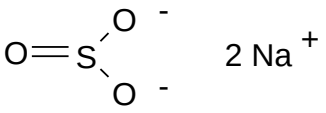
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7757-83-7
	Sodium sulfite
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue rationale

In case of missing or insufficient data on sodium sulfite, also data from other S(IV) compounds have been included, as there is a pH dependent equilibrium with the different forms of S(IV) being bisulfite, sulfite, metabisulfite and sulfur dioxide in the aqueous milieu of biological systems. Sodium metabisulfite (CAS No. 7681-57-4) has already been assessed in the OECD HPV Chemicals Programme.

Human Health

Sodium sulfite is rapidly absorbed from the gastro-intestinal tract. Sulfate is the main metabolite formed by the action of sulfite oxidase in many tissues. Tissue accumulation of sulfite-derived S is highest in stomach, skin and hair, intestine and kidney. Excretion is rapid, mainly in the urine.

With oral LD_{50} values ≥ 3,560 mg/kg bw in rats and 820 – 920 mg/kg bw in mice, the acute toxicity of sodium sulfite is moderate to low. There are no acute standard inhalation tests and no LC_{50} values available. Acute inhalation of sodium sulfite aerosols caused bronchoconstriction in guinea pigs (LOAE~~L~~C 0.204 mg/m^3). Acute dermal toxicity of sodium sulfite has not been investigated.

In studies according to OECD TG 404 and 405 sodium sulfite was not irritating to the skin or the eyes of experimental animals.

No dermal sensitization studies in animals are available. In humans some cases of sensitization from topical contact with sodium sulfite have been described. Only 1.4% of a population of 1762 eczema patients showed a positive reaction to sodium sulfite in patch tests. For S(IV) compounds, single cases of hypersensitivity have been reported for the respiratory tract and for the oral route. These reactions seem to be restricted to highly reactive persons, when considering the wide use of sodium sulfite as food preservative.

In dogs, exposed for 290 days to a well characterized aerosol of S(IV) particles, at a single concentration of 0.3 mg S(IV)/m^3 (corresponding to 1.2 mg/m^3 sodium sulfite), only minor changes were observed in pulmonary function parameters. Specific limited studies in the respiratory tract indicated 0.3 mg/m^3 to be a LOAEC for impairment of bacterial defense, for hyperplastic and inflammatory changes in the nasal cavity, and for histological changes in the larynx, trachea and alveolar region.

In a 90-day feeding study, a NOAEL for male rats of 2% in diet corresponding to 1670 mg/kg bw/day was found. The LOAEL was 4% in diet based on decreased body weight gain and increased relative weights of testis and brain. In female rats, the highest tested dose of 4% in diet was the NOAEL corresponding to 3070 mg/kg bw/day.

There is no chronic toxicity study available with sodium sulfite. Waiving is possible based on chronic studies with other sulfites, especially a detailed study on 2-year feeding of sodium metabisulfite ($Na_2S_2O_5$) to rats. An overall NOAEL of 0.5% in the diet was derived, which is equivalent to a dose of 144 mg/kg bw/day calculated as sodium sulfite. The LOAEL for local effects (forestomach and glandular stomach hyperplasia or inflammation) corresponded to 1.0% in diet being equivalent to a dose of 300 mg/kg bw/day calculated as sodium sulfite. The NOAEL for systemic effects corresponded to the highest dose of 2% in diet which would be equivalent to 625 mg/kg bw/day calculated as sodium sulfite.

In vitro, sodium sulfite gave no indication of mutagenic or clastogenic activity up to cytotoxic concentrations both in the absence and presence of metabolic activation systems when tested in Ames tests/*Salmonella typhimurium* reversion assays, in gene mutation tests with *Saccharomyces cerevisiae* and in mammalian V79 cells (without metabolic activation), in a DNA damage and repair assay with *Escherichia coli*, as well as in a chromosomal aberration test with CHL cells (without metabolic activation). There are no *in vivo* tests with application of pure sodium sulfite. Several genotoxicity studies *in vivo* with sulfites other than sodium sulfite were negative. The negative findings in whole animals are regarded as consistent with the high reactivity of sulfite e.g. with proteins and its rapid inactivation in mammals due to metabolism. However, in contrast to the consistent negative findings in earlier studies, recent investigations of a single working group demonstrated dose-dependent increases of micronuclei in bone marrow and DNA damage in tissues of mice after intraperitoneal injection of a mixture of Na_2SO_3 and $NaHSO_3$. No parallel investigations were performed with the pure compounds as controls.
In conclusion, from the available data, there are no indications of a genotoxic potential of sodium sulfite per se.

There are no carcinogenicity studies available with administration of sodium sulfite.

As there are no indications of a carcinogenic action of sodium metabisulfite, when applied in long term studies in the diet or drinking water in rats or mice, there is no principal concern about a carcinogenic potential of sodium sulfite.

There are no reproductive toxicity studies with sodium sulfite investigating effects on male or female fertility. In a 3-month feeding study with male rats no relevant effects of sodium sulfite were seen in the testes. In a three-generation study with sodium metabisulfite ($Na_2S_2O_5$), there was no suggestive evidence of reproductive toxicity or impairment of fertility in rats that received up to 2% in the diet. No effects on gonads were seen histologically. This NOAEL for reproductive toxicity would be equivalent to a dose of 625 mg/kg bw/day calculated as sodium sulfite, which is higher than the NOAEL for chronic toxicity of 0.5% in the diet (based on local irritation of the stomach), being equivalent to a dose of 144 mg/kg bw/day calculated as sodium sulfite.

No teratogenic effect of sodium sulfite was found in rats (feeding of sodium sulfite heptahydrate). Maternal toxicity was indicated by reduced body weight gain at 1650 mg/kg bw/day. The NOAEL for teratogenicity was 1650 mg /kg bw/day, the NOAEL for the maternal toxic dose was 1050 mg/kg bw/day (both as sodium sulfite).

Environment

Sodium sulfite is a white solid. The anhydrous substance is stable in dry air at ambient temperatures or at 100°C. In aqueous solutions, the substance is completely dissociated into sodium cations and the sulfite anion. Sodium sulfite is a salt of sulfurous acid (H_2SO_3). In aqueous solutions, sulfurous acid dissociates, the dissociation constants are pKa_1 of 1.8 and pKa_2 of 7.0 at 25°C. At neutral pH, a mixture of 50% sulfite (SO_3^{2-}) and 50% bisulfite (HSO_3^-) is present. At concentrations above 1M, bisulfite anions will dimerise with the elimination of water to form metabisulfite ($S_2O_5^{2-}$). At low concentrations, metabisulfite will hydrolyse to form bisulfite.

The water solubility of sodium sulfite was reported to be 313 g/L at 25°C and the relative density to be 2.633.
The octanol-water partitioning coefficient has limited relevance as the chemical is inorganic and dissociates in aqueous solution.

In surface waters, sulfite is oxidized to sulfate either catalytically by air oxygen or by microbial action. The half-life in deionized water was determined to be 77 hours. The presence of cations like iron, copper or manganese in the environment accelerates the oxidation rate significantly.

Experimental data on photodegradation of sodium sulfite are not available. Due to the molecular structure,

photodegradation can be excluded.

Because of its ionic structure, volatilization from the hydrosphere is unlikely. As well, sorption onto soil or sediment solids is not expected.

For the environmental hazard assessment, data from related sulfite salts are considered in addition. Numerous studies on the acute toxicity to fish, daphnids and algae are available. For the interpretation of the test results the instability of the test solutions has to be considered. Sulfite is rapidly oxidized to sulfate, the reaction is accompanied with consumption of dissolved oxygen. Therefore, the observed effects can be caused either by sulfite toxicity or by lack of oxygen. The available results indicate that algae represent the most sensitive trophic level, followed by daphnids and fish. The 96h-LC_{50} for *Leuciscus idus* was determined to be between 170 and 370 mg/L (nominal concentrations). In a short-term test on *Daphnia magna*, a 48h-EC_{50} of 118 mg/L (nominal concentrations) was obtained. Growth inhibition tests on 3 algal species (*Chlamydomonas reinhardtii*, *Chlorella vulgaris* and *Scenedesmus basiliensis*) exhibited identical effect values (96h-EC_{50} = 63 – 126 mg/L, nominal concentrations).

Long-term tests were conducted on daphnids and algae. The 21d-NOEC for *Daphnia magna* was determined to be >13 mg/L (nominal concentrations). At a concentration of 12.6 mg/L, inhibitory effects between 0 and 33% were observed at 18 different algal species. However, it has to be taken into account, that for sulfites reliable experimental toxicity results on 25 different algal species as the most sensitive taxonomic group are available. In addition, the compound is a normal metabolite present in living organisms and it is oxidized in aquatic compartments.

Exposure

Sodium sulfite is primarily produced by treating a suspension of sodium hydroxide or sodium carbonate with sulfur dioxide. Some sodium sulfite is obtained from scrubbing of SO_2-containing off-gases. In 1987, 95,200 tons sodium sulfite were produced and 454 tons were imported in the USA. For the year 2002, the demand was estimated to be 107,000 tons. The envisaged production amount in the Japanese lead company was estimated to be approximately 10,000 t/year.

The major amounts of sodium sulfite are used in chemical industry, leather processing industry, photographic industry, polymers industry, pulp & paper industry, in the personal/domestic sector, and many other applications.

Sodium sulfite is expected to be released into waste waters during production and use. There are no quantitative data about release amounts available. In the environment sulfite is formed from sulfur dioxide being released into the atmosphere by natural and anthropogenic sources. Sulfur dioxide may reach soils or surface waters by dry and wet deposition.

Occupational exposure to sodium sulfite is possible in a variety of industries as described above, mainly to sodium sulfite solutions. Sodium sulfite dusts were measured at a production site. The highest values up to 40 mg/m^3 were obtained for filling and cleaning operations. However, workers are recommended to wear protective gear such as a mask, rubber gloves and goggles.

Sulfite is present in the human body as a normal metabolite and intermediate of sulfur-containing amino acids, as a metabolite of sulfur dioxide inhaled via polluted air, and from ingestion of sulfiting agents used widely in foods and beverages. The daily intake varies widely depending on the diet. The US population has been estimated to consume an average of 10-15 mg/person of total sulfites. An acceptable daily intake (ADI) of 0.7 mg/kg body weight (total sulfites expressed as sulfur dioxide) was established by the Food and Agriculture Organisation of the United Nations and the World Health Organisation (FAO/WHO). Another source of exposure is from pharmaceutical preparations containing sodium sulfite as an antioxidant preservative and from its use as reducing agent in cosmetic formulations (up to 0.4%), mainly in hair dyes and colors (up to 3%).

RECOMMENDATIONS AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human health: The chemical is considered to be a candidate for further work. The chemical possesses properties indicating a hazard for human health (respiratory tract reactivity and dermal sensitization). Member countries are invited to perform an exposure assessment for consumers and workers, and, if then indicated, a risk assessment.

Environment: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for environment (acute toxicity to aquatic plants). However, the chemical has limited potential for bioaccumulation and rapidly degrades.