

Lithium and its compounds – Addendum: re-evaluation of the BAR

Assessment Values in Biological Material – Translation of the German version from 2026

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Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area re-evaluated the data of inorganic lithium compounds (as Li [7439-93-2]) to update the biological reference value (BAR). As lithium is an essential component of modern technologies, lithium-ion batteries in electric vehicles and portable electronic devices in particular have led to increasing occupational exposure and a possible increase in environmental pollution in recent years. In current studies, the 95th percentiles of background concentrations in the urine of occupationally unexposed persons in Germany were in the range of 100 µg lithium/l urine. Therefore, a BAR of 100 µg lithium/l urine has been derived. Sampling time is not fixed in the steady state.

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BAR (2025)**100 µg lithium/l urine**

Sampling time: not fixed in the steady state

Lithium [7439-93-2]**and more irritating lithium compounds (such as lithium amide, lithium hydride, lithium hydroxide, lithium nitride, lithium oxide, lithium tetrahydridoaluminate, lithium tetrahydroborate)****MAK value**

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Lithium compounds, inorganic**(as Li [7439-93-2]) with the exception of lithium and more irritating lithium compounds (such as lithium amide, lithium hydride, lithium hydroxide, lithium nitride, lithium oxide, lithium tetrahydridoaluminate, lithium tetrahydroborate)****MAK value (2013)****0.2 mg lithium/m³**

Prenatal toxicity

Pregnancy Risk Group C

Re-evaluation

Lithium is a silvery-white, soft alkali metal. This light metal is ubiquitous in nature; however, due to its high reactivity, it does not occur in its elemental form. Lithium is ingested through the diet, so background exposure may vary significantly by region. In psychiatry, lithium salts have been used therapeutically for decades to treat bipolar disorder and recurrent depressive episodes. Lithium is an essential component of modern technologies. In recent years, increases in occupational exposure as well as possible increases in environmental exposure have resulted particularly from the use of lithium-ion batteries in electric vehicles and portable electronic devices. To account for this growing significance for affected workers, the biological reference value (BAR) for lithium, which was last evaluated in 2011 (translated in Schaller 2021), has been re-evaluated based on the current literature.

Metabolism and toxicokinetics

Lithium can be absorbed orally, by inhalation and, to a lesser extent, through the skin. 80–100% of orally ingested lithium is absorbed into the gastrointestinal tract. Lithium binds only to a small extent to plasma proteins and is also not metabolised. 90–95% is excreted via the kidneys; the elimination half-life is 12–27 hours (Hartwig 2014).

Critical toxicity

Since lithium has been used for the treatment of psychiatric illnesses since the mid-20th century, its effects – but also its side effects – on the human body are well known. As lithium only possesses a narrow therapeutic index, therapeutic drug monitoring is indicated. The therapeutic range lies between 0.5–1.5 mmol/l serum/plasma (Lewitzka and Haußmann 2022).

In 2002, the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG) comprehensively investigated the side effects of lithium and created a table of the most frequent side effects based on concentrations of lithium in blood (Table 1).

Tab. 1 Side effects based on lithium concentration in serum/plasma (NEG 2002)

Lithium in serum/plasma		Side effect
[mM Li]	[µg/l]	
0.5–0.8	3470–5552	reversible moderate nephrogenic diabetes insipidus, fine hand tremor, weight gain, increased TSH values, hypothyreosis, diarrhoea, oedema, acne-like eruptions
0.6–0.8	4164–5552	no significant changes of tubular functions or GFR
0.75–0.95	5205–6593	decreased urine concentrating ability, increased urine volume
1.0–1.5	6940–10 410	tremor, lethargy, irritability, muscle weakness, slurred speech
1.6–2.5	11 104–17 350	disorientation, confusion, drowsiness, restlessness, unsteady gait, coarse tremor, dysarthria, muscle fasciculations
> 2.5	> 17 350	impaired consciousness (with progression to coma), delirium, ataxia, generalised fasciculation, extrapyramidal symptoms and convulsions

GFR: glomerular filtration rate; TSH: thyroid-stimulating hormone

Reversible, moderate nephrogenic diabetes insipidus was observed as the most frequent side effect with a prevalence of 25%, followed by weight gain and slight hand tremors at prevalence rates of 20% and 15%, respectively. Hypothyroidism has a prevalence of 5% in women over 40 years of age.

Further information on local effects as well as effects on the central nervous system, the kidneys, the thyroid gland, the male reproductive system, and on developmental toxicity have been described in Hartwig (2014). Moreover, information on the effects on the central nervous system is likewise available at low lithium levels (Liaugaudaite et al. 2022; Memon et al. 2020).

Selection of indicators

Lithium and its inorganic compounds can be measured in the following biological fluids: whole blood, serum, plasma, urine, and saliva (see also translated in Schaller 2021). The determination of lithium has been established for blood and urine. Therapeutic monitoring of lithium levels in serum or plasma is standardised clinical practice. Up to 96% of lithium is excreted via the kidneys. Indications for the parameter lithium in urine as a reference value for environmental exposure can be found in the literature. It should be noted that nephrotoxic effects have been reported at higher lithium concentrations, which in turn may lead to dilution effects and thus potentially inaccurate lithium levels in the urine.

Analytical methods

Primarily ICP-MS (inductively coupled plasma mass spectrometry; Heitland and Köster 2004, 2006, 2021) and, to a lesser extent, ICP-OES methods (inductively coupled plasma optical emission spectrometry; see also Schaller 2021) have been applied as investigative methods. A reliable ICP-OES method has been published by the Commission (Schramel et al. 1997), and a validated ICP-MS method for determining lithium in urine is due to be published shortly (Göen et al. 2027). Given their limits of detection and quantification, the available methods are suitable for reliably determining lithium concentrations in the background level range. In earlier studies, AAS (atomic absorption spectroscopy) has also proved to be a valid method for determining lithium levels (Trapp 1985).

Background exposure

Given that the exposure was predominantly diet-related, two German studies were selected in 2011 to establish an initial BAR of 50 µg lithium/l urine (Schaller 2021). Since then, further studies on background exposure have been published (Barbosa et al. 2023; Bertram et al. 2023; Chai et al. 2022; Enderle et al. 2020; Heitland and Köster 2021; Hoet et al. 2013;

Jayawardene et al. 2021; Liu et al. 2021). In the studies by Bertram et al. (2023) and by Heitland and Köster (2021), lithium was determined in urine. Table 2 summarises the results of German studies on background exposure levels of lithium.

Tab. 2 Lithium in whole blood, serum, plasma and urine: background exposure in Germany

Material	Persons	Lithium [µg/l]					Literature
		Mean	Median	GM	Range	95 th perc.	
Plasma	928	–	0.96	–	–	(1.37) ^{a)}	Enderle et al. 2020
	396 ♀	–	1.03	–	–	(1.43) ^{a)}	
	532 ♂	–	0.92	–	–	(1.32) ^{a)}	
Whole blood	102 (64 ♂, 38 ♀)	0.93	–	0.82	0.41–9.9	1.4	Heitland and Köster 2021
Serum	102	1.3	–	1.03	0.3–16.9	3.2	
Urine	102	27.6	–	–	2–416	103	
Urine	87 (40 ♂, 43 ♀) ^{b)}	35	–	23	4–237	115	Heitland and Köster 2006
Urine	63 (♂, ♀ n.s.)	18	–	14	3–86	47	Heitland and Köster 2004
Urine	88						Bertram et al. 2023
	Group 1: 22 ♂	29.5	–	–	5.8–87.5	86.7	
	Group 2: 35 ♂	56.2	–	–	4.1–336.4	259.1 ^{c)}	
	Group 3: 31 (21 ♂, 10 ♀)	59.8	–	–	1.0–287.1	254.6 ^{c)}	

a) 75th percentile

b) Information from the publication

c) Occupational exposure could not be ruled out, samples from the outpatient clinic at RWTH Aachen:

Group 1: 22 workers from a steel-processing plant

Group 2: 35 workers from a copper-processing plant

Group 3: 31 individuals (heterogeneous occupational backgrounds regarding exposure to metals or non-occupational background)

GM: geometric mean; n.s.: not specified

Re-evaluation of the BAR

According to current studies, the 95th percentile of background exposure to lithium in urine of the general population is generally well above the previous BAR of 50 µg lithium/l urine. In the study by Bertram et al. (2023), which involved three exposure groups, occupational exposure to lithium cannot be ruled out. The 95th percentile of 86.7 µg lithium/l urine calculated for one exposure group lies within the range described by Heitland and Köster.

Under consideration of the current literature in Germany, in which the 95th percentiles for background exposure to lithium in urine were found to be 115 µg/l (Heitland and Köster 2006) and 103 µg/l (Heitland and Köster 2021),

a BAR of 100 µg lithium/l urine is derived.

There are no restrictions on sampling time.

Interpretation

The BAR is based on normally concentrated urine for which the creatinine concentration should lie within a range of 0.3–3 g/l. For urine samples outside of the aforementioned range, it is generally recommended to repeat measurement with normally hydrated subjects (translated in Bader et al. 2016). Due to the risk of nephrotoxicity associated with lithium, an additional blood analysis is recommended in cases of a significant exceedance of the BAR.

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (https://www.dfg.de/mak/conflicts_interest) ensure that the content and conclusions of the publication are strictly science-based.

The views expressed in these publications are those of the individual authors acting in their personal capacity as experts and do not represent the positions of their respective institutions or employers.

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