Sodium hydrogen sulphite

(CAS No: 7631-90-5)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

The present document contains the assessment of the health hazard of sodium hydrogen sulphite by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by AAE Wibowo, Ph.D. (Coronel Institute, Academic Medical Centre, Amsterdam, the Netherlands).

In April 1998, literature was searched in the on-line databases Medline, Embase, and Chemical Abstracts, starting from 1966, 1988, and 1970, respectively, using the following key words: sodium bisulfite, natrium bisulfite, sodium hydrogen sulfite, and 7631-90-5. HSELINE, CISDOC, MHIDAS, and NIOSHTIC (covering the period up to and including 1997) and POLTOX (from 1986-December 1994), databases available from CD-ROM, were consulted as well.

In February 2001, the President of the Health Council released a draft of the document for public review. Comments were received from the following individuals or organizations: L Whitford (Health and Safety Executive, London, England). These comments were taken into account when deciding on the final version of the document.

An additional search in Toxline and Medline in February 2005 did not result in information changing the committee's conclusions.

2 Identity

name	: sodium hydrogen sulphite
synonyms	: sodium bisulfite; sodium bisulphite; hydrogen sulfite sodium; sulfurous acid, monosodium salt; sodium acid sulfite; sodium sulhydrate
molecular formula	: $NaHSO_3$
CAS number	: 7631-90-5

3 Physical and chemical properties

molecular weight	: 104.1
boiling point	: decomposes
melting point	: decomposes
flash point	: -
vapour pressure	: -
solubility in water	: soluble (30 g/100 mL)
log $P_{octanol/water}$	: -7.51 (estimated)
conversion factors	: not applicable

Data from ACG02, NLM04, http://www.syrres.com/esc/est_kowdemo.htm.

Sodium hydrogen sulphite is a white, crystalline powder with a slight odour of sulphur dioxide (ACG02).

In aqueous solutions, there exist equilibria between $SO_2.H_2O$, HSO_3^-, and SO_3^{2-} that depend on the pH and the acidic dissociation constants, the latter being affected by the temperature and the ionic strength of the solution. At pH<ca. 2, the equilibrium shifts towards $SO_2.H_2O$, at ca. 2>pH<ca. 7 towards HSO_3^- (with an optimum at pH of ca. 4.5), and at pH>ca. 7 towards SO_3^{2-}. Under physiological conditions (pH 7.4 and 37°C), approximately equal concentrations of sulphite and hydrogen sulphite ions will be present (irrespective of the species which may have been initially introduced into solution). Further, at high concentrations (>1 M) hydrogen sulphite anions can dimerise into $S_2O_5^{2-}$ (disulphite anion), while disulphite anions will hydrolyse into hydrogen sulphite anions at low concentrations (Gun87, Nai03).

4 Uses

Sodium hydrogen sulphite has a wide variety of uses in the paper, tanning, chemical, and food industry; as a selective inhibitor of yeast and bacteria in winemaking; and as a source of sulphur dioxide. It has been used as a disinfectant, bleach, and antioxidant (ACG02). It is used in a wide variety of cosmetic products (hair dyes, colours, care products; skin care products) (Nai03).

5 Biotransformation and kinetics

The committee did not find quantitative data on the uptake during occupational exposure to sodium hydrogen sulphite. Since the compound exists as crystalline

powder and since it is very soluble in water, occupational exposure by inhalation or hand-oral mediated uptake may occur.

Considerable endogenous sulphite production occurs via normal decomposition of the sulphur-containing amino acids, cysteine and methionine, and other sulphur-containing compounds. Endogenous sulphite levels are maintained at low, steady-state concentrations by mitochondrial sulphite oxidase, a molybdenum-containing haemoprotein found in most body tissues, which catalyses the oxidation of sulphite into sulphate, which is excreted in the urine. Considerable variability of sulphite oxidase activity exists among species. Sulphite oxidase activity in human liver is slightly less than that in rhesus monkey and rabbit but only about 5-10% of that in rat liver . Activity in human lung was reported to be 135 times less that that in human liver. Non-enzymatic oxidation, catalysed by compounds such as superoxide anion, dimethyl sulphoxide, and trace metals, can occur as well. Sulphite can also be metabolised through non-oxidative pathways by non-enzymatic reactions with disulphide bonds in low molecular weight compounds, such as cystine and oxidised glutathione, or macromolecules, such as proteins, to *S*-sulphonate ('sulphitolysis'), or by enzymatic reactions with 3-mercaptopyruvate to thiosulphate. *S*-sulphonate and thiosulphate were detected only at very small amounts in 'normal' humans and rats, suggesting that these are insignificant metabolism routes. However, large amounts were excreted by those deficient in sulphite oxidase. Exogenous sulphite entering the body via inhalation, ingestion, or injection is metabolised by sulphite oxidase into sulphate as well. Inhalation studies in dogs (SO_2), oral studies in rats (hydrogen sulphite), and intravenous studies in rats, rabbits, and monkeys showed that sulphite is rapidly cleared from the plasma and excreted as sulphate in the urine; 10% or less of the amount administered were excreted unchanged (FAO87, Gun87, Nai03).

Togawa et al. studied qualitatively the metabolic pathways of intravenously injected sodium hydrogen sulphite in rabbits. Most of the administered sulphite was oxidised into sulphate, but small amounts of thiosulphate, *S*-sulphoalbumin, *S*-sulphoglutathione, and *S*-sulphocysteine were found as well. When *S*-sulphocysteine was injected intraveneously, it was partially transformed into inorganic sulphate and thiosulphate. These metabolites showed the presence of the many and complicated metabolic pathways of sulphite *in vivo* (Tog90). A metabolism scheme is presented in Annex I.

6 Effects and mechanism of action

Human data

Citing unpublished information from medical records presented to the TLV Committee, the American Conference of Governmental Industrial Hygienists (ACGIH) stated that acute exposure to sodium hydrogen sulphite induced mild eye and respiratory responses (no more data given) (ACG02).

There were reports relating exposure to sodium hydrogen sulphite-containing food or pharmaceutical products to systemic immunological reactions. Cases of generalised urticaria have been reported (Pre76, Jim96). Jiminéz-Aranda et al. studied 36 patients (29 females and 7 males; age: 4-62 years) with clinical diagnostic of chronic urticaria. They performed oral challenge tests, skin prick tests, complete blood counts, coprology, immunological tests, and X-ray of the paranasal sinuses. They found that 33.3% (12/36) of the patients had positive reaction to sodium hydrogen sulphite (Jim96). Cases of bronchial asthma induced by sodium hydrogen sulphite have also been reported (Val93, Pel96, Hon89). Hong et al. studied 36 subjects with bronchial asthma. In 5 of these subjects, oral challenge with sodium hydrogen sulphite induced a bronchoconstructive response, which was defined as declines in values of FEV_1 (forced expiratory volume in 1 sec) or MMEF (maximum mixed-expiratory flow) of 20 and 25%, respectively, or greater (Hon89). Vena et al. reported a few cases of contact skin allergy caused by sodium hydrogen sulphite. They studied 2894 patients suffering from eczema with a patch test. Fifty of them showed positive reactions to both sodium hydrogen sulphite and dipotassium disulphite. In 7 cases, dermatitis had an occupational origin (Ven94).

Isolatedly, effects on the central nervous system were also reported. Meisel and Welford and Gregory et al. reported cases of seizures following intravenous administration of high doses of morphine containing sodium hydrogen sulphite as a preservative (Gre92, Mei92).

Animal data

Irritation and sensitisation

Semi-occlusive application of 0.5 g of sodium hydrogen sulphite to the flank of rabbits (n=3) caused very slight erythema, but no oedema (primary irritation

index: 1.0; maximum score possible: 8.0) (ECE95). A 38% solution was not found to be corrosive at observations 24 and 48 hours after application to the clipped back skin of rabbits (n=6) under occlusion for 4 hours (McA73).

The committee did not find data from experimental animal studies on the potential eye irritation of sodium hydrogen sulphite. *In vitro*, Green et al. reported that application of sodium hydrogen sulphite at a concentration of 0.1% during 5 minutes to the corneal endothelium isolated from New Zealand White rabbits induced rapid swelling at the rate of about 85 μm/hour (Gre95).

Acute toxicity

The committee did not find data from acute inhalation studies on sodium hydrogen sulphite.

ACGIH reported an oral LD_{50} of about 2000 mg/kg bw in rats (ACG02). Intravenous LD_{50} values of 115, 130, 65, and 95 mg/kg bw were reported for rats, mice, rabbits, and hamsters, respectively (Hop51). Intraperitoneal LD_{50} values were 244, 300, 475, 487, 675, and 779 mg/kg bw in dogs, rabbits, rats, hamsters, mice, and guinea pigs, respectively (NIO04).

Repeated-dose toxicity

The committee did not find data from repeated inhalation studies on sodium hydrogen sulphite.

Fitzhugh et al. investigated the effects of repeated oral exposure to sodium hydrogen sulphite in 3 experiments, all using a balanced incomplete block design method. In the first experiment, Osborne-Mendel rats (n=9/sex/group) were given nominal sodium hydrogen sulphite concentrations of 5000, 10,000, and 20,000 ppm in 3 different diets - a ‘normal’ diet, a diet supplemented with thiamine, and a diet with a reduced thiamine content - for 1 year. A 10th group receiving an untreated diet was included as a control group. In the second experiment, animals (n=9/sex/group) were given nominal hydrogen sulphite concentrations of 0, 1000, 2500, 10,000, and 20,000 in diets prepared to last 5-6 weeks and refrigerated, 0, 10,000, and 20,000 ppm in freshly prepared diets, and 10,000 and 20,000 sulphate, for 1.5 years. In the 3rd experiment, animals (n=12/sex/group) received dietary hydrogen sulphite concentrations of 0, 125, 250, and 500 ppm and sodium sulphide concentrations of 2500 and 10,000 ppm, for 2 years. At concentrations of 1000 ppm or more, decreased body weights and body weight gains were observed. Decreased average survival times were seen at concentrations of 2500 ppm or more. The lowest concentration producing

histological lesions was 1000 ppm. For doses of 2500 ppm or more, macroscopic and microscopic lesions included stunting of growth, clinical polyneuritis, 'spectacle' eyes, bleached incisor teeth, brown uteri, atrophy of various viscera, calcified renal tubular casts, atrophy of bone marrow or bone, focal myocardial necrosis and fibrosis, and gastric squamous epithelial hyperplasia. According to Fitzhugh et al., the greater amount of these effects induced by sodium hydrogen sulphite might have been due to the destruction of vitamins (Fit46). The skulls and teeth of 43 rats of the study described above were utilised to study vitamin deficiencies. At sodium hydrogen sulphite doses up to 250 ppm, slight deficiency of pigmentation of the incisor and slight atrophy of the enamel organ were seen. At higher doses of 5000 ppm and more, there were more and more pronounced effects among which that were indicative of vitamin A and vitamin E deficiency (Irv52).

From the Fitzhugh study, a NOAEL and a LOAEL of ca. 20 and 45 mg/kg bw/day, respectively, could be calculated* (being equivalent to 12 and 45 SO_2 mg/kg bw/day). However, the committee is of the opinion that this study cannot be used to draw conclusions on dose-response relationship for systemic effects following oral exposure to (hydrogen) sulphite. First, sulphite was sometimes considerably lost from the treated food due to chemical reactions which compromises the estimates of hydrogen sulphite intake dose levels. Further, Fitzhugh et al. might have failed to separate effects induced by (hydrogen) sulphite from effects of (hydrogen) sulphite on the composition of the diet such as thiamine but probably also other factors. Til and Feron showed that sulphite in semi-purified diets may react with unsaturated fatty acids fast leading to formation of polymers of unsaturated fatty acids and/or other toxic substances that may induce untoward effects (Til92). Finally, none of the studies performed later in the 1960s and 1970s with several sulphite species have corroborated the findings by Fitzhugh et al. Generally, a well-controlled study in which 3 generation of rats were given nominal dietary concentrations of disodium disulphite of 125-20,000 ppm (actual levels: 98-19,200 ppm) for 2 years (Til72) was considered the key study in assessing the effects of sulphite exposure (FAO87, Gun87, Til92). In this study, there was no clear evidence of systemic toxicity at levels of 10,000 or 20,000 ppm. Based on the occurrence of occult blood in he faeces and hyperplastic changes of the gastric epithelium, which are considered to be local effects, at the next higher dose, the nominal concentration of 250 ppm (actual level: 215 ppm), being equivalent to 72 mg

* Taken male body weights of 600 and 300 mg, respectively, female body weights of 330 and 230 mg, respectively, male feed consumption of 20 and 15 mg/day, respectively, and female feed consumption of 15 and 10 mg/day.

SO_2/kg bw/day was the NOAEL (Til72). In a later study in which rats were given oral (drinking water) doses of disodium disulphite for 5-8 weeks, Hui et al. established a NOAEL of 70 mg SO_2/kg bw/day (Hui89).

In vivo experiments in rats (Her90) and rabbits (Wan84) using routes irrelevant for occupational risk assessment (injection into the cerebrospinal fluid) and *in vitro* experiments using human neuroblastoma cells (Ser87) or isolated frog neuromuscular junction (Ste82) suggested that sodium hydrogen sulphite might affect the nervous system.

The committee did not find data from carcinogenicity studies on sodium hydrogen sulphite. However, no evidence of carcinogenic effects was found in the Fitzhugh study with sodium hydrogen sulphite or in studies performed with several other sulphite-generating substances (see Gin87, Nai03, Til92, IARC92).

Mutagenicity and genotoxicity

Hydrogen sulphite is involved in reactions that may cause irreversible genetic damage. *In vitro*, hydrogen sulphite specifically deaminates the nucleoside cytosine to uracil which would result in a cytosine-to-thymidine transition mutation. This reaction occurs predominantly in single-stranded DNA, and the rate of deamination is optimal at concentrations of 1 M and at a pH between 5 and 6, i.e., at non-physiological conditions. The deamination rate falls off as pH increases to about 1% of the maximum at physiological pH. At lower concentrations, hydrogen sulphite can catalyse transamination leading to protein-nucleic acid cross-linking or damage DNA by generating free radicals (Sha83).

Mutagenic and genotoxicity studies with hydrogen sulphite were reviewed and summarised by the International Agency for Research on Cancer (IARC) (IARC92) and Nair and Elmore (Nai03).

- *In vitro* tests:
  - Gene mutation tests. Under acidic conditions and at concentrations lower than required for deamination of cytosine, sodium hydrogen sulphite caused mutations in *S. typhimurium* strains that contain the *his*G46 (base-pair substitution-sensitive) and *his*D6610 (frameshift-sensitive) mutations while results were negative in strains carrying *his*C3076 or *his*D3052 mutations. Under acid conditions and at very high concentrations, it induced clear plaque mutations in phage lambda but was negative in phage T4. Under similar conditions, sodium hydrogen sulphite was found

positive in *E. coli* strains at loci containing cytosine-guanine bases. However, negative results were obtained in the *lacI* gene of repair-competent *E. coli*. At neutral pH and low concentrations, sodium hydrogen sulphite did not induce mutations in *S. typhimurium* strains ((TA98, TA100, TA1530, TA1535, TA1537, TA1538, G46) and *E. coli* strains (WP2 and WP2-derived).

Sodium hydrogen sulphite did not induce mutations at two loci (*hprt* and Na^+/K^+ ATPase) in Chinese hamster V79 or Syrian hamster embryo cells. Negative results were obtained in *S. typhimurium* strains TA1530 and G46 in a host-mediated assay in which groups of 10 mice were given single or repeated (for 5 days) oral (gavage) doses of 1.5, 15, or 150 mg/kg bw/day.

- Cytogenicity assays. Sodium hydrogen sulphite caused increases in the frequency of sister chromatid exchanges (SCE), chromosomal aberrations, and micronuclei in human lymphocytes and of SCEs in Chinese hamster ovary and Syrian hamster embryo cells. No increased incidences in chromosomal aberrations were found in human tissue cells and in Syrian hamster cells.
- Other genotoxicity assays. Sodium hydrogen sulphite failed to induce detectable levels of repair replication of DNA strand breaks, but decreased the number of functioning replicons in Syrian hamster embryo cells. Sodium hydrogen sulphite caused an increase in recombinant frequency in *S. cerevisiae* strain D3, but not in a host-mediated assay in which groups of 10 mice were given single or repeated (for 5 days) oral (gavage) doses of 1.5, 15, or 150 mg/kg bw/day.

- *In vivo* tests:

  Sodium hydrogen sulphite did not induce dominant-lethal mutations when male random bred rats (n=10/group) were given one single or 5 daily oral (gavage) doses of 1.5, 15, or 150 mg/kg bw and then mated with non-treated virgin females. Likewise, negative results were obtained in a dominant-lethal assay in rats and a dominant-lethal and heritable translocation assay in mice. In the former study, male Sprague-Dawley rats were fed daily doses of 4.5, 15, or 45 mg/kg bw for 10 weeks and then mated for 7 days with 2 groups of non-treated females. In the latter study, male $(101xC3H)F_1$ mice were given 38 intraperitoneal doses of 300 mg/kg bw or 20 injections of 400 mg/kg bw. In the translocation study, they were mated with two sets of two females. In the dominant-lethal study, males were mated with females at various intervals up to 14.5 days after the last injection. In addition, females were treated with a single intraperitoneal dose of 550 mg/kg bw and mated with untreated males within 4.5 days after the injection.

No increase in the incidence of chromosomal aberrations was found in bone marrow obtained from male albino rats given single or repeated (for 5 days) oral (gavage) doses of 1.5, 15, or 150 mg/kg bw.
Dose-dependent, statistically significant increase in the frequency of micronucleated polychromatic erythrocytes obtained from bone marrow from male and female Kunming mice (n=10/sex/group) 24 hours after the last of 2 intraperitoneal injections of doses of a 3:1 mixture of sodium sulphite and sodium hydrogen sulphite of 20, 100, 500, or 750 mg/kg bw. Given two injections of 500 mg/kg bw, a maximum increase (ca. 4.3-4.8 times that of saline-controls; $p<0.01$) was reached when animals were killed 24 hours after the final injection. At 72 hours, incidences in treated animals were similar to those of controls (Men02).

- Other tests:
  Sodium hydrogen sulphite induced dose-dependent increases in the frequency of morphological transformations in Syrian hamster embryo cells in two separate studies, while negative results were reported in a third study using Syrian hamster embryo and C3H/10T-1/2 mouse cells.

Reproduction toxicity

Single intraperitoneal injections of doses of sodium hydrogen sulphite of 500-1000 mg/kg bw or repeated injections of 200 and 400 mg/kg bw, 20, 30, or 40 times during 28, 42, and 56, respectively, did not induce effects on the population of various types of spermatogonia of mice (Bha80).

Burnett et al. investigated the reproduction toxicity of various hair dyes. Sodium hydrogen sulphite was one of the compounds in 2 of the formulations tested. The formulations were applied topically to groups of 20 Charles River CD female rats at doses of 2 mL/kg bw on gestational days 1, 4, 7, 10, 13, 16, and 19. Three untreated control groups and one positive (acetylsalicilic acid) control group were taken along in the experiment. There were no significant soft tissue or skeletal changes. Similarly, the mean numbers of corpora lutea, implantation sites, live fetuses, and resorptions per pregnancy, as well as numbers of litters with resorptions, were not significantly affected by the dye treatment (Bur76).

Sodium hydrogen sulphite did not induce effects on nidation, on maternal or fetal survival or body weights, or significant increases in fetal abnormalities in either soft or skeletal tissues in groups of pregnant rabbits (Dutch-belted; n=10-14/group) given daily oral (gavage) doses of 1-100 mg/kg bw during gestational days 6 through 18 and sacrificed on day 29 (Foo74). In experiments

performed by the same laboratory, similar negative results were obtained in pregnant rats (Wistar; n=21-24/group), mice (CD-1; n=18-21/group), and golden hamsters (n=21-22/group) given oral doses of 1-110 mg/kg bw from gestational days 6-15 (Caesareans: day 20), 2-150 mg/kg bw from days 6-15 (Caesareans: day: 17), and 1-120 mg/kg bw/day from days 6-10 (Caesareans: day 14), respectively (Foo72).

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for sodium hydrogen sulphite in the Netherlands is 5 mg/m^3, 8-hour TWA.

Existing occupational exposure limits for sodium hydrogen sulphite in other European countries and the USA are summarised in Annex II.

8 Assessment of health hazard

In aqueous solutions, there exist equilibria between several sulphite species ($SO_2.H_2O$, HSO_3^-, and SO_3^{2-}) particularly depending on pH. Under physiological conditions, approximately equal concentrations of sulphite (SO_3^{2-}) and hydrogen sulphite (HSO_3^-) will be present, irrespective of the species which may have been initially introduced into solution.

The committee did not find data on the biotransformation and kinetics following exposure to sodium hydrogen sulphite. Endogenous sulphite is produced via normal decomposition of the sulphur-containing amino acids and other sulphur-containing compounds and its levels are maintained at low, steady-state concentrations by mitochondrial sulphite oxidase, which catalyses the oxidation of sulphite into sulphate, which is excreted in the urine. There is considerable variability of sulphite oxidase activity among species. Sulphite oxidase activity in human liver is slightly less than that in rhesus monkey and rabbit but only about 5-10% of that in rat liver. This suggests that the rat might be a poor experimental toxicological model. Activity in human lung was reported to be 135 times less that that in human liver. Metabolism can proceed through other non-enzymatic oxidative and non-oxidative pathways, resulting in substances such as *S*-sulphonate and thiosulphate, but these routes are probably insignificant relevance in ‘normal’ (i.e., not sulphate oxidase-deficient) humans. In intravenously treated rabbits, besides sulphate, small urinary amounts of thiosulphate, *S*-sulphoalbumin, *S*-sulphoglutathione, and *S*-sulphocysteine were found.

Due to its physical and chemical properties, the committee expects irritation of the eyes and upper respiratory tract to be one of the critical effects of sodium hydrogen sulphite after exposure by inhalation, but did not find convincing substantiating data. Cases of generalised urticaria, bronchial asthma, and contact allergic dermatitis have been reported. Subjects with these disorders should be considered as groups at extra risk.

Sodium hydrogen sulphite caused only very slight erythema when applied semi-occlusively to the skin of rabbits. The committee did not find data on the potential eye irritation. Acute lethal toxicity data include an oral LD_{50} of 2000 mg/kg bw in rats, intravenous LD_{50} values ranging from 65 mg/kg bw in rabbits to 130 mg/kg bw in mice, and intraperitoneal LD_{50} values ranging from 244 mg/kg bw in dogs to 779 mg/kg bw in guinea pigs. The committee did not find data from adequate repeated dose studies with sodium hydrogen sulphite. Long-term oral studies with other sulphite-generating substances showed that local effects – occult blood in the faeces; hyperplastic changes of the gastric epithelium – were the critical effects, 72 mg SO_2/kg bw/day being a NOAEL in rats. In these studies, there was no evidence of a carcinogenic potency.

Under specific conditions, sodium hydrogen sulphite was mutagenic in bacterial systems. It was negative in mammalian cell systems and in a host-mediated assay using mice and *S. typhimurium* strains. It caused increases in the frequency of sister chromatid exchanges, chromosomal aberrations, and micronuclei in mammalian cell systems in some of the tests performed. Sodium hydrogen sulphite caused an increase in recombinant frequency in yeast, but not in a host-mediated assay. *In vivo*, negative results were obtained in dominant-lethal in rats and mice and a heritable translocation assay in mice following oral and intraperitoneal administration. It was positive in a bone marrow micronucleus test in intraperitoneally treated mice. In view of the high capacity of rodents to convert sulphite into sulphate, the committee is of the opinion that this positive result is difficult to explain and that these findings should be verifed.

Oral (gavage) administration of doses of 100-120 mg/kg bw during organogenesis did not induce maternal or reproduction toxicity in rats, mice, rabbits, or hamsters.

The committee considers the toxicological database on sodium hydrogen sulphite too poor to justify recommendation of a health-based occupational exposure limit.

The committee concludes that there is insufficient information to comment on the level of the present MAC value.

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Annex I

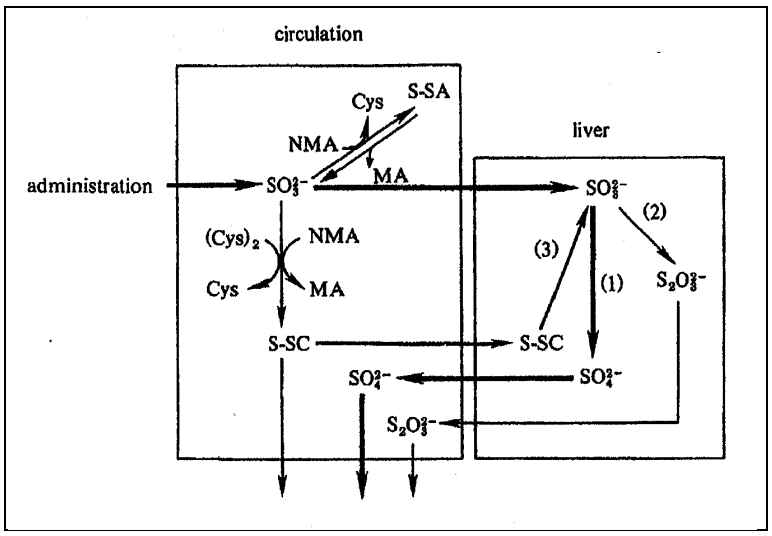

Figure 1 Proposed metabolism scheme for sulphur-containing compounds *in vivo* (Tog90). The conversions designated as (1), (2), and (3) are mediated by sulphite oxydase, 3-mercaptopyruvase sulphur-transferase, and thioltransferase, respectively.

Abbreviations:
- S-SC: *S*-sulphocysteine
- S-SA: *S*-sulphoalbumine
- MA: mercaptalbumine
- NMA: non- mercaptalbumine

Annex II

Occupational exposure limits for sodium hydrogen sulphite in various countries.

country - organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	reference[b]
	ppm	mg/m^3				
the Netherlands						
- Ministry of Social Affairs and Employment	-	5	8 h	administrative	-	SZW05
Germany						
- AGS	-	-				TRG04
- DFG MAK-Kommission	-	-				DFG05
Great-Britain						
- HSE	-	5	8 h	OES	-	HSE02
Sweden	-	-				Swe00
Denmark	-	5	8 h			Arb02
USA						
- ACGIH	-	5	8 h	TLV	A4[c]	ACG05
- OSHA	-	-				ACG04
- NIOSH	-	5	10 h	REL	-	ACG04
European Union						
- SCOEL	-	-				EC05

[a] S = skin notation; which means that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

[b] Reference to the most recent official publication of occupational exposure limits.

[c] Classified in carcinogenicity category A4, i.e., not classifiable as a human carcinogen: agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of a lack of data. *In vitro* or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories.