

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 esculanta*
 - Swiss male and female mice fed raw *Gyromitra esculanta* 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
 - Metabolized to the carcinogens formaldehyde and acetaldehyde, and to radical intermediates: Gannett *et al.* (1991)
- Structure activity considerations
 - Structurally similar to other hydrazine compounds that induce tumors in animals: Toth (1975), Gannett *et al.* (1991)
 - 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

References¹

Gannett PM, Garrett C, Lawson T, Toth B (1991). Chemical oxidation and metabolism of *N*-methyl-*N*-formylhydrazine. Evidence for diazenium and radical intermediates. *Food Chem Toxicol* **29**:49-56.

Toth B (1975). Synthetic and naturally occurring hydrazines as possible cancer causative agents. *Cancer Res* **35**:3693-3697.

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*-methyl-*N*-formylhydrazine of the false morel mushroom *Gyromitra esculenta*. *J Cancer Res Clin Oncol* **93**:109-121.

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.

Toth B, Patil K (1980). Carcinogenesis by a single dose of N-methyl-N-formylhydrazine. *J Toxicol Environ Health* **6**:577-584.

Toth B, Patil K (1982). Tumorigenicity of minute dose levels of N-methyl-N-formylhydrazine of *Gyromitra esculenta*. *Mycopathologia* **78**:11-16.

Toth B, Patil K (1983). Tumorigenic action of repeated subcutaneous administration of N-methyl-N-formylhydrazine in mice. *Neoplasma* **30**:437-441.

Toth B, Patil K, Erickson J, Kupper R (1979). False morel mushroom *Gyromitra esculenta* toxin: N-methyl-N-formylhydrazine carcinogenesis in mice. *Mycopathologia* **68**:121-128

Toth B, Patil K, Pyysalo H, Stessman C, Gannett P (1992). Cancer induction in mice by feeding the raw false morel mushroom, *Gyromitra esculenta*. *Cancer Res* **52**:2279-2284.