

Incompatibility and stability. The incompatibility and stability of sulfites are discussed under Sulfur Dioxide, below.

Sodium Sulfite

Anhydrous Sodium Sulphite; E221; Exsiccated Sodium Sulphite; Natrii Sulfis; Natrii sulfis anhydricus; Natrii Sulfis Siccatus; Natrii Sulphis; Natrio sulfitas, bevandenis; Natriumsulfitti, vedetön; Natriumsulfitt, vattenfritt; Siñžitan sodný; Sodium (sulfite de) anhydre; Sodium Sulphite; Sodu siarczyn; Sulfito sódico; Vízmentes nátrium-szulfitt.

$\text{Na}_2\text{SO}_3 = 126.0$.
CAS — 7757-83-7.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.* Also in *USNF*.

Eur. also includes the heptahydrate.

Ph. Eur. 6.2 (Sodium Sulphite, Anhydrous; Natri Sulfis Anhydricus). A white or almost white powder. Freely soluble in water; very slightly soluble in alcohol. Store in airtight containers.

Ph. Eur. 6.2 (Sodium Sulphite Heptahydrate; Natrii Sulfis Heptahydricus). Colourless crystals. Freely soluble in water; very slightly soluble in alcohol.

USNF 26 (Sodium Sulfite). Colourless crystals. Freely soluble in water; very slightly soluble in alcohol. Store in airtight containers.

Incompatibility and stability. The incompatibility and stability of sulfites are discussed under Sulfur Dioxide, below.

Sulfur Dioxide

Dióxido de azufre; E220; Kükürt Dioksit; Siarki dwutlenek; Sulphur Dioxide.

$\text{SO}_2 = 64.06$.
CAS — 7446-09-5.

Pharmacopoeias. In *USNF*.

USNF 26 (Sulfur Dioxide). A colourless non-flammable gas with a strong suffocating odour characteristic of burning sulfur. It condenses readily under pressure to a colourless liquid that boils at -10° and has a wt per mL of about 1.5 g. Soluble 36 in 1 of water and 114 in 1 of alcohol by vol. at 20° and standard pressure. Soluble in chloroform and in ether. Store in cylinders. It is usually packaged under pressure in liquid form.

Incompatibility and stability. Sulfite antioxidants can react with and inactivate sympathomimetics such as adrenaline.¹ Measures need to be taken to prevent such a reaction if sulfites have to be used. Cisplatin is another compound that can be inactivated.² Phenylmercuric nitrate may be inactivated or its activity enhanced.^{3,4} Sulfites are reported to react with chloramphenicol.¹ Hydrogen peroxide generation has been reported on exposure to light of amino acid solutions containing sulfites.⁵ When used in foods there can be a noticeable taste and a reduction in thiamine content.⁶ Stability is affected by air and moisture,⁷ and there is decomposition at very low pH.⁷ There can be adsorption on to rubber closures.⁸

- Higuchi T, Schroeter LC. Reactivity of bisulfite with a number of pharmaceuticals. *J Am Pharm Assoc (Sci)* 1959; **48**: 535–40.
- Garren KW, Repta AJ. Incompatibility of cisplatin and Reglan Injectable. *Int J Pharmaceutics* 1985; **24**: 91–9.
- Richards RME, Reary JME. Changes in antibacterial activity of thiomersal and PMN on autoclaving with certain adjuvants. *J Pharm Pharmacol* 1972; **24** (suppl): 84P–89P.
- Collins AJ, et al. Incompatibility of phenylmercuric acetate with sodium metabisulfite in eye drop formulations. *J Pharm Pharmacol* 1985; **37** (suppl): 123P.
- Brawley V, et al. Effect of sodium metabisulfite on hydrogen peroxide production in light-exposed pediatric parenteral amino acid solutions. *Am J Health-Syst Pharm* 1998; **55**: 1288–92.
- FAO/WHO. Evaluation of the toxicity of a number of antimicrobials and antioxidants: sixth report of the joint FAO/WHO expert committee on food additives. *WHO Tech Rep Ser* 228 1962.
- Stewart JT. Sodium metabisulfite. In: Rowe RC, et al. eds. *Handbook of pharmaceutical excipients*. 5th ed. London and Chicago: The Pharmaceutical Press, and the American Pharmaceutical Association 2006: 690–2.
- Schroeter LC. Sulfurous acid salts as pharmaceutical antioxidants. *J Pharm Sci* 1961; **50**: 891–901.

Adverse Effects and Precautions

Gastric irritation due to liberation of sulfurous acid can follow ingestion of sodium metabisulfite and other sulfites. Large doses of sulfites may cause gastrointestinal upsets, respiratory or circulatory failure, and CNS disturbances.

Concentrated solutions of salts of sulfurous acid are irritant to skin and mucous membranes.

Sulfur dioxide is highly irritant to the eyes, skin, and mucous membranes. Inhalation results in irritation of the respiratory tract which may lead to bronchoconstriction and pulmonary oedema; very high concentrations may cause respiratory arrest and asphyxia. Contact with liquid sulfur dioxide results in acid burns. Allergic reactions including anaphylaxis and deaths have been reported.

The symbol † denotes a preparation no longer actively marketed

Hypersensitivity. Hypersensitivity reactions including bronchospasm, anaphylaxis, and some deaths have occurred in subjects, especially those with a history of asthma or atopic allergy, exposed to sulfites used as preservatives in foods.¹ These reactions have led to restrictions by the FDA on such use.² There have been case reports of reactions to sulfites in medicines;^{3,9} such reports are considered to be few in number and the FDA has not extended the restriction on sulfites in foods to apply to their use in drugs since it was felt that in certain cases there was no suitable alternative to a sulfite.² It was even accepted that adrenaline recommended for use in treating allergic reactions could itself contain sulfite and that its presence should not preclude use of the adrenaline preparation even in sulfite-sensitive patients.²

- Anonymous. Sulfites in drugs and food. *Med Lett Drugs Ther* 1986; **28**: 74–5.
- Anonymous. Warning for prescription drugs containing sulfites. *FDA Drug Bull* 1987; **17**: 2–3.
- Baker GJ, et al. Bronchospasm induced by metabisulphite-containing foods and drugs. *Med J Aust* 1981; **ii**: 614–17.
- Twarog FJ, Leung DYM. Anaphylaxis to a component of isotherarine (sodium bisulfite). *JAMA* 1982; **248**: 2030–1.
- Koepke JW, et al. Dose-dependent bronchospasm from sulfites in isotherarine. *JAMA* 1984; **251**: 2982–3.
- Mikolich DJ, McCloskey WW. Suspected gentamicin allergy could be sulfite sensitivity. *Clin Pharm* 1988; **7**: 269.
- Deziel-Evans LM, Hussey WC. Possible sulfite sensitivity with gentamicin infusion. *DICP Ann Pharmacother* 1989; **23**: 1032–3.
- Campbell JR, et al. Allergic response to metabisulfite in lido-caine anesthetic solution. *Anesth Prog* 2001; **48**: 21–6.
- Riemersma WA, et al. Type IV hypersensitivity to sodium metabisulfite in local anaesthetic. *Contact Dermatitis* 2004; **51**: 148.

Pharmacokinetics

Sulfites and metabisulfites are oxidised in the body to sulfate and excreted in the urine. Any sulfurous acid or sulfur dioxide is also converted to sulfate.

Uses

Sulfur dioxide and the sulfites that produce sulfur dioxide and sulfurous acid are strong reducing agents and are used as antioxidants. Concentrations of the sulfites in pharmaceutical preparations have ranged from 0.01 to 1.0%. At higher concentrations and preferably at an acid pH sulfur dioxide and the sulfites exhibit antimicrobial activity.

Sulfur dioxide and the sulfites are used in the food industry as antioxidants, antimicrobial preservatives, and anti-browning agents. They are used in wine making where tableted sodium metabisulfite is commonly known as Campden Tablets. Concentrations of sulfites above 500 ppm impart a noticeable unpleasant taste to preparations. There is concern over the risk of severe allergic reactions arising from the use of sulfites in foods (see Hypersensitivity, above).

Tar Acids

Alquitrán, ácidos de.

Description. Tar acids are phenolic substances derived from the distillation of coal tar or petroleum fractions. The lowest boiling fraction of coal tar, distilling at 188° to 205° , consists of mixed cresol isomers. The middle fraction, known as 'cresylic acids', distils at 205° to 230° and consists of cresols and xylenols. The 'high-boiling tar acids', distilling at 230° to 290° , consist mainly of alkyl homologues of phenol, with naphthalenes and other hydrocarbons. Cresol is described on p.1641.

- Black Fluids** are homogeneous solutions of coal-tar acids, or similar acids derived from petroleum, or any mixture of these, with or without hydrocarbons and with a suitable emulsifying agent.
- White Fluids** are finely dispersed emulsions of coal-tar acids, or similar acids derived from petroleum, or any mixture of these, with or without hydrocarbons.
- Modified Black Fluids and Modified White Fluids** may contain, as an addition, any other active ingredients, but if these are used, the type and amount must be disclosed, if required.

Adverse Effects and Treatment

As for Phenol, p.1656.

Tar acids are generally very irritant and corrosive to the skin, even when diluted to concentrations used for disinfection.

Poisoning. A report of fatal self-poisoning in a 59-year-old man after the ingestion of about 250 mL of a xylene-containing disinfectant (*Stericol Hospital Disinfectant*).¹

- Watson ID, et al. Fatal xylene self-poisoning. *Postgrad Med J* 1986; **62**: 411–12.

Uses

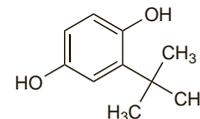
Tar acids are the phenolic components of coal tar and are used in the preparation of a range of fluids of varied activity used for household and general disinfection purposes.

Hydrocarbons are often used to enhance the activity of the tar acids in disinfectant fluids; they also help to reduce crystallisation of phenols.

Tertiary Butylhydroquinone

Butilhidroquinona terciaria; TBHQ, 2-tert-butylhydroquinone.

$\text{C}_{10}\text{H}_{14}\text{O}_2 = 166.2$.
CAS — 1948-33-0.



Profile

Tertiary butylhydroquinone is an antioxidant preservative used in foods. It has some antimicrobial activity.

Tetrabromocresol

3,4,5,6-Tetrabromo-*o*-cresol.

$\text{C}_7\text{H}_4\text{Br}_4\text{O} = 423.7$.
CAS — 576-55-6.



Profile

Tetrabromocresol is a brominated phenolic antiseptic. It has been used for hand disinfection and is applied topically in preparations for the treatment of fungal infections of the skin and bromhidrosis.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: *Austral:* Pedoz; *Ger:* Gehwol Fungizid†.

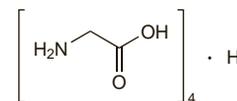
Tetraglycine Hydroperiodide

Tetraglicina, hidroperioduro de.

Гидропериодид Тетраглицина

$\text{C}_{16}\text{H}_{42}\text{I}_7\text{N}_6\text{O}_{16} = 1490.9$.

CAS — 7097-60-1.



Profile

Tetraglycine hydroperiodide is an iodine-based disinfectant that is used in the emergency treatment of drinking water (p.1623).

Preparations

Proprietary Preparations (details are given in Part 3)

UK: Potable Aqua; **USA:** Potable Aqua.

Thiomersal (BAN, rINN)

Mercuriothiolate; Mercuriothiolate Sodique; Sodium Ethyl Mercuriothiosalicylate; Thimerosal; Thiomersalate; Thiomersalum; Thiomersaali; Thiomersal; Thiomersalis; Tiomerzál. Sodium (2-carboxyphenylthio)ethylmercury.

Тиомерсал

$\text{C}_9\text{H}_9\text{HgNaO}_2\text{S} = 404.8$.

CAS — 54-64-8.

ATC — D08AK06.

ATC Vet — QD08AK06.

