

SULPHUR DIOXIDE**ICSC: 0074**

**Date of Peer
Review: October
2006**


Sulfurous oxide
Sulfurous anhydride
Sulfur oxide

CAS # 7446-09-5 **SO₂**
RTECS # WS4550000 **Molecular mass: 64.1**
UN # 1079
EC Annex 016-011-00-9
1 Index #
EC/EINECS 231-195-2
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TYPES OF HAZARD / EXPOSURE	ACUTE HAZARDS / SYMPTOMS	PREVENTION	FIRST AID / FIRE FIGHTING
FIRE	Not combustible. Heating will cause rise in pressure with risk of bursting.		In case of fire in the surroundings: use appropriate extinguishing media.
EXPLOSION			In case of fire: cool cylinder by spraying with water but avoid contact of the substance with water. Combat fire from a sheltered position.

EXPOSURE		STRICT HYGIENE!	IN ALL CASES CONSULT A DOCTOR!
Inhalation	Cough. Shortness of breath. Sore throat. Laboured breathing.	Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Artificial respiration may be needed. Refer for medical attention.
Skin	ON CONTACT WITH LIQUID: FROSTBITE.	Cold-insulating gloves.	ON FROSTBITE: rinse with plenty of water, do NOT remove clothes. Refer for medical attention.
Eyes	Redness. Pain.	Safety goggles face shield or eye protection in combination with breathing protection.	First rinse with plenty of water (remove contact lenses if easily possible). Refer for medical attention.
Ingestion			

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Evacuate danger area! Personal protection: complete protective clothing including self-contained breathing apparatus. Consult an expert! Ventilation. NEVER direct water jet on liquid.	<p>Note: 5</p> <p>EU Classification Symbol: T R: 23-34 S: (1/2-)9-26-36/37/39-45</p> <p>UN Classification UN Hazard Class: 2.3 UN Subsidiary Risks: 8</p> <p>GHS Classification Warning Contains refrigerated gas; may cause cryogenic burns or injury Toxic if inhaled Causes eye irritation Causes damage to respiratory tract if inhaled Causes damage to respiratory tract through prolonged or repeated exposure if inhaled Harmful to aquatic life</p>
EMERGENCY RESPONSE	STORAGE
Transport Emergency Card: TEC (R)-20S1079 or 20G2TC NFPA Code: H 3; F 0; R 0	Ventilation along the floor. Dry.
<p>IPCS International Programme on Chemical Safety</p>  <p>Prepared in the context of cooperation between the International Programme on Chemical Safety and the Commission of the European Communities © IPCS, CEC 2005</p> <p>SEE IMPORTANT INFORMATION ON BACK</p>	

SULPHUR DIOXIDE

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IMPORTANT DATA	
<p>PHYSICAL STATE; APPEARANCE: COLOURLESS GAS OR COMPRESSED LIQUEFIED GAS , WITH PUNGENT ODOUR.</p> <p>PHYSICAL DANGERS: The gas is heavier than air.</p> <p>CHEMICAL DANGERS: The solution in water is a medium strong acid. Reacts violently with sodium hydride. Attacks plastic.</p> <p>OCCUPATIONAL EXPOSURE LIMITS: TLV: 2 ppm as TWA, 5 ppm as STEL; A4 (not classifiable as a human carcinogen); (ACGIH 2006). MAK: 0.5 ppm, 1.3 mg/m³; Peak limitation category: I(1); Pregnancy risk group: C; (DFG 2006).</p>	<p>ROUTES OF EXPOSURE: The substance can be absorbed into the body by inhalation.</p> <p>INHALATION RISK: A harmful concentration of this gas in the air will be reached very quickly on loss of containment.</p> <p>EFFECTS OF SHORT-TERM EXPOSURE: Rapid evaporation of the liquid may cause frostbite. The substance is irritating to the eyes and the respiratory tract. Inhalation may cause asthma-like reactions.</p> <p>EFFECTS OF LONG-TERM OR REPEATED EXPOSURE: Repeated or prolonged inhalation exposure may cause asthma.</p>
PHYSICAL PROPERTIES	
Boiling point: -10°C	

Melting point: -75.5°C Relative density (water = 1): 1.4 at -10°C (liquid) Solubility in water, ml/100 ml at 25°C: 8.5 Vapour pressure, kPa at 20°C: 330 Relative vapour density (air = 1): 2.25	
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ENVIRONMENTAL DATA

The substance is harmful to aquatic organisms.

NOTES

Depending on the degree of exposure, periodic medical examination is suggested. The symptoms of asthma often do not become manifest until a few hours have passed and they are aggravated by physical effort. Rest and medical observation are therefore essential. Anyone who has shown symptoms of asthma due to this substance should avoid all further contact. Do NOT spray water on leaking cylinder (to prevent corrosion of cylinder). Turn leaking cylinder with the leak up to prevent escape of gas in liquid state.

ADDITIONAL INFORMATION

LEGAL NOTICE	Neither the CEC nor the IPCS nor any person acting on behalf of the CEC or the IPCS is responsible for the use which might be made of this information
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SULFUR DIOXIDE

CHEMICAL NAMES	Sulfur dioxide; sulfurous acid anhydride
EMPIRICAL FORMULA	SO ₂
MOLECULAR WEIGHT	64.1
DEFINITION	Sulfur dioxide contains not less than 95% SO ₂
DESCRIPTION	A colourless, non-inflammable gas with a strong, pungent, suffocating odour. Soluble in water and ethanol.
USE	As an antimicrobial preservative and as an anti-browning agent.

SODIUM SULFITE

CHEMICAL NAME	Sodium sulfite
EMPIRICAL FORMULA	Anhydrous: Na ₂ SO ₃ Heptahydrate: Na ₂ SO ₃ .7H ₂ O
MOLECULAR WEIGHT	Anhydrous: 126.05 Heptahydrate: 252.16
DEFINITION	Anhydrous sodium sulfite contains not less than 95.0% Na ₂ SO ₃ . Sodium sulfite heptahydrate contains not less than 48.0% Na ₂ SO ₃ .
DESCRIPTION	Anhydrous sodium sulfite is a white powder, with not more than a faint odour of sulfur dioxide; 1 g is soluble in 4 ml of water. Sodium sulfite heptahydrate is a transparent white crystalline solid, with not more than a faint odour of sulfur dioxide; 1 g is soluble in 2 ml of water.
USE	As an antimicrobial preservative and as an anti-browning agent.

SODIUM METABISULFITE

CHEMICAL NAME	Sodium pyrosulfite
EMPIRICAL FORMULA	Na ₂ S ₂ O ₅
MOLECULAR WEIGHT	190.1
DEFINITION	Sodium pyrosulfite contains not less than 95.0% of Na ₂ S ₂ O ₅ .
DESCRIPTION	A white crystalline solid, with an odour of sulfur dioxide. 1 g is soluble in 2 ml of

water.

USE As an antimicrobial preservative and as an anti-browning agent.

SODIUM HYDROGEN SULFITE

CHEMICAL NAMES Sodium hydrogen sulfite; sodium bisulfite; sodium acid sulfite

EMPIRICAL FORMULA NaHSO_3

MOLECULAR WEIGHT 104.06

DEFINITION Sodium hydrogen sulfite contains not less than 95% of NaHSO_3 .

DESCRIPTION A white crystalline or granular solid, with an odour of sulfur dioxide. 1 g is soluble in 2.5 ml of water.

Biological Data

Biochemical aspects

Sulfite is oxidized in the body to sulfate. Bisulfite reacts with aldehydes and ketones, including aldehydic sugars. This is a reversible reaction; the equilibrium concentrations depend on temperature. The acute effects of sulfite in foods are related to the amount and concentration of free sulfur dioxide and to the speed at which the additive compounds liberate the bound sulfur dioxide. Sulfite may also react reversibly with disulfide linkages in proteins. The disulfide is split into one part containing a thiol group and another part with an S-sulfonic acid group.¹ Sulfite reacts with dried yeast to form a component with anti-thiamine activity.²

Acute toxicity

In rabbits, the oral LD_{50} of sulfite, measured as SO_2 , was found to be between 600 and 700 mg/kg body-weight.³

Animal Reference	Route	LD_{50} (mg/kg body-weight)		
		Sodium bisulfite	Sodium sulfite	
Mouse	Intravenous	130	175	4
Rat	Intravenous	115	-	4
Hamster	intravenous	95	-	4
Rabbit	Intravenous	65	-	4

In man, a single oral dose of 4 g of sodium sulfite caused toxic symptom in 6 of 7 persons. In another subject, 5.8 g caused severe irritation of the stomach and intestine.³

The vomiting reflex in man appeared regularly with doses of sulfite equivalent to less than 250 mg SO_2 , i.e. 3.5 mg SO_2 per kg

body-weight.⁵

Short-term studies

Rat. In thiamine-deficient rats, daily oral administration of fruit syrup containing 350 ppm of sulfur dioxide in a dose of 0.5 ml/150 g rat for 8 weeks failed to influence growth.⁶

Groups of weanling rats numbering 5 per group were fed 0.6% sodium metabisulfite (not less than 3400 ppm as SO₂) for 6 weeks. The diets were either freshly sulfited or stored at room temperature before use. A reduction in growth occurred in rats receiving the fresh diet which was attributed to lack of thiamine. Rats fed the diet which had been stored for 75 days developed signs of thiamine deficiency and additional toxic effects including diarrhoea and stunting of growth which could not be reversed by the administration of thiamine.²

(Work in progress) Three groups of 20 to 30 rats containing equal numbers of males and females received daily doses of sulfite dissolved in water or added to wine, and a control group received the same volume of water. The levels of sulfite in the 2 groups receiving wine were equivalent to 105 mg and 450 mg SO₂ per litre respectively and the aqueous solution contained potassium metabisulfite equivalent to 450 mg SO₂ per litre. The effect of this treatment was studied in 4 successive generations, the duration being 4 months in females and 6 months in males. Groups of animals from the second generation were treated for 1 year. No effect was observed on weight gain, efficiency of utilization of protein, biological value of the same protein or reproduction. There was also no effect on the macroscopic or microscopic appearance of organs or organ weights. The only effect observed was a slight diminution in the rate of tissue respiration by liver slices in vitro.⁷

(Work in progress) About 120 rats containing equal numbers of each sex were divided into 2 groups, one receiving potassium metabisulfite equivalent to 0.6% SO₂ in the drinking-water, the other group serving as controls. No effect was observed after treatment for 3 months on reproduction, mortality or blood count. The second and third generations were treated in the same way for 3 months, the only effect observed being a significant reduction in the size of the litters of treated mothers. No effect of sulfite on digestive enzymes in vitro was observed at a level equivalent to 360 mg SO₂ per gram of protein. No effect on the incidence of dental caries in the rat was produced by 0.5% potassium metabisulfite in the dietary regime. Work is in progress on the effects of sulfite on the metabolism of thiamine, vitamin A and calcium.⁸

Rabbit. One rabbit given 3 g of sodium sulfite by stomach tube each day for 185 days lost weight, but all organs were normal post mortem. Two rabbits given 1.08 g daily for 127 days gained weight. Autopsy showed haemorrhages in the stomach. Three rabbits given 1.8 g daily for between 46 and 171 days lost weight and autopsy showed stomach haemorrhages.³

Dog. A dose of 3 g of sodium sulfite daily was given by stomach tube to a dog weighing 17 kg for 23 days. Another weighing 34 kg was given 6-16 g of sodium sulfite daily for 20 days (total dose 235 g). No abnormalities were observed on autopsy in the first dog, but the second dog had haemorrhages in several organs. Sodium sulfite was given by stomach tube to 16 growing dogs in daily doses of 0.2-4.8 g for 43-419 days; no damage was observed in any of the dogs. Sodium

bisulfite was given to 2 dogs by the same method and for the same length of time as in the preceding experiment in daily doses of 1.08-2.51 g. Examination of heart, lungs, liver, kidney and intestine showed no damage. A total of 91-265 g of sodium sulfite fed to 5 pregnant dogs over a period of 60 days had no effect on the weight of the mothers or on the weight gain of the litters.³

Long-term studies

Rat. Groups of rats numbering from 18 to 24 per group were fed sodium bisulfite in dosages of 0.0125%, 0.025%, 0.05%, 0.1%, 0.25%, 0.5%, 1% or 2% of the diet for periods ranging from 1 to 2 years. The rats fed 0.05% sodium bisulfite (307 ppm as SO₂) for 2 years showed no toxic symptoms. Sulfite in concentrations of 0.1% (615 ppm as SO₂), or more, in the diet inhibited the growth of the rats, probably through destruction of thiamine in the diet.⁹

Three groups of weanling rats containing 18, 13 and 19 animals received drinking-water containing sodium metabisulfite at levels of 0 ppm SO₂, 350 ppm SO₂ and 750 ppm SO₂. Prior interaction of the sulfite with dietary constituents was thus prevented. The experiment lasted 2 years and extended over 3 generations of rats. No effects were observed on food consumption, fluid intake, faecal output, reproduction, lactation or the incidence of tumours.¹⁰

Comment on experimental studies reported

Sufficient data are not available to indicate the lowest dosage causing acute effects in man or the highest dosage that will normally be tolerated without producing harmful effects. The position of the lowest level at which sulfite produced a significant effect in the long-term feeding experiments in rats may have been determined by the destruction of thiamine and possibly other essential dietary components rather than by a direct action of sulfite on the animals. The absence of toxic effect on long-term ingestion of sulfite in the drinking-water (750 ppm as SO₂) is consistent with this. Although the toxicity of sulfite in the drinking-water was lower than that in the food, this was not considered sufficient evidence for alteration of the evaluation given previously in the Sixth Report of the Joint FAO/WHO Expert Committee on Food Additives.

Evaluation

Level causing no significant toxicological effect in the rat

0.05% of sodium bisulfite (= 307 ppm as SO₂) in the diet, equivalent to 15 mg/kg body-weight per day, calculated as SO₂.

0.1% of sodium metabisulfite (= 750 ppm as SO₂) in the drinking-water, equivalent to 37 mg/kg body-weight per day, calculated as SO₂.

Estimate of acceptable daily intakes for man (calculated as SO₂)

	<u>mg/kg body-weight</u>
Unconditional acceptance	0-0.35
Conditional acceptance	0.35-1.5

SULFUR DIOXIDE AND SOME SULFITES, BISULFITES AND METABISULFITES (Group 3)

For definition of Groups, see [Preamble Evaluation](#).

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Sulfur dioxide

CAS No.: 7446-09-5

Sodium sulfite

CAS No.: 7757-83-7

Sodium bisulfite

CAS No.: 7631-90-5

Sodium metabisulfite

CAS No.: 7681-57-4

Potassium metabisulfite

CAS No.: 16731-55-8

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Sulfur dioxide is produced commercially by burning sulfur or various sulfides or by recovering it from flue gases or non-ferrous metal smelting gases. Large quantities are used as intermediates in the manufacture of sulfuric acid and sulfite pulp. It is also used in agriculture and in the food and beverage industries as, among other things, a biocide and a preservative. Sulfite pulp workers have been exposed to fluctuating levels of sulfur dioxide, often exceeding 10 ppm (26 mg/m³), but levels have decreased with modernization of facilities and processes. In metal industries, the roasting of ores and the combustion of various sulfur-containing fuels have resulted in mean exposures to sulfur dioxide in the range of 1-10 ppm (2.6-26 mg/m³) in copper smelters, but at about 1 ppm (2.6 mg/m³) or less in other facilities. Mean levels exceeding 1 ppm (2.6 mg/m³) have also been reported in the manufacture of sulfuric acid and of superphosphate fertilizers, as well as at certain fire sites during fire fighting. Levels of sulfur dioxide in ambient air do not usually exceed 0.05 ppm (0.1 mg/m³), except in some urban areas.

Sodium sulfite is used mainly in the pulp industry. Both sodium and potassium metabisulfite are used in food processing, chemical industries, water treatment, photoprocessing and the textile industry. Levels of occupational exposure have not been reported.

5.2 Human carcinogenicity data

In four US and one Swedish cohort studies of copper smelters, increased lung cancer risks were observed in relation to exposure to arsenic, but no independent effect of sulfur dioxide was seen.

One proportionate mortality study from the USA and Canada, as well as two US and one Finnish cohort studies, analysed cancer risks among sulfite pulp mill workers. Three of them suggested an increase in risk for stomach cancer; however, potential confounding factors were not adequately controlled. Lung cancer risks were not elevated in any of these studies.

In case-control studies performed at a chemical facility in Texas with a complex exposure environment, increased risks for lung cancer and brain tumours were indicated in workers with high exposure to sulfur dioxide; however, the findings using two different control groups were not consistent.

A population-based case-control study from Canada suggested an increased risk for stomach cancer in men exposed to sulfur dioxide, but no excess was indicated for lung cancer.

No epidemiological study was available on cancer risks associated with exposure to sulfites, bisulfites or metabisulfites.

5.3 Carcinogenicity in experimental animals

Sulfur dioxide was tested for carcinogenicity in one study in mice by inhalation exposure. A significant increase in the incidence of lung tumours was observed in females.

Sulfur dioxide was tested for enhancement of carcinogenicity when administered with benzo[*a*]pyrene in two studies in rats and in one study in hamsters. One incompletely reported study found an increase in the incidence of lung tumours in rats exposed to sulfur dioxide in conjunction with benzo[*a*]pyrene. The other study in rats suffered from limitations owing to the high incidence of lung tumours in controls given benzo[*a*]pyrene. The study in hamsters was inadequately reported.

Potassium metabisulfite was tested for carcinogenicity in one study in mice by oral administration in the drinking-water and *sodium metabisulfite* in one study in rats by oral administration in the diet. No increase in tumour incidence was observed in mice, and there was no indication of a dose-related increase in tumour incidence in rats, but both studies had some inadequacies in reporting of data.

Potassium metabisulfite was tested for enhancement of carcinogenicity in one study in rats. It significantly increased the incidence of gastric adenocarcinoma after initiation with *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine.

No data were available on the carcinogenicity in experimental animals of sulfites or bisulfites.

5.4 Other relevant data

At high concentrations, sulfur dioxide irritates the upper airways and can induce acute and chronic bronchitis. At lower levels (less than 0.25 ppm [0.65 mg/m³]), no effect of sulfur dioxide is seen on the airways of sensitive individuals in the general population who take exercise, presumably since this relatively hygroscopic gas is removed by the nose and mouth.

Conflicting results for the induction of chromosomal aberrations in lymphocytes were obtained in two studies of workers exposed to sulfur dioxide, among other agents. In a single

study, no increase was reported in the frequency of sister chromatid exchange in lymphocytes of exposed workers.

Sulfur dioxide and its aqueous forms did not induce sister chromatid exchange, chromosomal aberrations or micronucleus formation in bone marrow of mice or Chinese hamsters. In a single study, sister chromatid exchange and chromosomal aberrations were induced in human lymphocytes. In cultured mammalian cells, bisulfite induced transformation and sister chromatid exchange but not gene mutation, chromosomal aberrations or DNA repair synthesis. In plants, chromosomal aberrations, micronuclei and gene mutation were induced. Sulfur dioxide and bisulfite induced gene mutation but not gene conversion in yeast. Mutations were induced in bacteria and phage.

Bisulfite solutions at high concentrations caused deamination of cytosine in DNA *in vitro*.

5.5 Evaluation

There is *inadequate evidence* for the carcinogenicity in humans of sulfur dioxide, sulfites, bisulfites and metabisulfites.

There is *limited evidence* for the carcinogenicity in experimental animals of sulfur dioxide.

There is *inadequate evidence* for the carcinogenicity in experimental animals of sulfites, bisulfites and metabisulfites.

Overall evaluation

Sulfur dioxide, sulfites, bisulfites and metabisulfites *are not classifiable as to their carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see [Preamble Evaluation](#).

Synonyms for Sulfur dioxide

- Sulfurous acid anhydride
- Sulfurous anhydride
- Sulfurous oxide
- Sulfur oxide [SO₂]
- Sulphur dioxide
- Sulfur superoxide

Synonyms for Sodium sulfite

- Anhydrous sodium sulfite
- Disodium sulfite
- Sodium sulphite
- Sulfurous acid, disodium salt

Synonyms for Sodium bisulfite

- Hydrogen sulfite sodium

- Monosodium sulfite
- Sodium acid sulfite
- Sodium bisulphite
- Sodium hydrogen sulfite
- Sodium sulfite [NaHSO₃]
- Sulfurous acid, monosodium salt

Synonyms for Sodium metabisulfite

- Disodium disulfite
- Disodium metabisulfite
- Disodium pyrosulfite
- Disulfurous acid, disodium salt
- Pyrosulfurous acid, disodium salt
- Sodium disulfite
- Sodium metabisulphite
- Sodium pyrosulfite

Synonyms for Potassium metabisulfite

- Dipotassium disulfite
- Dipotassium metabisulfite
- Dipotassium pyrosulfite
- Disulfurous acid, dipotassium salt
- Potassium disulfite
- Potassium metabisulfite
- Potassium pyrosulfite
- Pyrosulfurous acid, dipotassium salt