HBM Biological Application Data Sheet

Update: May 2010

ACRYLONITRILE

Identity

Name (parent)	Acrylonitrile
UN number	1093
CAS number	107-13-1
Intervention value (AGW in mg/m3)	50 (irritation, reprotoxicity)
Structure	C3H3N

Occurrence

Chemical state (at 20°C)	Liquid
Physical appearances	Colorless to pale-yellow liquid, with a sharp onion / garlic-like odor; highly flammable
Industrial products	Production of plastics, synthetic rubber, and acrylic fibers

Physicochemical properties

Molecular weight	53.06
Vapor pressure (mbar at 20°C)	124
Octanol/water partition coefficient (log Po/w)	-0.9
Water solubility (in mg/L at 25 °C)	73,000

Toxicokinetics (parent)

Uptake by inhalation	Approximately 50% of inhaled acrylonitrile is absorbed though the lungs: In a human experiment with 6 male volunteers, 52% of inhaled dose of acrylonitrile was absorbed through the lungs [1]. In three volunteers a retention of 46± 1.6% was observed [2].
Uptake by skin absorption	Acrylonitrile can be absorbed both as a vapor and a liquid through the skin: - After application on the forearms skin of 4 human volunteers absorption was estimated to be 0.6 mg/cm2/hr [2]. - The extent of absorption of acrylonitrile vapor through the skin of rabbits was 1% of that absorbed through the lungs [3].
Uptake via gastrointestinal tract	Acrylonitrile is extensively absorbed in animals: in male rats absorption after oral ingestion was nearly complete [3].
Distribution	Rapid distribution throughout the body after inhalation exposure and oral exposure [2].
Metabolism	- Main pathway: conjugation of acrylonitrile. Involved enzymes: GSH transferase, glutathionase [2]. - Oxidation pathway: cytochrome P450, mainly CYP2E1 [2, 4].
Excretion via lungs	In rats, ten days after a single oral dose, 13% of the dose was excreted in exhaled air as unchanged acrylonitrile, CO2 and hydrogen cyanide [3].
Excretion via urine	In rats, ten days after a single oral dose, 61% of the dose was excreted in urine Predominant as unmetabolized acrylonitrile and metabolites thiocyanate, 2-cyanoethylmercapturic acid [3].
Excretion via feces	Minor excretion route. In rats, ten days after a single oral dose, 3% of the dose was excreted in feces [3].
Elimination kinetics	First-order kinetics, with a half-life of 7 to 8 hours [1].

Toxicodynamics

Mechanisms of toxicity	Oxidative metabolism leads to the formation of cyanoethylene oxide (CEO) and cyanide. Acrylonitrile and CEO both bind to tissue thiols, leading to depletion of glutathione. CEO is reacts with DNA and is mutagenic. Cyanide affects the central nervous system [2].
Classifications for carcinogenicity	Group 2B (IARC); possibly carcinogenic to humans [5].
Classifications for reprotoxicity	Acrylonitrile is teratogenic in rats: inhalation and oral exposure resulted in fetal malformations [2]. Acrylonitrile induces male reprotoxicity, both in animals and humans. In acrylonitrile exposed workers, sperm density and sperm numbers per ejaculum

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	were significantly lower than in controls [6].
Classifications for sensitizing properties	Can cause skin sensitization with allergic rashes [7].

Biological monitoring

Biomarkers	Hemoglobin adducts of acrylonitrile (N-2-cyanoethylvaline)	Acrylonitrile in urine	2-Cyanoethylmercapturic acid (CEMA) in urine	Thiocyanate in urine
Molecular weight	170.2	53.06	216.3	58.08
Enzymatic metabolism	Cytochrome P450 (CYP2E1)	-	GSH transferase, glutathionase	Cytochrome P-450 system
Biological material	Venous blood sample	Urine	Urine	Urine
Type of sample	Whole blood	Spot urine	Spot urine	Spot urine
Sampling strategy	Collection of blood samples within a few weeks after exposure.	< 24 h	< 24 h	< 96 h
Excretion pattern	Linear elimination during lifespan of erythrocytes (126 days) [8] (zero order kinetics)	Elimination half-life: approximately 8 hours (1st order kinetics)	Elimination half-life: 7-9 hours [1] (1st -order kinetics)	Elimination thiocyanate (in serum): 2.7 days ± 1.1 (1st-order kinetics) [9]
Materials	Test tubes containing an anticoagulant agent, such as heparin or EDTA.	Polystyrene universal container	Polystyrene universal container	Polystyrene universal container
Transportation	Transportation within 24 hours to the laboratory for separation of the red blood cells	Cooled: 4°C	Cooled: 4°C	Cooled: 4°C
Storage	Fresh blood can be stored for up to 24 hours at 4 °C; separated and rinsed red blood cells should be stored below -20°C.	-20°C	4°C (refrigerated) [1] Below 0°C	-20°C
Stability	Not reported	Not reported	Not reported	Not reported
Measurement principle	GC-MS-MS [8]	Static head space analysis combined with GC/ nitrogen phosphorus detector [2] Azeotropic distillation – GC [2]	GC-FID [1]	Colorimetric König reaction, after anion exchange. Absorbance is measured at 608 nm [10]
Aliquot for 1 analysis	7.5 mL [8]	2.5 mL	2.5 mL [1]	2.5 mL
Limit of quantification	4 pmol / g globin (limit of detection) [8] / 2 pmol / g globin (limit of detection) [11]	- 2 ng/mL (HS-GC) [2] - 5 ng/mL	1 mg CEMA / L urine [1]	1 µg/mL [10]

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			(azeotropic distillation – GC) [2]		
Recommended adjustments	Correction by globin; correction for smoking		- Specific gravity - Adjustment for creatinine	- Specific gravity - Adjustment for creatinine	- Specific gravity - Adjustment for creatinine
Preferred units for expression of results	pmol / g globin		mg / L mg/mmol creatinine [12]	mg / L	mg/L
Conversion factor	10 µg N-2-cyanoethylvaline / L blood = 408 pmol / g globin [13]		1 mg/L = 18.85 * 10^{-3} mmol/L	1 mg/L = 4.62 *10^{-3} mmol/L	1 mg/L = 17.22 * 10^{-3} mmol/L
Biological exposure US	-		-	-	-
Biological exposure value Germany [14]	Acrylonitrile in air (mg/m^3) 0.3 0.5 1 7	Cyanoethylvaline in erythrocytes (µg/L blood) 16 35 60 420	-	-	-
BIOMONECS background in non-smoking m/f adults (based P0.95)	-		-	-	-
Background values	< 2 pmol / g globin [11] (non-smokers) 106 pmol / g globin (smokers) [11]		2 µg / g creatinine (non-smokers) [15]	Not reported	2.5 mg / g creatinine (non-smokers) [15]
Possible confounders	Active smoking, intake of thiocyanate-containg food, thiocyanogenic glucosides and cyanogenic glucosides, the use of the drug sodium nitroprusside.				

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