1,3-PROPANE SULTONE

Data were last reviewed in IARC (1974) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

1. Exposure Data

1.1 Chemical and physical data

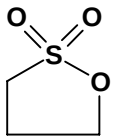
1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 1120-71-4

Chem. Abstr. Name: 1,2-Oxathiolane, 2,2-dioxide

Synonyms: 3-Hydroxy-1-propanesulfonic acid, γ-sultone; propane sultone

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_3H_6O_3S$ Relative molecular mass: 122.14

1.1.3 *Chemical and physical properties of the pure substance*

(from American Conference of Governmental Industrial Hygienists, 1992)

(*a*) *Description*: White crystalline solid or colourless liquid

(*b*) *Boiling-point:* 112°C

(*c*) *Melting-point:* 31°C

(*d*) *Solubility:* Moderately soluble in water (100 g/L) and most organic solvents; insoluble in aliphatic hydrocarbons

(*e*) *Conversion factor:* $mg/m^3 = 5.0 \times ppm$

1.2 Production and use

No information on the global production of 1,3-propane sultone was available to the Working Group.

1,3-Propane sultone has been used as a chemical intermediate to introduce the propylsulfonate ($–CH_2CH_2CH_2SO_3^–$) group into molecules and to confer water solubility and anionic character. It is also a chemical intermediate in the production of fungicides, insecticides, cation-exchange resins, dyes, vulcanization accelerators and a variety of other

chemicals (American Conference of Governmental Industrial Hygienists, 1992; Lewis, 1993).

1.3 Occurrence

No data were available to the Working Group.

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has not proposed any occupational exposure limit for 1,3-propane sultone in workplace air but does list it as an animal carcinogen. Australia, Belgium, Finland, France, Germany, Sweden and Switzerland list 1,3-propane sultone as a probable human carcinogen (International Labour Office, 1991).

No international guideline for 1,3-propane sultone 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

1,3-Propane sultone was tested for carcinogenicity by oral, intravenous and prenatal exposure in rats, producing tumours at various sites; a local carcinogenic effect was induced in mice and rats when it was given subcutaneously. It was carcinogenic in rats after single-dose exposures (IARC, 1974).

3.1 Oral administration

Rat: 1,3-Propane sultone (purity 91%) was administered orally by gavage to groups of 26 male and 26 female weanling Sprague-Dawley rats at doses of 28 and 56 mg/kg bw per day twice per week for 60 weeks or 32 weeks. The animals were then observed without further dosing up to 60 weeks. Two groups of rats, one of 16 males and 16 females and one of 26 males and 26 females, were used as matched and pooled controls. Survival at 52 weeks among male and female rats, respectively, was 62% and 39%, in the 28 mg/kg bw group and 15% and 23%, respectively, in the 56 mg/kg bw group. Administration of the high dose was stopped at week 32 because numerous mammary tumours had developed in the females from week 18 and there was high mortality among the males. Significant increases in the incidence of certain tumours were found. The incidences in the matched control, low-dose and high-dose groups, respectively, were: male rats—malignant glioma (cerebrum), 1/16, 10/26 and 11/26; malignant glioma (cerebellum), 0/16, 6/26 and 11/26; and female rats—malignant glioma (cerebrum), 1/16,

12/26 and 12/26; malignant glioma (cerebellum), 0/16, 8/26 and 4/26; mammary adenocarcinoma, 0/16, 6/26 and 13/26 (Weisburger *et al*., 1981).

3.2 Subcutaneous administration

Rat: Eighty random-bred male albino rats (weighing 70–140 g) were divided into groups of five or 10 [no controls] and given 1–7 subcutaneous injections of 1,3-propane sultone at doses of 62, 125 or 166 mg/kg bw. Multiple doses were given at 15-day intervals. Neoplastic lesions varying from well differentiated to anaplastic adenocarcinomas were seen in the lungs of 17/73 rats 21–25 weeks after injection of 1,3-propane sultone (Gupta *et al*., 1981). [The Working Group noted the limited reporting of the data.]

3.3 Skin application

Mouse: Groups of 25 male and 25 female mice of each of three strains (CF1, C3H and CBah, a hairless strain), six weeks of age, were treated twice weekly by painting with approximately 0.05–0.1 mL benzene per mouse for four weeks and then toluene for one year or with 2.5% w/v 1,3-propane sultone (purity, 99.9%) in the same solvents and for the same time; control groups were left untreated. In the control groups, survival at the end of the experiment (58 weeks) was at least 60%. No CF1 or C3H mice survived exposure to 1,3-propane sultone for 58 weeks and only 12% of the CBah mice survived to this time. No skin tumours were seen in the untreated or solvent control groups, whereas, in the 1,3-propane sultone-treated groups of male and female mice, respectively, the numbers of tumour-bearing mice were: CF1, 15/21, 3/24; C3H, 20/22, 6/25; CBah, 20/23, 18/25. In addition, there was clearly a higher proportion of CF1 mice with lymphoreticular neoplasms: untreated control males, 1/24, females, 1/23; solvent control males, 0/22, females, 3/25; 1,3-propane sultone-treated males, 12/21, females, 17/24. No significant increase in these neoplasms was seen in either the C3H or the CBah strains of mice (Doak *et al*., 1976).

Groups of 48 male and 48 female CF1 mice were painted with either approximately 0.05–0.1 mL per mouse toluene or 1,3-propane sultone in toluene administered as a single application of 2.5% or 25% w/v or as 10 applications of a 2.5% w/v solution on alternate days. The experiment was terminated after 78 weeks. No skin tumour was found in the toluene controls of either sex, whereas in the 1,3-propane sultone-treated groups, the numbers of tumour-bearing mice were: single application of 2.5%, 0/48 males and 1/48 females; 10 applications of 2.5%, 3/48 males and 2/48 females; single application of 25%, 29/36 males and 26/46 females (Doak *et al*., 1976).

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

4.1 Absorption, distribution, metabolism and excretion

No data were available to the Working Group.

4.2 Toxic effects

No data were available to the Working Group.

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)

1,3-Propane sultone causes DNA damage and mutation in bacteria and induces mitotic recombination in yeast. It induces mutations and chromosomal aberrations in plant cells. In cultured mammalian cells, it induces chromosomal aberrations, sister chromatid exchanges and, according to single studies, cell transformation in C3H 10T½ cells, but not in Syrian hamster embryo cells. DNA strand breaks are induced in brain cells from rats injected with 1,3-propane sultone.

1,3-Propane sultone reacts with guanosine and DNA at pH 6–7.5 *in vitro*, with *N*7-alkylguanosine accounting for > 90% of the total reaction products. Minor products that have been identified are *N*1-alkylguanosine (approx. 1.6%) and O^6-alkylguanosine (approx. 0.5%) (Hemminki, 1983).

5. Summary of Data Reported and Evaluation

5.1 Exposure data

1,3-Propane sultone has been used as an intermediate in the production of a variety of chemical products.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

1,3-Propane sultone is carcinogenic in rats by all routes of administration (oral, dermal, intravenous, subcutaneous or prenatal), producing tumours at various sites

Table 1. Genetic and related effects of 1,3-propane sultone

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, Prophage, *umu* induction, SOS repair test, DNA strand breaks, cross-links or related damage	+	NT	16	Nakamura *et al*. (1987)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	2.5	Simmon (1979a)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	6	Bartsch *et al*. (1983)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	NT	2.5	Simmon (1979a)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	NT	6	Bartsch *et al*. (1983)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	NT	NG	Simmon (1979a)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	NT	NG	Simmon (1979a)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	NT	NG	Simmon (1979a)
SAS, *Salmonella typhimurium* TA1536, reverse mutation	–	NT	NG	Simmon (1979a)
SCH, *Saccharomyces cerevisiae*, homozygosis by mitotic recombination or gene conversion	+	+	1000	Simmon (1979b)
HSM, *Hordeum* species (barley), mutation	+	NT	611	Kaul & Tandon (1981)
HSM, *Hordeum* species (barley), mutation	+	NT	975	Singh & Kaul (1985)
HSC, *Hordeum* species (barley), chromosomal aberrations	(+)	NT	611	Kaul & Tandon (1981)
SIC, Sister chromatid exchange, Chinese hamster lung fibroblasts *in vitro*	+	NT	1.2	Abe & Sasaki (1977)
CIC, Chromosomal aberrations, Chinese hamster lung fibroblasts *in vitro*	+	NT	12	Abe & Sasaki (1977)
CIC, Chromosomal aberrations, Chinese hamster lung Don cells *in vitro*	+	NT	63	Ishidate (1988)
TCM, Cell transformation, C3H 10T½ CL8 mouse cells *in vitro*	(+)	NT	50	Oshiro *et al*. (1981)
TCS, Cell transformation, Syrian hamster embryo cells, clonal assay *in vitro*	–	NT	10	Pienta *et al*. (1977)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	+	NT	61	Kaul (1985)
CHL, Chromosomal aberrations, human lymphocytes *in vitro*	+	NT	122	Kaul (1985)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
TIH, Cell transformation, human newborn foreskin epithelial cells	+	NT	7.5	Milo *et al*. (1981)
HMM, Host-mediated assay, *Salmonella typhimurium* TA1530 and TA1538 in Swiss-Webster mice	+		12 im × 1	Simmon *et al*. (1979)
DVA, DNA strand breaks, male Sprague-Dawley rat brain cells *in vivo* (alkaline elution assay)	+		31 ip × 1	Robbiano & Brambilla (1987)

[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; im, intramuscular; ip, intraperitoneal

including the brain and mammary gland. In mice, it was carcinogenic after skin application and subcutaneous injection producing local tumours.

5.4 Other relevant data

1,3-Propane sultone is mutagenic in bacteria. It is positive for many genetic activity end-points *in vitro* in rodent and human cells. 1,3-Propane sultone induces DNA strand breaks *in vivo* in rat brain cells.

5.5 Evaluation

No epidemiological data relevant to the carcinogenicity of 1,3-propane sultone were available.

There is *sufficient evidence* in experimental animals for the carcinogenicity of 1,3-propane sultone.

Overall evaluation

1,3-Propane sultone is *possibly carcinogenic to humans (Group 2B).*

6. References

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