all exposed mice. Atypical thickening (hyperplasia) of the bronchial respiratory epithelium (lining) was observed in male and female mice exposed to 200 ppm 2,3-hexanedione. The presence of bronchial epithelial hyperplasia and atypical hyperplasia in exposed mice indicates that a toxic concentration of 2,3-hexanedione reached the airways; however, 2,3-hexanedione did not cause airway fibrosis or obliterative bronchiolitis-like lesions.

Conclusions: *The results showed that after whole body inhalation exposure for 12 days, inhaled 2,3-hexanedione vapor targeted the same sites in the respiratory tract as 2,3-butanedione; however, 2,3-hexanedione did not cause airway fibrosis or obliterative bronchiolitis-like lesions in the exposed mice. Although 2,3-hexanedione caused respiratory tract irritation and lesions in mice exposed to the flavoring agent, 2,3-hexanedione was found to be less toxic than 2,3-butanedione.*