STYRENE

Identity

Name (parent)	Styrene
UN number	2055
CAS number	100-42-5
Intervention value (AGW in mg/m^3)	1000
Structure	C_8H_8

Occurrence

Chemical state (at 20°C)	Liquid
Physical appearances	Colorless liquid with a sweet smell
Industrial products	Combustion product (automobile exhaust, cigarette smoke), styrene is used to produce plastic and rubber.

Physicochemical properties

Molecular weight	104.2
Vapor pressure (mbar at 20°C)	7
Octanol/water partition coefficient (log Ko/w)	3.2
Water solubility (in g/100 mL)	0.03

Toxicokinetics (parent)

Uptake by inhalation	Retention of inhaled styrene in humans was found to range from 42% to 97% [1].
Uptake by skin absorption	Skin absorption of its vapor phase is negligible [1]. In a human experiment, where liquid styrene was applied to the forearms of male volunteers, it was found that the absorption rate of liquid styrene was 9 to 15 mg/cm^2/hr, and the absorption rates from aqueous solutions were 40-180 µg/cm^2/hr at a mean (range) dose of 66 (5-269) mg/L [2]. In a human experiment with male volunteers who dipped their right hand into liquid styrene, the absorption rate of styrene was 1 ± 0 5 µg /cm^2 / min [3].
Uptake via gastrointestinal tract	Uptake of styrene from the gastrointestinal tract was rapid and complete in rats deprived of food overnight and administered, via gavage, 9.3 mg/kg styrene in aqueous solution. The uptake was much slower when styrene was administered in vegetable oil [4].
Distribution	Styrene is distributed throughout the body, with highest concentrations in adipose tissue.
Metabolism	There are several metabolic pathways for styrene: The primary pathway is oxidation of the side chain by cytochrome P450 to form styrene 7,8-oxide. Styrene oxide is predominantly metabolized by epoxide hydrolase to form styrene glycol; styrene glycol is subsequently converted to mandelic acid, phenylglyoxylic acid, and hippuric acid. Styrene 7,8-oxide can also be conjugated with glutathione to ultimately form phenylhydroxylethylmercapturic acids. A minor pathway of styrene metabolism involves the formation of phenylacetaldehyde from styrene 7,8-oxide or cytochrome P450 conversion of styrene to phenylethanol and subsequent metabolism to phenylacetic acid. An alternative minor pathway involves ring oxidation resulting in the production of styrene 3,4-oxide, which is further metabolized to 4-vinylphenol [5].
Excretion via lungs	After subcutaneous injection of styrene-ß-^{14}C in rats, 12% was excreted as CO_2 and 3% as unchanged styrene after 24 hours [6]. < 5% is excreted as unchanged styrene with expired air [1].
Excretion via urine	Major route of elimination. Excretion as unchanged styrene or metabolites (e.g. mandelic acide and phenylglyoxylic acid). After subcutaneous injection of styrene-ß-^{14}C in rats, 71% was excreted in urine after 24 hours [6].

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Excretion via feces	Minor excretion route. After subcutaneous injection of styrene-ß-^{14}C in rats, <3% was excreted in feces after 24 hours [6].

Toxicodynamics

Toxicity	Neurotoxicity: the central nervous system is the critical target organ [5]. Irritation of the skin, eyes and mucous membranes [5]
Classifications for carcinogenicity	Group 2B, IARC-classification [7]
Classifications for reprotoxicity	Animal studies: Teratogenic effects of styrene are only seen at exposure levels causing maternal toxicity [8].
Classifications for sensitizing properties	Exposure to styrene can cause allergic contact dermatitis and asthma [9, 10].

Biological monitoring

Biomarkers	**Mandelic acid (MA) in urine**	**Phenyl glyoxylic acid (PGA) in urine**	**Styrene in whole blood**
Molecular weight	152.1	150.1	104.2
Involved enzymatic metabolism	CYP 450 and epoxide hydrolase, alcohol dehydrogenase, aldehyde dehydrogenase [5]	CYP 450 and epoxide hydrolase, alcohol dehydrogenase, aldehyde dehydrogenase [5]	-
Biological material	Urine	Urine	Blood
Type of sample	Spot urine	Spot urine	Whole blood
Sampling strategy	< 24 h	< 24 h	< 1 h
Excretion pattern	Bi-phasic elimination pattern, with half-lives of 4-9 h (fast elimination phase) and 17 – 25 h (slow elimination phase) [11]	Half-life of 11 h in a one compartment model simulation [11]	Excretion pattern styrene from blood: bi-phasic with half-lives of 0.58 and 13.0 hours [5]
Materials	Polystyrene universal container	Polystyrene universal container	Vacutainers containing heparin
Transportation	Room temperature [12]	4°C (within 4 hours) [12]	4°C
Storage	4°C or -20°C	-20°C [12]	4°C
Stability	Up to 70 days at 4°C and -20°C [12]	4 days at 4°C [13]; Up to 70 days at -20°C [12]	Not reported
Measurement principle	HPLC	HPLC	GC-MS[14]; headspace solid-phase microextraction (SPME) / GC / MS [15]
Aliquot for 1 analysis	1 mL [16]	1 mL [16]	3 mL
Limit of quantification	0.015 g / L (limit of detection) [16]	0.002 g / L (limit of detection) [16]	LOD 0.008 ng / mL (GC-MS) [14]; 30 pg/mL (SPME-GC-MS) [15]
Recommended adjustments	Creatinine	Creatinine	n/a
Preferred units for expression of results	mg / g creatinine	mg / g creatinine	mg/L
Conversion factor	1 mg / g creatinine = 0.74 mmol / mol creatinine	1 mg / g creatinine = 0.75 mmol / mol creatinine	1 mg/L = 9.60 * 10^{-3} mmol / L
Biological exposure value US [17]	400 mg / g creatinine (MA + PGA in urine; end of shift)		0.2 mg/L (end of shift)

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Biological exposure value Germany [18]	600 mg/ g creatinine (excretion of MA + PGA in urine)	n/a
Background value	Not available	Median: 172 ng/L Range: 7 – 963 ng/L [19]
Possible confounders	Active smoking; Ethanol in combination with styrene reduces the elimination rate of MA and PGA [1]	Active smoking

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