ARSENIC

3. Biological monitoring of arsenic

Identity

Name (parent)	Arsenic	Arsine	Arsenic trioxide	Arsenic pentoxide	Arsenic acid
UN number	1558	2188	1561	1559	1553 (liquid), 1554 (solid)
CAS number	7440-38-2	7784-42-1	1327-53-3	1303-28-2	7778-39-4
Intervention value (AGW in mg/m^3)	-	1	-	-	-
Structure	As	AsH_3	As_2O_3	As_2O_5	H_3AsO_4
Oxidative state	n/a	III	III	V	V

Occurrence

Chemical state (at 20°C)	Solid	Gas	Solid	Solid	Liquid
Physical appearances	Silver-grey metallic solid, which becomes black when exposed to air	Colorless, flammable gas with a garlic-like or fishy odor. Often shipped as a liquefied compressed gas.	White or transparent, glassy, amorphous lumps or crystal powder	White hygroscopic powder	Clear syrupy liquid
Industrial products [1]	In metallurgy for hardening copper, lead and alloys, in the manufacture of certain types of glass.	Use a additive in the semiconductor industry and in the manufacture of crystals for fiber optics and computer chips; also in galvanizing, soldering, etching, burnishing, and lead plating.	Manufacturing of glass, Paris green, enamels, weed killers, metallic arsenic, for preserving hides, killing rodents and insects, in sheep dips and weed killers, textile mordant	Manufacturing of colored glass, in adhesives for metals, in wood preservatives, in weed control, as fungicide	Used in the production of arsenates and the manufacturing of pesticides

Physicochemical properties

Molecular weight	74.9	77.9	197.8	229.8	141.9
Vapor pressure (mbar at 20°C)	negligible	10300	$3.29 * 10^{-4}$ (at 25°C)	Not determined	Not determined
Water solubility (in	Scarcely soluble in	0.07	2.1 (at 25°C)	230	302

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g/100mL at 20°C)	water				

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Toxicokinetics (parent)

Uptake by inhalation	- Arsine is rapidly absorbed through the lungs into the blood stream. For humans, no quantitative data are available. An in vivo experiment with mice showed that approximately 64% of the administered dose was absorbed [2]. - As_2O_3 and As_2O_5 in air are solid and thus respiratory absorption is a two-stage process, involving deposition of the particles on to airway and lung surfaces, followed by absorption of arsenic from deposited particulates. The extent of absorption of arsenic is mainly dependent on the particle size and solubility. In lung cancer patients exposed to arsenic in cigarette smoke, deposition was estimated to be about 40% and absorption was 75–85 % [3] [4].
Uptake by skin absorption	Percutaneous absorption through abdominal skin of rhesus monkey of ^{73}As as H_3AsO_4 was 2.0 ± 1.2% (dose: 0.6 µg/cm^2) and 6.4 ± 3.9% (dose: 0.0004 µg/cm^2) in an aqueous solution and 3.2 ± 1.9 % (dose: 0.6 µg/cm^2) and 4.5 ± 3.2% (dose: 0.0004 µg/cm^2) in freshly mixed soil [5]. In vitro (human skin): percutaneous absorption of ^{73}As as H_3AsO_4 was 1.9% of arsenic acid in aqueous solution and 0.76% of arsenic acid in freshly mixed soil [5].
Uptake via gastrointestinal tract	For natural drinking water an absorption of 94.76 ± 2.27% was observed [6].
Distribution	As is generally bound to sulfhydryl groups of proteins and low-molecular-weight compounds such as glutathione (GSH) and cysteine. After absorption, arsenic is distributed throughout the body, cited in ATSDR [3]. Acute intoxication with arsenic, showed ubiquitous distribution of arsenic, with the highest concentrations in liver and kidneys [7].
Metabolism	Metabolism of inorganic arsenic: (1) reduction/oxidation reactions that interconvert As(III) and As(V), and (2) methylation reactions, which convert arsenite (As III) to MMA and DMA [3].
Excretion via lungs	Exhalation of arsine.
Excretion via urine	Primary route of excretion: the total amount of arsenic excreted in urine accounts for about 60% of the absorbed amount [8]; cited in ACGIH [4].
Excretion via feces	Minor excretion route.

Toxicodynamics

Mechanisms of toxicity	The trivalent state is more toxic than the pentavalent state. Acute toxicity after ingestion: abdominal pain, vomiting, diarrhea, vascular shock, death. Neurotoxicity, oxidative stress, genotoxicity [3].
Classifications for carcinogenicity	Human carcinogen (IARC class I) [9]
Classifications for reprotoxicity	Arsenic is teratogenic in animals: maternal oral treatment with inorganic arsenic increased the rate of neural tube defects in the offspring exposed in utero [10] . As measured in maternal human hair early in pregnancy was associated with decreased birth weight [11].
Classifications for sensitizing properties	Contact sensitivity to arsenic is not common, but has been confirmed in clinical and experimental studies [12].

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Biomarkers	**Total inorganic arsenic in urine**	**Inorganic arsenic species (As III and As V) in urine**
Remark	Measurement of total As (organic and inorganic) is not recommended because of contribution of less toxic organic arsenic (monomethylarsonic acid (MMA) and dimethylarsenic acid (DMA)), which are primarily derived from diet (sea-food).	
Molecular weight arsine	*77.9 (arsine is the compound detected)*	74.9
Involved enzymatic metabolism	Enzymatic methylation (arsenite methyltransferase, MMA reductase and MMA methyltransferase [3])	-
Biological material	Urine	Urine
Type of sample	Spot urine	Spot urine
Sampling strategy	First urine in the morning after awakening	First urine in the morning after awakening
Excretion pattern	Triphasic elimination: 2.1 days, 9.5 days and 38 days (determined in 6 male volunteers) [13]; 24 h, 84 h and 8 d (measured in volunteers), cited in ACGIH [4].	Triphasic elimination: 2.1 d, 9.5 d and 38 d (determined in 6 male volunteers) [13]; 24 h, 84 h and 8 d (measured in volunteers), cited in ACGIH [4].
Materials	Acid rinsed plastic containers	Acid rinsed plastic containers
Transportation	Within 24 hours at 4°C	Within 24 hours at 4°C
Storage	24 h at 4°C and > 6 month at -20°C.	24 h at 4°C and > 6 month at -20°C.
Stability	> 6 month at -20°C	> 6 month at -20°C
Measurement principle	1) For measurement inorganic arsenic: selective conversion of inorganic arsenic and its metabolites into arsine, separation of the arsine produced or a preliminary ion-exchange separation of the arsenic compounds; cited in ACGIH [4] 2) Atomic absorption spectrometry (AAS) with Zeeman background correction	HPLC-ICP-MS: measurement of AsIII and AsV [14]
Limit of quantification	1 µg/L, cited in ACGIH [4]	0.1 µg/L (HPLC-ICP-MS) [14]
Aliquot for 1 analysis	25 mL	5 mL
Recommended adjustments	Use creatinine for correction of density	Use creatinine for correction of density
Preferred units for expression of results	µg As/ g creatinine	µg As/ g creatinine
Conversion factor	1 µmol As / mol creatinine = 0.69 µg As/g creatinine 1 µg As/ g creatinine = 1.45 µmol As/mol creatinine	1 µmol As / mol creatinine = 0.66 µg As/g creatinine 1 µg As/ g creatinine = 1.51 µmol As /mol creatinine
Biological exposure value US [15]	Inorganic arsenic + methylated metabolites: 35 µg As/L, at the end of the workweek	Inorganic arsenic + methylated metabolites: 35 µg As/L, at the end of the workweek
Biological exposure value Germany	BLW (Biologischer Leit-Wert) for inorganic arsenic and	BLW (Biologischer Leit-Wert) for inorganic arsenic

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[16]	methylated metabolites in urine: 50 µg/L EKA arsenic trioxide: Air arsenic (mg/m^3) / Arsenic in urine (µg/L) at end of exposure or end of shift 0.01 / 50 0.05 / 90 0.10 / 130	including methylated metabolites in urine: 50 µg/L EKA arsenic trioxide: Air arsenic (mg/m^3) / Arsenic in urine (µg/L) at end of exposure or end of shift 0.01 / 50 0.05 / 90 0.10 / 130
Background value	< 10 µg/g creatinine (sum of inorganic arsenic and methylated metabolites) [17]	<1.5 µg/g creatinine (inorganic arsenic) [17]
BIOMONECS background in non-smoking m/f adults (based on P0.95) [18]	23.0 µg As/ g creatinine (sum total organic and inorganic As)	Not available
Possible confounders	Occupational exposure, consumption of seafood	

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