The MAK Collection for Occupational Health and Safety

Arsenic and its inorganic compounds (with the exception of arsine)

MAK Value Documentation, addendum – Translation of the German version from 2015

M. Bader[1], A. Hartwig[2,*], MAK Commission[3,*]

[1] *Occupational Medicine and Health Protection, GUA/CB, 67056 Ludwigshafen, Germany*

[2] *Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Geb. 50.41, 76131 Karlsruhe, Germany*

[3] *Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany*

* *email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)*

Keywords: arsenic and inorganic arsenic compounds; human carcinogen; cardiovascular; skin changes; neurologic; skin absorption

Citation Note: Bader M, Hartwig A, MAK Commission. Arsenic and its inorganic compounds (with the exception of arsine). MAK Value Documentation, addendum – Translation of the German version from 2015. MAK Collect Occup Health Saf [Original edition. Weinheim: Wiley-VCH; 2017 Oct;2(4):1459-1464]. Corrected republication without content-related editing. Düsseldorf: German Medical Science; 2026. https://doi.org/10.34865/mb744038vere5817_w

Republished (online): 07 Aug 2026

Originally published by Wiley-VCH Verlag GmbH & Co. KGaA; https://doi.org/10.1002/3527600418.mb744038vere5817

Addendum completed: 26 Feb 2014

Published (online): 27 Oct 2017

The commission established rules and measures to avoid conflicts of interest.

Arsenic and its inorganic compounds (with the exception of arsine)

MAK Value Documentation

M. Bader[1], A. Hartwig[2,*], MAK Commission[3,*]

DOI: 10.1002/3527600418.mb744038vere5817

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated the data available for absorption through the skin for arsenic [7440-38-2] and its inorganic compounds including gallium arsenide [1303-00-0]. Available publications are described in detail.
Dermal penetration has been demonstrated for pentavalent arsenic compounds, and it can also be assumed for trivalent arsenic compounds. The extent of skin penetration depends on the solubility of the substance. Arsenic and its inorganic compounds are classified in Category 1 for Carcinogenic Substances and in Category 3 A for Germ Cell Mutagens. No MAK value (maximum concentration at the workplace) could be established. No safe concentration range can therefore be estimated, so that an increased carcinogenic or genotoxic risk should be assumed even for low amounts absorbed percutaneously. Therefore, inorganic arsenic compounds, with the exception of arsenic itself and gallium arsenide, which are both very poorly soluble in water, are designated with an "H" (for substances that can be absorbed through the skin in toxicologically relevant amounts).

Keywords

arsenic; gallium arsenide; arsenic trioxide; arsenic(III) oxide; arsenous acid; arsenic(III) acid; trisodium arsenite; arsenic pentoxide; arsenic(V) oxide; arsenic acid; arsenic(V) acid; disodium arsenate; trisodium arsenate; absorption through the skin; occupational exposure; maximum workplace concentration; MAK value; toxicity; hazardous substance

Author Information

[1] BASF SE, Occupational Medicine and Health Protection, GUA/CB, 67056 Ludwigshafen, Germany
[2] Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Department of Food Chemistry and Toxicology, Institute for Applied Biosciences, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Geb. 50.41, 76131 Karlsruhe, Germany
[3] Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany

* Email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)

Arsenic and its inorganic compounds (with the exception of arsine)

[7440-38-2]

Supplement 2015

MAK value	**–**
Peak limitation	**–**
Absorption through the skin (2014)	**H** **all compounds except arsenic metal and gallium arsenide**
Sensitization	**–**
Carcinogenicity (1971)	**Category 1**
Prenatal toxicity	**–**
Germ cell mutagenicity (2002)	**Category 3 A**
BLW (2002)	**50 µg inorganic arsenic and its methylated metabolites/l urine**
BAR (2010)	**15 µg inorganic arsenic and its methylated metabolites/l urine**

Substance	CAS number	Formula	Molar mass (g/mol)	Solubility in water
Arsenic	7440-38-2	As	74.92	practically insoluble (IFA 2013 a)
Gallium arsenide	1303-00-0	GaAs	144.64	25 µg/l (ECHA 2014)
Trivalent arsenic compounds:				
Arsenic trioxide, Arsenic(+III) oxide	1327-53-3	As_2O_3	197.84	17 g/l at 16 °C (IFA 2013 b)
Arsenous acid, Arsenic(+III) acid	13464-58-9 36465-76-6[a)]	H_3AsO_3 (ortho form)	125.94	substance known only in aqueous solution (IFA 2013 c)
	13768-07-5	$HAsO_2$ (meta form)	107.94	

Salts of arsenic(+III) acid, e.g.				
Trisodium arsenite	13464-37-4 14060-38-9	Na_3AsO_3 (ortho form)	191.89	
Sodium arsenite	7784-46-5	$NaAsO_2$ (meta form)	129.91	readily soluble (IFA 2013 d)
Pentavalent arsenic compounds:				
Arsenic pentoxide, Arsenic(+V) oxide	1303-28-2	As_2O_5	229.84	readily soluble (IFA 2013 e)
Arsenic acid, Arsenic(+V) acid	7778-39-4	H_3AsO_4 (ortho form)	141.94	302 g/l at 12.5 °C (ATSDR 2007)
Salts of arsenic(+V) acid, e.g.				
Trisodium arsenate	13464-38-5	Na_3AsO_4	207.89	readily soluble (IFA 2013 f)
Disodium arsenate	7778-43-0	Na_2HAsO_4	185.91	soluble 1 : 3 parts in water (ATSDR 2007)
Disodium arsenate heptahydrate	10048-95-0	$Na_2HAsO_4 \times 7 H_2O$	312.0	

[a)] Arsonic acid

In this supplement only the data available for absorption through the skin are considered. The other end points are presented in the documentation from 2002 (documentation "Arsenic and its inorganic compounds (with the exception of arsine)" 2005) and in the supplement from 2014 (supplement "Arsenic and its inorganic compounds (with the exception of arsine)" 2014).

Absorption through the skin

For disodium arsenate heptahydrate absorption rates of 1.14 to 33 µg arsenic/cm² and hour were determined in rats after immersion of the tail into 0.01 to 0.2 molar aqueous solutions. The substance first accumulated in the skin and was then slowly released into the blood. After exposure to a 0.1 molar solution (about 7.5 g arsenic/l), 203 µg arsenic was absorbed; 30% of this dose was eliminated with the faeces and a further 30% with the urine over a period of 10 days. After dermal exposure, the arsenic concentration in the different tissues was as high as that after oral administration, but lower than that after intravenous or intratracheal exposure (Dutkiewicz 1977). The results are not presented in sufficient detail for the calculations to be fully understood. A flux cannot be calculated; the absorption of soluble arsenate through the skin, however, has been demonstrated.

Arsenic acid in water was applied semi-occlusively to the skin of Rhesus monkeys for 24 hours; the arsenic dose amounted to 0.000024 µg/cm² or 2.1 µg/cm² (5 µl/cm², 12 cm²). The high dose thus corresponds to an arsenic concentration of

0.42 g/l. The elimination of arsenic with the urine was monitored during the exposure and 6 days after the exposure and the dose absorbed through the skin was adjusted on the basis of the amount eliminated with the urine after intravenous administration. 6.4% of the low arsenic dose was absorbed and 2.0% of the high dose. After the application of soil material containing arsenic, 3.2% to 4.5% of the applied dose was absorbed through the skin (Wester et al. 1993). Thus, for the high dose in water, 2.1 µg/cm² × 12 cm² × 0.02 = 0.5 µg was absorbed, which represents a flux of 0.5 µg/12 cm² within 24 hours = 1.7 ng/cm² and hour.

Investigations by Lowney et al. (2007), who exposed monkeys semi-occlusively to soil material containing arsenic (1230 to 1400 mg arsenic/kg soil material) for 8 hours, showed that dermal absorption was negligible (< 0.5%). After 8-hour application of soluble sodium arsenate heptahydrate (presumably disodium arsenate) (2.8 g arsenic/l, 5 µl/cm², about 1400 µg arsenic on 100 cm², about 14 µg/cm²) with subsequent washing of the skin, between 1% and 16% (on avarage about 4%, about 60 µg arsenic) was eliminated with the urine. The 8-hour mean value corresponds to a flux of 72.5 ng/cm² and hour, and under standard conditions (2000 cm² skin area) to 145 µg arsenic.

In flow cells with dermatomed human skin (1 cm²), 2% of the applied amount of arsenic acid was absorbed, determined as the sum of the concentration in the receptor fluid and in the skin (Wester et al. 1993). As the data given in the publication were insufficient, a flux cannot be calculated, but the percentage amount absorbed is in agreement with that determined in monkeys (see above).

Sodium arsenate (no other details) was applied as the solid or in aqueous solution (5, 50 or 500 ng in 100 or 250 µl) and in soil material for 24 hours to excised full-thickness mouse skin (0.64 cm²) in a flow cell. The skin was washed and the amount that had penetrated into the receptor fluid (HEPES buffered Hanks' balanced salt solution) and the skin was determined. In the skin and the receptor fluid 30% to 62% of the dose was recovered if the arsenate was applied as the solid or as a solution, but only 0.3% if the substance was applied in soil material (Rahman et al. 1994). The flux calculated from these data is 500 ng × 0.6/0.64 cm² within 24 hours = 20 ng/cm² and hour.

Manifesto (absorption through the skin)

Arsenic and inorganic arsenic compounds are carcinogenic in humans. In addition, long-term exposure causes cardiovascular and neurological disorders, and skin changes.

Absorption through the skin. Arsenic and its inorganic arsenic compounds were previously not designated with an "H" (for substances that can be absorbed through the skin in toxicologically relevant amounts) (documentation "Arsenic and its inorganic compounds (with the exception of arsine)" 2005; supplement "Arsenic and its inorganic compounds (with the exception of arsine)" 2014).

In studies with rats, despite 24-hour occlusive dermal application of gallium arsenide doses as high as 10 000 mg, there was no evidence of clinical changes indicative of toxicity (supplement "Arsenic and its inorganic compounds (with the exception of arsine)" 2014). As there are no other data available that indicate relevant absorption through the skin, gallium arsenide is not designated with an "H".

There are no studies available for the trivalent arsenic compounds, but there are data for pentavalent arsenic compounds (see below) which indicate absorption through the skin. By analogy, the penetration behaviour of pentavalent arsenic compounds very likely also applies to trivalent arsenic compounds.

Animal experiments and in vitro studies with human and mouse skin are available with pentavalent arsenic compounds for arsenic acid (Wester et al. 1993) and sodium arsenate (Dutkiewicz 1977; Lowney et al. 2007; Rahman et al. 1994). Amounts of 2% to 6% were absorbed through human and monkey skin, and up to 60% through mouse skin. Fluxes of up to 72.5 ng/cm^2 and hour were calculated. Under standard conditions this flux corresponds to a daily intake of 145 µg arsenic, which is in the range of the previous provisional tolerable weekly intake of 15 µg arsenic/kg body weight (= 150 µg/day) established by the WHO (1989).

Arsenic and its inorganic arsenic compounds are classified in Category 1 for carcinogenic substances and in Category 3 A for germ cell mutagens. No MAK value could be established. No safe concentration range can therefore be estimated for exposure to the skin-penetrating compounds, so that an increased carcinogenic or genotoxic risk should be assumed even for low amounts absorbed percutaneously. Dermal penetration has been demonstrated for pentavalent arsenic compounds, for trivalent arsenic compounds it may be assumed. The extent of penetration doubtless depends on the solubility of the substance, so that the inorganic arsenic compounds, with the exception of arsenic itself and gallium arsenide, which are both very poorly soluble in water, are designated with an "H".

References

ATSDR (Agency for Toxic Substances and Disease Registry) (2007) Toxicological profile for arsenic. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, GA, USA, http://www.atsdr.cdc.gov/toxprofiles/tp2.pdf

Dutkiewicz T (1977) Experimental studies on arsenic absorption routes in rats. Environ Health Perspect 19: 173–177

ECHA (European Chemicals Agency) (2014) Information on registered substances. Dataset on gallium arsenide (CAS number 1303-00-0), joint submission, first publication 17.03.2011, last modification 11.03.2014, http://echa.europa.eu/web/guest/information-on-chemicals

IFA (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung) (Institute for Occupational Safety and Health of the German Social Accidence Insurance) (2013 a) Arsenic (CAS No. 7440-38-2), GESTIS databank, www.dguv.de/ifa/gestis-database

IFA (2013 b) Arsenic trioxide (CAS No. 1327-53-3), GESTIS databank, www.dguv.de/ifa/gestis-database

IFA (2013 c) Arsenous acid (CAS No. 13464-58-9), GESTIS databank, www.dguv.de/ifa/gestis-database

IFA (2013 d) Sodium arsenite (CAS No. 7784-46-5), GESTIS databank, www.dguv.de/ifa/gestis-database

IFA (2013 e) Arsenic pentoxide (CAS No. 1303-28-2), GESTIS databank, www.dguv.de/ifa/gestis-database

IFA (2013 f) Trisodium arsenate (CAS No. 13464-38-5), GESTIS databank, www.dguv.de/ifa/gestis-database

Lowney YW, Wester RC, Schoof RA, Cushig CA, Edwards M, Ruby MV (2007) Dermal absorption of arsenic from soils as measured in the Rhesus monkey. Toxicol Sci 100: 381–392

Rahman MS, Hall LL, Hughes MF (1994) In vitro percutaneous absorption of sodium arsenate in B6C3F1 mice. Toxicol In Vitro 8: 441–448

Wester RC, Maibach HI, Sedik L, Melendres J, Wade M (1993) In vivo and in vitro percutaneous absorption and skin decontamination of arsenic from water and soil. Fundam Appl Toxicol 20: 336–340

WHO (World Health Organization) (1989) Toxicological evaluation of certain food additives and contaminants. WHO Food Additives Series, No. 24. International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, http://www.inchem.org/documents/jecfa/jecmono/v024je08.htm

completed 26.02.2014