METHYL ACRYLATE

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

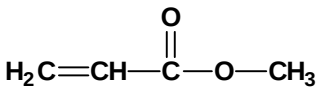
1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 96-33-3
Chem. Abstr. Name: 2-Propenoic acid, methyl ester
IUPAC Systematic Name: Acrylic acid, methyl ester
Synonym: Methyl propenoate

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_4H_6O_2$ Relative molecular mass: 86.09

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Liquid with an acrid odour (Budavari, 1996)
(*b*) *Boiling-point*: 80.6°C (American Conference of Governmental Industrial Hygienists, 1992)
(*c*) *Melting-point*: –76.5°C (Budavari, 1996)
(*d*) *Solubility*: Slightly soluble in water (6 g/100 mL at 20°C, 5 g/100 mL at 40°C); soluble in ethanol, diethyl ether, acetone and benzene (American Conference of Governmental Industrial Hygienists, 1992)
(*e*) *Vapour pressure*: 9.3 kPa at 20°C; relative vapour density (air = 1), 3.0 (Verschueren, 1996)
(*f*) *Flash point*: –2.8°C, closed cup; 6.7°C, open cup (American Conference of Governmental Industrial Hygienists, 1992)
(*g*) *Explosive limits:* upper, 25%; lower, 2.8% by volume in air (American Conference of Governmental Industrial Hygienists, 1992)
(*h*) *Conversion factor*: $mg/m^3 = 3.52 \times ppm$

1.2 Production and use

Production of methyl acrylate in the United States was reported to be 14 100 tonnes in 1983 (United States National Library of Medicine, 1997).

Methyl acrylate is used in manufacture of acrylic and modacrylic fibres, amphoteric surfactants, leather finish resins, textile and paper coatings and plastic films (United States National Library of Medicine, 1997).

1.3 Occurrence

1.3.1 *Occupational exposure*

National estimates of exposure were not available.

1.3.2 *Environmental occurrence*

Methyl acrylate is a volatile component of pineapples. It may be released into the environment in fugitive and stack emissions or in wastewater during its production and use in the manufacture of acrylic fibres and resins. Methyl acrylate has been detected at low levels in wastewater and ambient air samples (United States National Library of Medicine, 1997).

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has recommended 7 mg/m^3 as the threshold limit value for occupational exposures to methyl acrylate in workplace air. Similar values have been used as standards or guidelines in many countries (International Labour Office, 1991).

No international guideline for methyl acrylate 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

In one study, reported as an abstract, in which rats were exposed to methyl acrylate by inhalation for two years, no neoplastic effect was reported (IARC, 1986).

3.1 Inhalation exposure

Rat: In the full report of the study cited previously in IARC (1986), four groups of 86 male and 86 female Sprague-Dawley rats, 35 days of age, were exposed (whole body) to 0, 15, 45 and 135 ppm [0, 53, 158 and 475 mg/m^3] methyl acrylate (purity, > 99.8%; main impurities methyl propionate and ethyl acrylate) in air for 6 h per day on five days

per week for 24 months. Interim kills were performed after 12 (10 males and 10 females) and 18 months (15 males and 15 females) of exposure. No significant difference in mortality was observed between the groups. The incidence of soft-tissue sarcomas varied considerably among the groups but there was no dose-dependence. No increased frequency of any tumour type in any organ could be related to a carcinogenic effect of the test substance (Reininghaus *et al*., 1991).

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

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

Autoradiography of guinea-pigs exposed dermally to methyl [2,3-^{14}C]acrylate showed that the radioactivity was seen in the subcutaneous tissues and throughout the body. Following oral administration of methyl [2,3-^{14}C]acrylate to guinea-pigs, the radioactivity was distributed in internal organs, especially the liver and bladder, and brain within 2 h; at 16 h it was seen only in mucous linings of the stomach, intestine and mouth epithelium. One hour after intraperitoneal injection of the same dose (no vehicle), radioactivity was concentrated in the peritoneum and liver and present in most other organs. Radioactivity quickly decreased in most organs, except the liver and bladder. After 24 and 48 h most organs had lost the radioactive material, but some was retained in mucous linings. After an intraperitoneal dose of methyl [2,3-^{14}C]acrylate to young male guinea-pigs, 35% of the radioactivity was excreted as $^{14}CO_2$ in expired air within 8 h and 40% after 72 h (22.6% was excreted in the urine over 72 h) (IARC, 1986).

Conjugation with sulfhydryl groups appears to be an important detoxification process for methyl acrylate in the guinea-pig. The thioethers were identified as *N*-acetyl-*S*-(2-carboxyethyl)-L-cysteine and the corresponding monomethyl ester, with a ratio between the two metabolites of 20:1. In male rats exposed to methyl acrylate by inhalation, depletion of nonprotein sulfhydryl compounds was most pronounced in the lung, compared to liver, kidney and blood. After administration of methyl acrylate to Wistar rats, no hydroxymercapturic acid that might be derived from the epoxide of methyl acrylate was detected. It seems unlikely, therefore, that epoxidation of the acrylic esters occurs *in vivo* (IARC, 1986).

Two further metabolic studies of methyl [2,3-^{14}C]acrylate have confirmed these results (Sapota, 1988, 1993).

4.2 Toxic effects

4.2.1 *Humans*

Methyl acrylate in nail lacquer has been shown to be a possible cause of contact dermatitis (Kanerva *et al*., 1995, 1996).

4.2.2 *Experimental systems*

No exposure-related clinical signs or lesions of systemic toxicity were observed in male and female Sprague-Dawley rats exposed by inhalation to methyl acrylate for 6 h per day on five days per week, at concentrations of 0, 15, 45 and 135 ppm [0, 53, 158 and 475 mg/m^3] over 24 months (Reininghaus *et al*., 1991). Atrophy of the neurogenic epithelial cells and hyperplasia of reserve cells were observed in the nasal mucosa of all methyl acrylate-treated animals. These changes were dose-related and mainly affected the anterior part of the olfactory epithelium. Opacity and neovascularization of the cornea were seen in all methyl acrylate-exposed groups.

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 acrylate did not induce mutations in bacteria.

In mammalian cells treated *in vitro*, methyl acrylate induced mutations at the *tk* locus in mouse cells, in the absence of exogenous metabolic activation, but not at the *hprt* locus in Chinese ovary hamster cells. It induced chromosomal aberrations in mouse and Chinese hamster cells *in vitro.*

Of three micronucleus assays of methyl acrylate using mouse bone marrow *in vivo*, two were negative.

4.4.3 *Mechanistic considerations*

Methyl acrylate appears to be clastogenic to mammalian cells *in vitro*. The preferential induction of small colonies rather than large ones in the mouse lymphoma L5178Y *tk* mutagenicity assay is thought to indicate that mutations arise from chromosomal damage rather than by point mutation. The clastogenic activity of methyl acrylate seen *in vitro* is not readily detected *in vivo*.

Table 1. Genetic and related effects of methyl acrylate

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation (spot test)	–	–	258	Florin *et al.* (1980)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	590	Hachiya *et al.* (1982)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	1250	Waegemaekers & Bensink (1984)
SA5, *Salmonella typhimurium* TA1535, reverse mutation (spot test)	–	–	258	Florin *et al.* (1980)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	590	Hachiya *et al.* (1982)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	1250	Waegemaekers & Bensink (1984)
SA7, *Salmonella typhimurium* TA1537, reverse mutation (spot test)	–	–	258	Florin *et al.* (1980)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	590	Hachiya *et al.* (1982)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	1250	Waegemaekers & Bensink (1984)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	590	Hachiya *et al.* (1982)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	1250	Waegemaekers & Bensink (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation (spot test)	–	–	258	Florin *et al.* (1980)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	590	Hachiya *et al.* (1982)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	1250	Waegemaekers & Bensink (1984)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	NT	14	Moore *et al.* (1988)
GCO Gene mutation, Chinese hamster ovary CHO cells, *hprt* locus *in vitro*	–	NT	18	Moore *et al.* (1989)
GCO Gene mutation, Chinese hamster ovary CHO cells, *hprt* locus *in vitro*	–	NT	60	Moore *et al.* (1991)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
GCO, Gene mutation, Chinese hamster ovary A552 cells, *xprt* locus *in vitro*	–	NT	25	Oberly *et al.* (1993)
CIM, Chromosomal aberrations, mouse lymphoma L5178Y cells *in vitro*	+	NT	16	Moore *et al.* (1988)
CIC, Chromosomal aberrations, Chinese hamster lung cells *in vitro*	+	NT	6.5	Ishidate *et al.* (1981)
CIC, Chromosomal aberrations, Chinese hamster lung cells *in vitro*	+	NT	75	Sofuni *et al.* (1984a)
CIC, Chromosomal aberrations, Chinese hamster ovary cells *in vitro*	+	NT	14	Moore *et al.* (1989)
MVM, Micronucleus test, ddY mouse bone-marrow cells *in vivo*	–		250 po × 1	Hachiya *et al.* (1981)
MVM, Micronucleus test, BALB/c mouse bone-marrow cells *in vivo*	+		37.5 ip × 2	Przybojewska *et al.* (1984)
MVM, Micronucleus test, ddY mouse bone-marrow cells *in vivo*	–		2100 ppm inh 3 h	Sofuni *et al.* (1984b)

[a] +, 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; po, orally; ip, intraperitoneally; inh, inhalation

5. Evaluation

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

There is *inadequate evidence* in experimental animals for the carcinogenicity of methyl acrylate.

Overall evaluation

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

6. References

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