Arsenic and compounds

Safety Data Sheet

Division of Occupational Health and Safety
National Institutes of Health

WARNING:

Compounds in this class are acutely toxic, carcinogenic, teratogenic, and mutagenic. They are readily absorbed by various body tissues through the skin, respiratory and intestinal tracts, and transplacentally. They may cause severe irritation of tissues (skin, eyes, mucous membranes, and lungs). Avoid formation and breathing of aerosols or vapors.

Laboratory operations should be conducted in a fume hood, glove box, or ventilated cabinet.

Avoid skin contact: if exposed, wash with dilute boric acid solution followed by water. Avoid rubbing of skin or increasing its temperature.

For eye exposure, irrigate immediately with dilute boric acid solution followed by large amounts of water. For ingestion, induce vomiting. Refer for gastric lavage. For inhalation, remove victim promptly to clean air. Administered rescue breathing if necessary. Refer to physician.

In case of laboratory spill, wear protective clothing during cleanup. Avoid skin contact or breathing of aerosols or vapors. Use dilute nitric acid solution to dissolve arsenic metal, and dilute hydrochloric acid for other arsenic compounds. Use absorbent paper to mop up spill. Wash down area with soap and water. Dispose of waste solutions and materials appropriately. Monitor laboratory air and check for arsenic residues after clean-up.

A. Background

Elementary arsenic is a gray metallic-looking crystalline powder; arsine is a colorless gas; arsenites and arsenates are white crystalline powders. The alkali salts are highly soluble in water but the calcium and lead salts are not.

All arsenic compounds are moderately toxic (arsine is highly toxic), mutagenic in some but not all test systems, and teratogenic. With regard to carcinogenicity, IARC (1980) states that "there is inadequate evidence for the carcinogenicity of arsenic compounds in animals. There is sufficient evidence that inorganic arsenic compounds are skin and lung carcinogens in humans." Since that time, several investigations have demonstrated carcinogenicity in several animal species also.

Major uses of arsenic in various forms are as pesticides (insecticides, herbicides, and sheep and cattle dips) and in drugs. The use of "Fowler's solution" (potassium arsenite) in the treatment of psoriasis has been almost entirely discontinued.

Arsenic may be found in any of four valence states: -3 (arsine), 0 (elementary arsenic), +3 (arsenites), and +5 (arsenates). Nearly all experimental work on arsenites and arsenates has been carried out on their sodium or potassium salts, and most of the pertinent physical and chemical properties are listed for these salts. The term "arsenic" is used when the valence state is not specified and generally refers to arsenite and/or arsenate.

The current permissible exposure limit at work places has been established at 0.2 mg/m^3 for arsenic, its soluble compounds (as As), and arsine, averaged over an 8-hour period ((ACGIH, 1987). The latest 8-hour time-weighted average is 0.15 mg/m^3 for lead arsenate (ACGIH, 1987). For a review of the development of these limits, see Sittig (1985).

Recent reviews of the chemical and biological properties of arsenic compounds include Landrigan (1981), Fowler (1983), Lederer and Fensterheim (1983), Sunderman (1984), and IARC (1986).

B. Chemical and Physical Properties

For properties and listed under individual entries, see the end of this section.

Arsenic

1. Chemical Abstract No.: 7440-38-2
2. Synonyms: Gray arsenic; metallic arsenic; As and As Compounds
3. Chemical formula: As; atomic weight: 74.92
4. Density: 5.727 g/cm^3 as 20° C relative to water at 4° C.
5. Solubility: Insoluble in water; soluble in nitric acid to form arsenious and arsenic acids.
6. Description: Gray, shiny, metallic-looking rhombohedra.
7. Boiling point: 613° C (sublimes); Melting point: 817° C at 28 atmospheres.
8. Stability: High in the absence of oxidizers or reducers.
9. Chemical reactivity: Forms arsine (highly toxic) in the presence of nascent hydrogen.

Arsenic pentoxide

1. Chemical Abstract No.: 1303-28-2
2. Synonyms: Arsenic acid anhydride; Arsenic [V] oxide; Arsenic oxide [As205] (9CI)
3. Chemical formula: As_2O_5; molecular weight: 229.84
4. Density: 4.32 g/cm^3.
5. Solubility: Highly soluble in water (150 g/100 ml at 16° C), ethanol, dilute mineral acids, and alkali hydroxides.
6. Description: Deliquescent white powder.
7. Melting point: 315° C with decomposition.
8. Stability: Deliquesces in moist air to form arsenic acid. Decomposes on heating above 300° C to As_2O_3 and O_2.
9. Chemical reactivity: Acts as an oxidant in acid solution.

Arsenic trioxide

1. Chemical Abstract No.: 1327-53-3
2. Synonyms: Arsenic (III) oxide; Arsenous acid; Arsenic sesquioxide; White arsenic; Arsenous oxide; Arsenous acid anhydride; Arsenic oxide (As_2O_3) (9CI)
3. Chemical formula: As203; molecular weight: 197.84
4. Density: 3.738 g/cm^3.
5. Volatility: 1 mm Hg at 212.5° C. (For other values, see Weast, 1979, p. D-199.)
6. Solubility: 3.7 g/100 ml at 20° C in water[A]; soluble in HC1, alkali hydroxides; practically insoluble in ethanol or ether.
7. Description: Amorphous or crystalline (claudetite, arsenolite) powder.
8. Melting point: 312.3° C; [A] sublimes if heated slowly.
9. Stability: Stable to heat and light.
10. Chemical reactivity: Reduced to arsenic by heating with charcoal or in HCl solution by stannous chloride; reduced to arsine by nascent hydrogen (2n + HCl); oxidized to arsenate by various oxidants in alkaline solution.

Arsine

1. Chemical Abstract No.: 7784-42-1
2. Synonyms: Arsenic hydride; Hydrogen arsenide
3. Chemical formula: AsH3; molecular weight: 77.95
4. Density: 2.695 as a gas (air=1).
5. Volatility: 1 mm Hg at – 142.6° C. (For other values, see Weast, 1979, p. D-199.)
6. Solubility: Slightly soluble in water (20 ml/100 ml); soluble in chloroform and benzene.
7. Description: Colorless gas.
8. Boiling point: -55° C.
9. Melting point: -116.3° C.
10. Stability: Decomposes on heating below 300° C to arsenic and hydrogen. Decomposition is accelerated by light in the presence of moisture. Stable in air at Room temperature but ignitable to yield arsenic, arsenic trioxide, or arsenic Pentoxide (depending on oxygen supply).
11. Chemical reactivity: Oxidized by oxidants (permanganate, bromine water); reduces silver nitrate solutions to metallic silver.

Calcium arsenate

1. Chemical Abstract No.: 7778-44-1
2. Synonyms: Tricalcium arsenate; Pencal; Arsenic acid (H_3AsO_4), calcium salt (2:3) (9CI)

[A] These values are for the amorphous forms. Those for the crystalline forms are listed in Weast (1979), p. B-57.

3. Chemical formula: $Ca_3(AsO_4)2$; molecular weight: 398.08

Lead arsenate

1. Chemical Abstract No.: 7784-40-9
2. Synonyms: Arsenic acid (H_3As0_4), lead(2+) salt (1:1) (9CI); Acid lead arsenate; Schultenite; Lead di-ortho-arsenate
3. Chemical Formula: $PbHAsO_4$; molecular weight: 347.12
4. Solubility: Very slightly soluble in water; soluble in nitric acid, alkali.

Potassium arsenate[B]

1. Chemical Abstract No.: 7784-41-0
2. Synonyms: Arsenic acid (H_3AsO_4), monopotassium salt (9CI); Potassium dihydrogen arsenate; Macquer's salt
3. Chemical formula: KH_2AsO_4; molecular weight: 180.04

Potassium arsenite[C]

1. Chemical Abstract No.: 13464-35-2
2. Synonyms: Arsenous acid, potassium salt (9CI); Potassium metaarsenite
3. Chemical formula: KH((As02)2; molecular weight: 253.93
4. Note: "Fowler's solution" is a 1% aqueous solution of KH(As02)2.

Sodium arsenate (heptahydrate) [D]

1. Chemical Abstract No.: 10048-95-0
2. Synonyms: Dibasic sodium arsenate heptahydrate; Sodium orthoarsenate, mono H, heptahydrate; Arsenic acid (H_3AsO_4), disodium salt, heptahydrate (9CI)
3. Chemical formula: Na_2HasO_4 TH2O); molecular weight: 311.9
4. Stability: Loses 5 molecules of water at 50° C; becomes anhydrous at 100° C. Converted to sodium pyroarsenate (Na4s2O7) at 150° C or above. A decahydrate is also known.

Sodium arsenite

1. Chemical Abstract No.: 7784-46-5
2. Synonyms: Arsenious acid, sodium salt Sodium
3. Chemical formula: $NaAsO_2$; molecular weight: 129.91

[B] Other forms are listed in Weast (1979).
[C] Other forms are listed in Weast (1979).
[D] Other forms are listed in Weast (1979).

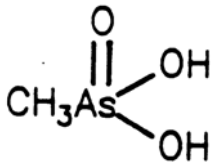
Other properties

There are no data for any of the above arsenic compounds regarding optical absorption characteristics, flash point, autoignition-temperature, or explosive limits. Alkali arsenites and arsenates are water soluble and sparingly soluble in ethanol; the calcium and lead salts are nearly insoluble in water. Arsenites and arsenates are amorphous or crystalline while powders with practically no volatility. Arsenates are stable to heat, light, and moisture (except as noted otherwise); there are no data on their chemical reactivity. Alkali arsenites are somewhat hygroscopic and decompose in the presence of atmospheric in CO_2. They react with metals like aluminum and zinc to produce highly toxic arsine. Aqueous solutions of arsenites (40 or 400 ug As/ml) are stable over 4 weeks at 4^{o} C; at room temperature, up to 40% is oxidized to arsenate in this time (Vahter and Norin, 1980).

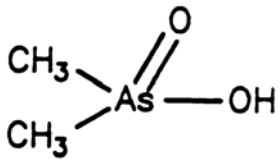
Exposure of arsenite solutions to ultraviolet light results in quantitative transformation to arsenate (Reay and Asher, 1977; Marafante *et al*., 1985).

Products of arsenic metabolism:

monomethylarsonic acid (MMA):



dimethyl arsinic acid (cacodylic acid, DMA):



C. Fire, Explosion, and Reactivity Hazard Data

1. Fire fighters should wear a full-face-piece, self-contained breathing apparatus in positive pressure mode. While arsenic compounds are not flammable themselves, fires can produce volatile toxic products. There are no explosion hazards.
2. Conditions contributing to instability include heat and reducing materials.
3. Incompatibilities, particularly for metallic arsenic, arsenic trioxide, and alkali arsenites, are aluminum and zinc in the presence of acid.
4. Arsenic compounds do not require nonspark equipment.

D. Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe Operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The NIH Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving arsenic compounds.

It should be emphasized that this data sheet and the NIH Guidelines are intended as starting points for the implementation of good laboratory practices when using this compound. The practices and procedures described in the following sections pertain to the National Institutes of Health and may not be universally applicable to other institutions. Administrators and/or researchers at other institutions should modify the following items as needed to reflect their individual management system and current occupational and environmental regulations.

1. Chemical inactivation: No validated method reported.
2. Decontamination: Turn off equipment that could be affected by arsenic compounds or the materials used for cleanup. If there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 911) for assistance. Use absorbent paper to mop up spill. Wipe Off surfaces with acidified water, then wash with copious quantities of water. Glassware should be rinsed in a hood with acidified water, followed by soap and Water. Animal cages should be washed with water.
3. Disposal: No waste streams containing arsenic compounds shall be disposed of in sinks or general refuse. Surplus arsenic compounds or chemical waste streams contaminated with arsenic compounds shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (*e.g.*, animal carcasses and bedding) containing arsenic compounds shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Nonchemical waste (*e.g.*, animal carcasses and bedding) containing arsenic compounds shall be handled and packaged for incineration in accordance with the NIH medical- pathological waste disposal system. Potentially infectious waste (*e.g.*, tissue cultures) containing arsenic compounds shall be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (*e.g.*, absorbent bench top liners) minimally contaminated with arsenic compounds shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (*e.g.*, associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing arsenic compounds shall be handled in accordance with the NIH radioactive waste disposal system.
4. Storage: Store solid arsenic compounds and their solutions in tightly closed glass containers. Avoid contact with container materials consisting of or containing aluminum or zinc. Avoid exposure of solid arsenic compounds to atmospheric moisture and carbon dioxide.

E. Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

For recent reviews of sampling for analysis and analytical procedures see: Lewis (1977); Brooks et al. (1981); IARC (1986), chapters 10-12 and individual methods.

1. Sampling: Officially recommended methods for air sampling (NIOSH, 1977) are: for particulate arsenic compounds, filtration through cellulose membranes followed by ashing and solubilization in nitric acid (Procedure S-309-1-7; a portable sampling unit is described); for arsine, adsorption on charcoal and description with dilute nitric acid (Procedure S229-1-8). Both procedures use atomic absorption spectrometry for evaluation. A simple method for sampling and analysis of arsenic trioxide in air consists of collection on filter paper, dissolving in 1 N NaOH, and spectrometry at 222 nm (Snyder and Isola, 1979).

   Lewis (1977) cautions that significant absorption of As from biological material Onto soft glass containers may lead to low analytical results; Teflon and Polyethylene bottles are recommended for sample storage.

2. Analysis

   a. Total arsenic: Most methods for the analysis of water, urine, and other biological materials involve first wet ashing with nitric, sulfuric, and perchloric acid (proper control of residual acid [Kang and Valentine, 1977] and of the order oxidizing acids [Cox, 1980] has been emphasized). Krynitsky (1987) recommends the use of nitric acid and hydrogen peroxide for wet ashing. This is usually followed by reduction with either zinc hydrochloride or sodium borohydride to arsine. In colorimetric procedures, the AsH_3 is absorbed in a pyridine solution

of silver diethyldithiocarbamate to produce a red color (Burke and Diamondstone, 1977). In recent years, atomic absorption spectrometry (AAS) has become the preferred method. It has been adopted by NIOSH as the method of choice for the analysis of air and urine and these methods have been described in detail (IARC, 1986). AAS is usually preceded by graphite furnace combustion and arsine generation. Addition of EDTA to the sample mixture prevents interference from copper, iron, and nickel (Uthus *et al*., 1981). The advantages and disadvantages of AAS in comparison with neutron-activation-γ spectrometry, molecular absorption spectrometry, atomic emission spectrometry, electrometric methods, x-ray emission, and atomic fluorescence spectrometry have been discussed oritically (Brooks *et al*., 1981; Maitani *et al*., 1987).

b. Arsenic speciation: Differential determination of arsenite, arsenate, and organoarsenic compounds usually uses AAS preceded by high pressure liquid chromatography. Some applications to environmental samples have been described (Ricci *et al*., 1981; Aggett and Kadwani, 1983; IARC, 1986; Chana and Smith, 1987). HPLC coupled with atomic emission spectrometry is stated to have a twenty-fold higher sensitivity (Morita *et al*., 1981) but employs a far more expensive spectrometer.

F. Biological Effects (Animal and Human)

1. Absorption: Arsenites and arsenates are absorbed by ingestion and parenteral injection; sodium arsenite, arsenic trioxide, and arsine are absorbed by inhalation. Skin absorption of arsenates, while slight, has been demonstrated and may be considered to be significant for arsine (though there is no documentation). Sodium arsenite and arsenate are absorbed through the placenta.

2. Distribution and pharmacokinetics; Injected arsenites and arsenates are first concentrated in red blood cells and subsequently distributed to other organs (highest concentrations in liver, lung, kidney, and spleen), followed by urinary excretion. Whole body autoradiography following intravenous injection of either arsenite or arsenate into mice and hamsters illustrates this distribution. There is also a significant accumulation of arsenate in the skeleton, presumably by exchange with phosphate (Lindgren *et al*., 1983). The same distribution pattern applies to inhaled arsine. Application of pentavalent arsenic to skin results first in an accumulation of arsenic in the skin, followed by distribution to other organs, followed by urinary excretion. Significant deposition in hair and nails has been demonstrated in man and animals.

3. Metabolism and excretion: The pathways of arsenic metabolism vary with the type of arsenic compound administered, route of administration, and animal species. Some aspects have been reviewed (Klevay, 1976; Odanaka *et al*., 1980; Peoples, 1983). Biotransformation of arsenite to arsenate occurs in the mouse (this is probably a detoxication mechanism) while the reverse reaction has been observed in dogs (Tsukamoto, 1983). Urinary and fecal excretion products are inorganic arsenic and the result of successive methylation to MAA and DMA (for structures see B, above) in most species including man (Buchet *et al*., 1981; Bertolero *et al*., 1981; Marafante *et al*., 1985); however, there is no methylation in the marmoset monkey (Vahter *et al*., 1982), and the rat is an inappropriate species for studying arsenic metabolism since in this species nearly all of the administered arsenic is stored in red blood cells (Peoples, 1983).

4. Toxic effects: In general, arsenites are much more toxic than arsenates; the oral LD_{50} of arsenates in rats and mice is about 100 mg/kg and that of arsenites about 10 mg/kg; the acute oral LD_{50} of arsenic trioxide is 15 mg/kg in rats and 39 mg/kg in mice, and that of calcium arsenate is 812 mg/kg in rats. The LD_{50} of arsine by inhalation in mice has been estimated to be 0.67 mg/kg (0.5 mg/l) after 2-4 min; 3-10 ppm will produce symptoms in man after several hours of exposure. The intraperitoneal LD_{50} in mice is about 2.5 mg/kg in several strains

Acute and chronic effects of arsenic intoxication in man have been summarized (Landrigan, 1981; IARC, 1980; Arena and Drew, 1986). They include a burning sensation of mouth and throat; metallic, garlicky odor of breath and feces; difficulty in swallowing; vomiting; diarrhea; and cyanosis. Chronic effects include hyperpigmentation and keratosis (characteristics of prolonged treatment with Fowler's solution), vascular effects ("blackfoot disease"), cirrhosis of the liver, and effects on the hematopoietic system (leukopenia, anemia). The chief toxic effect of inhaled arsine is due to its binding to hemoglobin, resulting in extensive hemolysis and hematuria followed by jaundice; the usual cause of death is renal failure.

5. Carcinogenic effects: As late as 1980 it was believed that arsenic compounds were not carcinogenic in experimental animals, and this conclusion was drawn from a summary of largely negative results (IARC, 1980). Since that time evidence has appeared which indicates carcinogenicity in rats (Ivankovic *et al*., 1979), mice (Rudnai and Borzsonyi, 1980), and Syrian golden hamsters (Ishinishi *et al*., 1983; Yamamoto *et al*., 1987). While some of these experiments may be questioned on the basis of inadequate controls or low though statistically significant incidence of tumors, the previous position can no longer be justified.cally significant incidence of tumors, the previous position can no longer be justified.

   The evidence for carcinogenicity of arsenic compounds in man is more positive, and this has been reviewed (Landrigan, 1981; IARC, 1980, 1982; Furst, 1983). A correlation was established between the appearance of skin cancer and arsenic concentration in the well water in certain regions of Taiwan (Tseng, 1977). Skin cancers were also noted repeatedly in patients after prolonged treatment with Fowler's solution (potassium arsenite) and in vineyard workers employing arsenical pesticides. Lung cancers have been noted in men involved in the production of arsenicals (Mabuchi *et al*., 1980). Other studies (involving workers in copper smelters and mines) are not as Clear-out since exposure to other materials occurred concomitantly. There is still an open question whether arsenic compounds are primary carcinogens or co-carcinogens, but the bulk of the evidence is in favor of the former.

6. Mutagenic and teratogenic effects: Sodium arsenite and arsenate are not mutagenic in the Ames test or in E. coli (Sunderman, 1984) but are weakly positive in B. subtilis. Both are strongly teratogenic in the hamster (Ferm and Hanlon, 1985; Hanlon and Ferm, 1986a, 1986b) and in the mouse (Baxley *et al*., 1981).

G. Emergency Treatment

The treatment of poisoning by arsenic compounds, including use of BAL Therapy, has been discussed (Arena and Drew, 1986).

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with dilute boric and solution followed by water. Since some arsenic compounds are readily absorbed through the skin, avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with dilute boric acid solution followed by copious quantities of running water for at least 15 minutes. Obtain ophthalmological evaluation.

3. Ingestion: Induce vomiting. Refer to gastric lavage.

4. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

5. Refer to physician at once. Consider treatment for pulmonary irritation.

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