N-Methyl-N-Formylhydrazine

N-Methyl-N-formylhydrazine is a constituent of the false morel Gyromitra esculenta, an edible wild mushroom. Gyromitra esculenta grows wild and is consumed in North America and Europe. This mushroom contains at least six different compounds associated with carcinogenic activity.

N-Methyl-N-formylhydrazine passed the animal data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data

No cancer epidemiology studies were identified.

Animal carcinogenicity data

- Lifetime drinking water studies of N-methyl-N-formylhydrazine
  - Swiss male and female mice: Toth and Nagel (1978)
    - Increased liver, lung, gall bladder and bile duct tumors in males and females (by pairwise comparisons)
  - Swiss male and female mice: Toth et al. (1979)
    - Increased lung, liver, blood vessel, gall bladder, and bile duct tumors in males and females (by pairwise comparisons)
  - Swiss male and female mice: Toth and Patil (1982)
    - Increased lung tumors in males and females (by pairwise comparisons)
  - Syrian golden male and female hamsters: Toth and Patil (1979)
    - Increased liver, gall bladder, bile duct (males only) tumors and malignant histocytoma (by pairwise comparisons)

- Subcutaneous injection studies of N-methyl-N-formylhydrazine
  - Male and female Swiss mice (injected once and observed for life): Toth and Patil (1980)
    - Increased lung tumors in females and preputial gland tumors in males (by pairwise comparisons)
  - Male and female Swiss mice (given 40 weekly injections and observed for life: Toth and Patil (1983)
    - Increases in lung tumors in males and females (by pairwise comparisons)
• Lifetime feeding studies of raw *Gyromitra esculenta*
  o Swiss male and female mice fed raw *Gyromitra esculenta* three
days per week, and mushroom-free semisynthetic diet four days
per week: Toth *et al.* (1992)
  ▪ *Increased lung, nasal cavity, blood vessel, forestomach, glandular stomach (males only), cecum, and liver (males only) tumors in males and females (by pairwise comparisons)*

**Other relevant data**

• Metabolism
  o Metabolized to the carcinogens formaldehyde and acetaldehyde, and to radical intermediates: Gannett *et al.* (1991)

• Structure activity considerations
  o Structurally similar to other hydrazine compounds that induce
tumors in animals: Toth (1975), Gannett *et al.* (1991)
  o Hydrazine compounds listed as Proposition 65 carcinogens include:
    ▪ Hydrazine
    ▪ Hydrazine sulfate
    ▪ Methylhydrazine and its salts
    ▪ Phenylhydrazine and its salts
    ▪ 1,2-Diethylhydrazine
    ▪ 1,1-Dimethylhydrazine
    ▪ 1,2-Dimethylhydrazine
    ▪ 1,2-Diphenylhydrazine

**References**

Gannett PM, Garrett C, Lawson T, Toth B (1991). Chemical oxidation and
metabolism of *N*-methyl-*N*-formylhydrazine. Evidence for diazenium and radical

Toth B (1975). Synthetic and naturally occurring hydrazines as possible cancer

Toth B, Nagel D (1978). Tumors induced in mice by *N*-methyl-*N*-formylhydrazine
of the false morel *Gyromitra esculenta*. 60:201-204.

Toth B, Patil K (1979). Carcinogenic effects in the Syrian golden hamster of *N-

1 Excerpts or the complete publication have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.


