Sodium Thiosulfate

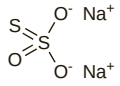
Disodium Thiosulfate Pentahydrate; Hiposulfito sódico; Natrii thiosulfas; Natrii Thiosulfas Pentahydricus; Natrio tiosulfatas; Natrium Thiosulfuricum; Natriumtiosulfaatti; Natriumtiosulfat; Nátrium-tioszulfát; Sodium Hyposulphite; Sodium, thiosulfate de; Sodium Thiosulphate; Sodu tiosiarczan; Sodyum Tiyosülfat; Thiosíran sodný pentahydrát; Tiosulfato sódico.

$Na_2S_2O_3,5H_2O$ = 248.2.

CAS — 7772-98-7 (anhydrous sodium thiosulfate); 10102-17-7 (sodium thiosulfate pentahydrate).

ATC — V03AB06.

ATC Vet — QV03AB06.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Sodium Thiosulphate). Colourless transparent crystals; efflorescent in dry air. It dissolves in its own water of crystallisation at about 49°. Very soluble in water; practically insoluble in alcohol. A 10% solution in water has a pH of 6.0 to 8.4. Store in airtight containers.

USP 31 (Sodium Thiosulfate). Large, colourless crystals, or a coarse, crystalline powder. Is deliquescent in moist air and effloresces in dry air at temperatures exceeding 33°. Soluble 1 in 0.5 of water; insoluble in alcohol. Its solutions are neutral or faintly alkaline to litmus. Store in airtight containers.

Incompatibility. Sodium thiosulfate may reduce the activity of some preservatives, including bronopol (p.1633), phenylmercuric salts (see Phenylmercuric Nitrate, p.1657), and thiomersal (p.1664).

Stability. Solutions of sodium thiosulfate 50% stored in air developed cloudiness or a deposit after autoclaving.[1] Addition of sodium phosphate 0.5% or 1.2% improved stability but solutions became cloudy or developed a deposit after 12 and 6 weeks respectively at 25°. Solutions containing sodium bicarbonate 0.5% became cloudy or developed a deposit after 12 weeks at 25°. No significant improvement in stability was obtained when the concentration of sodium thiosulfate was reduced to 30% or 15%, or when the injection was sealed under nitrogen.

1. Anonymous. Sodium thiosulphate injection–effect of additives on stability. *PSGB Lab Rep* P/75/3 1975.

Adverse Effects

Apart from osmotic disturbances sodium thiosulfate is relatively non-toxic. Large oral doses have a cathartic action.

Pharmacokinetics

Sodium thiosulfate is poorly absorbed from the gastrointestinal tract. After intravenous injection it is distributed throughout the extracellular fluid and rapidly excreted in the urine.

◊ An intravenous infusion of sodium thiosulfate 12 g/m^2 was given over 6 hours to 8 patients receiving intraperitoneal antineoplastic therapy.[1] The thiosulfate was rapidly eliminated, 95% being excreted within 4 hours of stopping the infusion; on average only 28.5% of the dose was recovered unchanged in the urine. The mean plasma elimination half-life was 80 minutes.

1. Shea M, *et al*. Kinetics of sodium thiosulfate, a cisplatin neutralizer. *Clin Pharmacol Ther* 1984; **35:** 419–25.

Uses and Administration

Sodium thiosulfate is used in the treatment of cyanide poisoning (p.2045). Sodium thiosulfate may be effective alone in less severe cases of cyanide poisoning, but it is often used with sodium nitrite (p.1464).

Sodium thiosulfate acts as a sulfur-donating substrate for the enzyme rhodanese, which catalyses the conversion of cyanide to relatively non-toxic thiocyanate, and thus accelerates the detoxification of cyanide.

The usual dosage regimen in adults is 300 mg of *sodium nitrite* (10 mL of a 3% solution) given intravenously over 5 to 20 minutes followed by 12.5 g of *sodium thiosulfate* (50 mL of a 25% solution or 25 mL of a 50% solution) given intravenously over a period of about 10 minutes. A suggested dosage regimen in children is about 4 to 10 mg/kg of *sodium nitrite*, given as a 3% solution (0.13 to 0.33 mL/kg) to a maximum of 300 mg (10 mL), followed by about 400 mg/kg of *sodium thiosulfate*, as a 25 or 50% solution (1.65 mL/kg of a 25% solution) to a maximum of 12.5 g (50 mL of a 25% solution). The methaemoglobin concentration should not be allowed to exceed 30 to 40%. If symptoms of cyanide toxicity recur, the injections of nitrite and thiosulfate may be repeated after 30 minutes at half the initial doses.

Sodium thiosulfate is used as an isotonic 4% solution in the management of extravasation of chlormethine and has been tried in the management of extravasation of some other antineoplastics (but see below).

Sodium thiosulfate has been used for its antifungal properties. Sodium thiosulfate and magnesium thiosulfate are included in mixed preparations for a variety of disorders.

Antineoplastic toxicity. Sodium thiosulfate may be used in the management of extravasation of chlormethine and some other antineoplastics (although this is a contentious area, see p.640). It is also used to inactivate some antineoplastics before disposal.

Sodium thiosulfate, given by intravenous infusion, has also been investigated for reducing the systemic toxicity of some antineoplastics. It has been reported to reduce the incidence of nephrotoxicity associated with intraperitoneal cisplatin (see Prophylaxis under Effects on the Kidneys, p.699) and to reduce hearing loss associated with carboplatin (see Effects on the Ears, p.693).

Bromate poisoning. Sodium thiosulfate has been used in the treatment of bromate poisoning[1,2] although its clinical efficacy is unclear;[3] it is thought to act by reducing bromate to the less toxic bromide ion, but evidence is lacking.[3,4] Although it has been given orally, this is no longer recommended since toxic sulfide may be formed.[4] However, intravenous sodium thiosulfate may have a role in some clinical circumstances.[4,5]

1. Lue JN, *et al.* Bromate poisoning from ingestion of professional hair-care neutralizer. *Clin Pharm* 1988; **7:** 66–70.
2. Lichtenberg R, *et al.* Bromate poisoning. *J Pediatr* 1989; **114:** 891–4.
3. McElwee NE, Kearney TE. Sodium thiosulfate unproven as bromate antidote. *Clin Pharm* 1988; **7:** 570, 572.
4. De Vriese A, *et al.* Severe acute renal failure due to bromate intoxication: report of a case and discussion of management guidelines based on a review of the literature. *Nephrol Dial Transplant* 1997; **12:** 204–9.
5. Johnson CE. Sodium thiosulfate unproven as bromate antidote. *Clin Pharm* 1988; **7:** 572.

Preparations

BP 2008: Sodium Thiosulphate Injection;
USP 31: Sodium Thiosulfate Injection.

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Azufracid; ***Austria:*** Schwefelbad Dr Klopfer; ***Braz.:*** Dessensibilizante Chauvin†; ***Canad.:*** Adasept; ***Cz.:*** Carbotox; ***Fr.:*** Desintex; Desintex Infantile; Desintex-Choline; Rhino-Sulfuryl; Vagostabyl; ***Ger.:*** Corti Jaikal†; Jaikal†; Schwefelbad Dr Klopfer; Sulfuretten†; ***Hung.:*** Schwefelbad Dr Klopfer; ***Ital.:*** Antimicotica Solforata; ***S.Afr.:*** Tripac-Cyano; ***USA:*** Cyanide Antidote Package; Tinver; Versiclear.

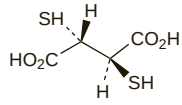
Succimer *(BAN, USAN, rINN)*

DIM-SA; DMSA; Succimère; Succímero; Succimero; Succimerum; Suksimeeri. *meso*-2,3-Dimercaptosuccinic acid; (*R**,*S**)-2,3-Dimercapto-butanedioic acid.

Сукцимер

$C_4H_6O_4S_2$ = 182.2.

CAS — 304-55-2.



Pharmacopoeias. In *Chin.*

Adverse Effects and Precautions

Succimer may cause gastrointestinal disorders, skin rashes, increases in serum transaminase, flu-like symptoms, drowsiness, and dizziness. Mild to moderate neutropenia has been reported in some patients and regular full blood counts are recommended during therapy. Succimer should be used with caution in patients with renal impairment or a history of hepatic disease.

Pharmacokinetics

Succimer is rapidly but incompletely absorbed after oral doses. It undergoes rapid and extensive metabolism and is excreted mainly in the urine with small amounts excreted in the bile and via the lungs.

◊ References.

1. Dart RC, *et al.* Pharmacokinetics of meso-2,3-dimercaptosuccinic acid in patients with lead poisoning and in healthy adults. *J Pediatr* 1994; **125:** 309–16.

Uses and Administration

Succimer is a chelator structurally related to dimercaprol (p.1444). It forms water-soluble chelates with heavy metals and is used in the treatment of lead poisoning. It has also been used in the treatment of poisoning with arsenic or mercury.

Succimer, labelled with a radionuclide, is used in nuclear medicine.

In the treatment of lead poisoning, succimer is given orally in a dose of 10 mg/kg or 350 mg/m^2 every 8 hours for 5 days then every 12 hours for an additional 14 days. The course of treatment may be repeated if necessary, usually after an interval of not less than 2 weeks.

Lead poisoning. Succimer is an effective lead chelator[1] and is used in the management of lead poisoning (see Treatment of Adverse Effects under Lead, p.2332). Succimer is also used in children with chronic lead exposure, and various dosage regimens have been studied.[2] It is generally only indicated if blood-lead concentrations are greater than 45 micrograms per 100 mL;[3] although short-term studies[4] in children with lower concentrations have shown effective reduction of blood lead, no effect on neurodevelopmental outcome has been shown in follow-up studies[5,6] and treatment of such children remains controversial.

1. Mann KV, Travers JD. Succimer, an oral lead chelator. *Clin Pharm* 1991; **10:** 914–22.
2. Farrar HC, *et al.* A comparison of two dosing regimens of succimer in children with chronic lead poisoning. *J Clin Pharmacol* 1999; **39:** 180–3.
3. American Academy of Pediatrics Committee on Environmental Health. Lead exposure in children: prevention, detection, and management. *Pediatrics* 2005; **116:** 1036–46. Also available at: http://pediatrics.aappublications.org/cgi/reprint/116/4/1036 (accessed 11/10/05)
4. Besunder JB, *et al.* Short-term efficacy of oral dimercaptosuccinic acid in children with low to moderate lead intoxication. *Pediatrics* 1995; **96:** 683–7.
5. Rogan WJ, *et al.* The effect of chelation therapy with succimer on neuropsychological development in children exposed to lead. *N Engl J Med* 2001; **344:** 1421–6.
6. Dietrich KN, *et al.* Effect of chelation therapy on the neuropsychological and behavioral development of lead-exposed children after school entry. *Pediatrics* 2004; **114:** 19–26.

Mercury poisoning. Succimer, given orally, increases the renal excretion of mercury and may be used in mercury poisoning (see Treatment of Adverse Effects under Mercury, p.2342). In patients with renal impairment, the succimer-mercury chelate may accumulate, and alternative methods have been tried. Extracorporeal infusion of succimer into the arterial blood line during haemodialysis, a procedure known as extracorporeal regional complexing haemodialysis, produced a substantial clearance of mercury in an anuric patient following intoxication with inorganic mercury.[1] Clearance was about ten times greater than that achieved with haemodialysis after intramuscular dimercaprol.

1. Kostyniak PJ, *et al.* Extracorporeal regional complexing haemodialysis treatment of acute inorganic mercury intoxication. *Hum Toxicol* 1990; **9:** 137–41.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Succicaptal; ***USA:*** Chemet.