METHYL IODIDE

Data were last reviewed in IARC (1986) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

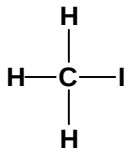
1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 74-88-4
Chem. Abstr. Name: Iodomethane
IUPAC Systematic Name: Iodomethane

1.1.2 *Structural and molecular formulae and relative molecular mass*



CH_3I Relative molecular mass: 141.94

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Colourless transparent liquid, with a sweet ethereal odour (American Conference of Governmental Industrial Hygienists, 1992; Budavari, 1996)
(*b*) *Boiling-point*: 42.5°C (Lide, 1997)
(*c*) *Melting-point*: –66.4°C (Lide, 1997)
(*d*) *Solubility*: Slightly soluble in water (14 g/L at 20°C); soluble in acetone; miscible with diethyl ether and ethanol (Budavari, 1996; Verschueren, 1996; Lide, 1997)
(*e*) *Vapour pressure*: 53 kPa at 25.3°C; relative vapour density (air = 1), 4.9 (Verschueren, 1996)
(*f*) *Octanol/water partition coefficient (P)*: log *P*, 1.51 (Hansch *et al*., 1995)
(*g*) *Conversion factor*: $mg/m^3 = 5.81 \times ppm$

1.2 Production and use

No information on the global production of methyl iodide was available to the Working Group. Production in the United States in 1983 was about 50 tonnes (IARC, 1986).

Because of its high refractive index, methyl iodide is used in microscopy. It is also used as an embedding material for examining diatoms, in testing for pyridine, as a methylating agent in pharmaceutical (e.g., quaternary ammonium compounds) and chemical synthesis, as a light-sensitive etching agent for electronic circuits, and as a component in fire extinguishers (IARC, 1986; American Conference of Governmental Industrial Hygienists, 1992; Budavari, 1996).

1.3 Occurrence

1.3.1 *Occupational exposure*

According to the 1981–83 National Occupational Exposure Survey (NOES, 1997), approximately 2000 workers in the United States were potentially exposed to methyl iodide (see General Remarks). Occupational exposures to methyl iodide may occur in its production and use in organic synthesis and as a laboratory reagent.

1.3.2 *Environmental occurrence*

Methyl iodide is produced by many marine photosynthetic organisms and therefore the ocean is thought to be a major natural source of methyl iodide. Some of this is released to the atmosphere and some reacts with seawater to form methyl chloride. Industrial emissions of methyl iodide may occur in conjunction with its use as a methylating agent and in organic synthesis. Humans are exposed to methyl iodide from the ambient air and from ingesting seafood (United States National Library of Medicine, 1998).

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has recommended 12 mg/m^3 as the 8-h time-weighted average threshold limit value for occupational exposures to methyl iodide in workplace air. Values of 1–28 mg/m^3 have been used as standards or guidelines in other countries (International Labour Office, 1991). Methyl iodide is considered to be a human carcinogen in Germany (Deutsches Forschungsgemeinschaft, 1998).

No international guideline for methyl iodide in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Methyl iodide was tested for carcinogenicity in one experiment in rats by subcutaneous administration and in a screening test for lung adenomas in strain A mice by intraperitoneal injection. It induced local sarcomas in rats after single or repeated subcutaneous injections; a marginally increased incidence of lung tumours was observed in mice (IARC, 1986).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

The inhalation of trace amounts of [^{132}I]methyl iodide was followed by a decrease in plasma radioactivity, a thyroid uptake pattern and urinary excretion that were similar to those observed after oral administration of inorganic iodide (IARC, 1986).

Methyl iodide incubated with human erythrocytes conjugates nonenzymatically with glutathione. In addition, an enzymatic conjugation was apparent with erythrocytes from 10/17 donors, but even among these people, the nonenzymatic process was dominant (Hallier *et al*., 1990).

4.1.2 *Experimental animals*

Data from several experiments with rats suggest that absorbed methyl iodide is excreted mainly in bile. Approximately 25% of an oral dose of 50 mg/kg bw was excreted in bile as *S*-methylglutathione, while 2% of the same subcutaneous dose was recovered from urine and 1% of a 76 mg/kg bw oral dose was present, unchanged, in expired air within 30 min. The urinary metabolites detected in rats after subcutaneous injection, presumed to originate from *S*-methylglutathione, were *S*-methylcysteine, *N*-acetyl-*S*-methylcysteine, *S*-methylthioacetic acid and *N*-(methylthioacetyl)glycine (IARC, 1986).

4.2 Toxic effects

4.2.1 *Humans*

Workers affected by non-fatal poisoning showed many neurological symptoms such as visual and psychological disturbances, vertigo and weakness (IARC, 1986).

4.2.2 *Experimental animals*

Toxic effects observed in rodents after exposure to methyl iodide included narcosis, lung congestion and liver and kidney damage. Oral administration to rats reduced non-protein thiol concentrations in liver and kidney (IARC, 1986).

4.3 Reproductive and developmental effects

No data were available to the Working Group.

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 1 for references)

Methyl iodide induces DNA damage and is mutagenic to bacteria in the presence or absence of an exogenous metabolic system. It induces mitotic recombination in yeast and mutations in cultured mammalian cells. It induces transformation in Syrian hamster embryo cells but not in C3H 10T½ cells.

DNA adducts were detected in the stomach, forestomach, liver and lung of male and female Fischer 344 rats exposed to [^{14}C]methyl iodide orally or by inhalation in a closed exposure system. [^{14}C]3-Methyladenine, [^{14}C]7-methylguanine and [^{14}C]*O*^{6}-methylguanine were identified by a combination of three different methods of hydrolysing DNA and subsequent high-performance liquid chromatography or gas chromatography–mass spectrometry analysis. The higher levels of methylated guanines were found in the stomach and forestomach following both oral and inhalation exposure (Gansewendt *et al*., 1991).

5. Evaluation

No epidemiological data relevant to the carcinogenicity of methyl iodide were available.

There is *limited evidence* in experimental animals for the carcinogenicity of methyl iodide.

Overall evaluation

Methyl iodide is *not classifiable as to its carcinogenicity to humans (Group 3)*.

6. References

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Table 1. Genetic and related effects of methyl iodide

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
ECD, *Escherichia coli pol A*/W3110-P3478, differential toxicity (spot test)	(+)	NT	23000	Rosenkranz & Poirier (1979)
SA0, *Salmonella typhimurium* TA100, reverse mutation	(+)	NT	NG	McCann *et al*. (1975)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	7.6	Simmon *et al*. (1977)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	250	Simmon (1979a)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	4600	Rosenkranz & Poirier (1979)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	250	Simmon (1979a)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	250	Simmon (1979a)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	23000	Rosenkranz & Poirier (1979)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	250	Simmon (1979a)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	250	Simmon (1979a)
SAS, *Salmonella typhimurium* TA1536, reverse mutation	–	–	250	Simmon (1979a)
ECW, *Escherichia coli* WP2 *uvr*A, reverse mutation	+	NT	NG	Hemminki *et al*. (1980)
EC2, *Escherichia coli* WP2, reverse mutation	+	NT	2850	Takahashi & Kawazoe (1987)
SCH, *Saccharomyces cerevisiae* D3, mitotic recombination	+	+	2300	Simmon (1979b)
ANR, *Aspergillus nidulans*, reverse mutation	–	NT	NG	Moura Duarte (1972)
VFC, *Vicia faba*, chromosomal aberrations	–	NT	140	Rieger *et al*. (1988)
GCO, Gene mutation, Chinese hamster ovary CHO cells, *hprt* locus *in vitro*	+	NT	0.75	Amacher & Zelljadt (1984)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	+	50	Clive *et al*. (1979)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	NT	7.5	Moore & Clive (1982)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	NT	7.5	Moore *et al*. (1985)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
G51, Gene mutation, mouse lymphoma L5178Y cells, *hprt* locus *in vitro*	NT	–	50	Clive *et al*. (1979)
G51, Gene mutation, mouse lymphoma L5178Y cells, *hprt* locus *in vitro*	(+)	NT	10	Moore & Clive (1982)
G51, Gene mutation, mouse lymphoma L5178Y cells, ouabain resistance *in vitro*	+	NT	3.6	Amacher & Dunn (1985)
TCM, Cell transformation, C3H 10T½ mouse cells	–	NT	250	Oshiro *et al*. (1981)
TCS, Cell transformation, Syrian hamster embryo cells, clonal assay	+	NT	1	Pienta *et al*. (1977)
BVD, Binding (covalent) to DNA, male and female Fischer 344 rat stomach, forestomach, liver and lungs *in vivo*	+		3.1 po × 1	Gansewendt *et al.* (1991)
BVD, Binding (covalent) to DNA, male and female Fischer 344 rat stomach, forestomach, liver and lungs *in vivo*	+		744 mg/m^3 inh 6 h × 1	Gansewendt *et al.* (1991)

[a] +, positive; (+), weak positive; –, negative; NT, not tested

[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL; in-vivo tests, mg/kg bw/day; NG, not given; po, oral; inh, inhalation

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