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Determination of trace elements in urine by inductively coupled plasma-tandem mass spectrometry – Biomonitoring of adults in the German capital region

Andy Schmied [a,*], Aline Murawski [b], Marike Kolossa-Gehring [b], Peter Kujath [a]

[a] Federal Institute for Occupational Safety and Health (BAuA), Berlin, Germany
[b] German Environment Agency (UBA), Berlin, Germany

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ABSTRACT

A method was developed and validated for multi-element analyses of human urine samples using inductively coupled plasma-tandem mass spectrometry. The combination of a simple sample preparation and the state-of-the-art technique allows high-throughput and lowest limits of quantification up to 1 ng/L. Thereby coefficients of variation ranges from 0.4% (V) to 3.7% (Be), and 0.9% (Cd) to 4.8% (Ni) for intraday and interday precision, respectively. The method's performance is demonstrated by successful participation in international interlaboratory comparison programs as external quality assurance.

Moreover, the method was applied for the analysis of first-morning void urine samples of adults (N = 77) living in the German capital region. 15 metals and metalloids (As_{total}, Be, Bi, Cd, Co, Cr, In, Mn, Mo, Ni, Pb, Sn, Tl, V, and Zn) were determined. With exception of indium, all elements were found in urine samples above the limit of quantification, demonstrating the suitability to measure the general population's exposure to these metals and metalloids. The method presented here shall be used for analysis of urine samples collected in the upcoming German Environmental Survey, GerES VI, a cross-sectional, population-representative study.

1. Introduction

Biomonitoring is an important tool to assess both the occupational and the general population's exposure to chemicals (Ganzleben et al., 2017; Louro et al., 2019). It aggregates exposure from different pathways and from different sources by measuring the concentration of a substance and/or its metabolites in human biological matrices, preferably urine and blood. For ubiquitous substances such as metals, metalloids, and their compounds, where exposure occurs e.g. through diet, at workplaces, and from different environmental sources, biomonitoring provides a more accurate estimation of the body burden compared to modelling approaches (Louro et al., 2019).

Several metals, metalloids, and their compounds possess hazardous properties (e.g. mutagenicity, carcinogenicity, and toxicity for reproduction), and have been proposed as substances of very high concern. To reduce exposure, their use has been restricted. At EU level there are restrictions for arsenic, cadmium, chromium, mercury, lead, and their compounds listed in the Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (EU, 2006). To evaluate the effectiveness of these measures and to identify the demand for additional regulation, accurate data on the general population's exposure are required. Furthermore, these data are necessary to assess and specifically address occupational exposure by supplying information on the background exposure of the general population for comparison. Therefore, several countries established human biomonitoring programs and carried out cross-sectional studies. In particular besides Germany: Belgium (Schoeters et al., 2012; Hoet et al., 2013), Canada (Saravanabhavan et al., 2017) the Czech Republic (Batáriová et al., 2006; Černá et al., 2007), France (Fréry et al., 2012), Italy (Aprea et al., 2018), and the USA (CDC, 2019).

Abbreviations: AM, arithmetic mean; As_{total}, total arsenic; BAR, Biological Reference Values for Chemical Compounds in the Work Area; CV coefficient of variation, CRC; collision reaction cell, GerES; German Environmental Survey, G-EQUAS; German External Quality Assessment Scheme, ICP-MS; inductively coupled plasma mass spectrometry ICP-MS/MS, inductively coupled plasma-tandem mass spectrometry; GM, geometric mean; HBM-1, human biomonitoring value 1; LOQ, limit of quantification; N, sample size; P, percentile; QMEQAS, Quebec Multielement External Quality Assessment Scheme; sf-ICP-MS, sector field ICP-MS.

* Corresponding author. Nöldnerstraße 40/42, 10317, Berlin, Germany.
E-mail address: Schmied.Andy@baua.bund.de (A. Schmied).

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In Germany, complementary to the human samples in the Environmental Specimen Bank collected from young occupationally not specifically exposed adults, the German Environmental Survey (GerES) as a population-representative, cross-sectional biomonitoring program for the general population has been established since the early 1980s (Kolossa-Gehring et al., 2012). GerES has repeatedly been conducted in close cooperation with the health examinations of the Robert Koch Institute on adults, children, and adolescents, completing the latest cycle, GerES V, on 3-17-year-olds in 2017 (Schulz et al., 2007, 2017). The last survey on adults aged 18–69 was GerES III, sampled 1997–1999.

Hence, for Germany there are no current, population-representative data on adult's exposure to metals and metalloids and only a limited number of elements has been determined in urine samples in the past German Environmental Surveys (Schulz et al., 2007). To close the data gap, a broader spectrum of elements shall be analysed in samples of the upcoming GerES VI.

Focus of this publication is the validation of a method that will be used to determine metal and metalloid concentrations in urine samples of GerES VI using inductively coupled plasma-tandem mass spectrometry (ICP-MS/MS). In general, inductively coupled plasma-mass spectrometry (ICP-MS) is the state-of-the-art technique for multi-element analysis in biological samples. In the biomonitoring studies mentioned above high-resolution sector field ICP-MS (sf-ICP-MS) or quadrupole-based ICP-MS instruments equipped with collision-reaction cells (ICP-CRC-QMS) were used to overcome spectral overlaps. In contrast, our method uses the advantages of tandem mass spectrometry to resolve spectral overlaps and to achieve low limits of quantification (LOQ). The methods performance is demonstrated by internal and external quality assurance. Furthermore, results from 77 adults participating in the GerES VI pilot study that took place in the German capital region, are shown.

2. Materials and methods

2.1. Reagents and chemicals

All solutions were prepared using ultrapure water provided by a water purification system (18.2 MΩ cm). All chemicals and single element standards used for analysis were of highest purity and suitable for ICP-MS. Nitric acid (Normatom®) was supplied by VWR (Darmstadt, Germany). Single Element standards were provided either by VWR or Agilent technologies (Waldbronn, Germany). Lyophilised control materials were supplied by Recipe (ClinChek® (Lot. 1227), Munich, Germany) and Invicon (Seronorm^{TM}, Lot. 1403080, 1706878, Munich, Germany). Samples of the 64th G-EQUAS (Erlangen-Nuremberg, Germany) were used as additional reference materials.

2.2. Instrumentation

Multi-element analysis was carried out on an Agilent 8900 ICP-MS/MS equipped with a SPS-4 autosampler and an ISIS 3 sample introduction system (Agilent technologies, Waldbronn, Germany). Operation conditions were optimised daily to obtain a maximum sensitivity, oxide ratio <1% ($^{140}Ce^{16}O^{+}/^{140}Ce^{+}$) and doubly charged ratio <2% ($^{140}Ce^{2+}/^{140}Ce^{+}$). To avoid interferences, helium was used as collision gas in the Single Quadrupole mode, whereas oxygen was applied as reaction gas in the MS/MS mode. According to the characteristic of each element the gas mode was chosen as listed in Table 1. Further operation conditions are summarised in Table 2.

2.3. Sample preparation

To avoid sample contamination, the sample preparation was performed under a laminar flow hood, metal free tubes were used for dilution steps, pipette tips were cleaned with 2% (v/v) nitric acid prior use, and the prepared samples were measured directly after preparation.

The deep frozen urine samples were thawed on an overhead rotator. For sample preparation 400 μL of a urine sample were mixed with 3.2 mL 2% (v/v) nitric acid and 400 μL of an internal standard solution. ^{103}Rh and $^{159}Tb(^{16}O)$ were used for internal standardization. The concentration of the internal standards was 2.5 μg/L in all prepared sample and calibration solutions.

Freeze-dried certified reference materials were reconstituted following the procedure provided by the manufacturer's instructions and then treated like thawed urine samples.

Certified reference materials were analysed at the start and end of each analytical run and after every 20th sample. In compliance with the FDA guideline on bioanalytical method validation (FDA, 2018) the total number of quality controls was at least 5% of the total number of unknown samples. Due to the lack of certified reference materials containing bismuth and indium, spiked pool urine samples were used for these elements.

Determination of the creatinine content was performed according to the Jaffé method (Blaszkewicz and Liesenhoff-Henze, 2010) using a Sunrise absorbance microplate reader (Tecan, Männedorf, Switzerland).

Table 1
Instrument modes, integration time and internal standards for analysed elements.

Element	Instrument mode	Integration time/s	Internal Standard
As	O_2, mass-shift	3	TbO
Be	No gas	2	Tb
Bi	No gas	2	Tb
Cd	O_2, on-mass	3	Rh
Co	He	1	Rh
Cr	He	1	Rh
In	He	1	Tb
Mn	He	1	Rh
Mo	O_2, mass-shift	1	TbO
Ni	He	1	Rh
Pb	No gas	2 each isotope	Tb
Sn	He	2	Tb
Tl	No gas	2	Tb
V	O_2, mass-shift	1	TbO
Zn	He	1	Rh

Table 2
ICP-MS/MS operating conditions.

RF Power	1550 W		
Nebulizer gas flow	1 L/min		
Auxiliary gas flow	0.9 L/min		
Plasma gas flow	15 L/min		
Nebulizer type	MicroMist		
Spray chamber	Scott type		
Replicates	3		
Sweeps/ Replicate	50		
Gas mode	No gas	He mode	O_2 mode
Cell gas flow	0 mL/min	He: 4.6 mL/min	O_2: 0.5 mL/min
m/z Q1			51 (V) 75 (As), 98 (Mo), 114 (Cd), 103 (Rh), 118 (Sn), 159 (Tb)
m/z Q2	9 (Be), 159 (Tb), 205 (Tl), 206, 207, 208 (Pb), 209 (Bi)	52 (Cr), 55 (Mn), 59 (Co), 60 (Ni), 66 (Zn), 103 (Rh), 115 (In), 118 (Sn), 159 (Tb)	67 (VO), 91 (AsO), 103 (Rh), 114 (Cd), 118 (Sn), 130 (MoO_2), 175 (TbO)

2.4. Calibration

A matrix-matched calibration was applied using a pooled urine sample.

First, multielement stock solutions were prepared freshly in PFA flasks by diluting 10 μg/L single element standards.

For the calibration standards, defined volumes of the stock solutions were mixed with 400 μL of the pooled urine sample and 400 μL of the internal standard solution and then filled up to a final volume of 4 mL with 2% (v/v) nitric acid.

With exception of tin, eight calibration solutions were prepared. The added concentrations were in the range from 0.005, to 2 μg/L. For the elements As, Mo, Zn the added concentrations in the same solutions were in the range from 0.05 to 20 μg/L. For tin ten calibration solutions were prepared. The added concentration in the two additional calibration solutions were 100 and 200 μg/L.

2.5. Study population sample collection

To ensure consistency with previous GerES cycles, first-morning void urine samples were collected. All participants (N = 77) were volunteer, non-specifically occupationally exposed adults, living in the area of Berlin. They provided informed consent and the Ethics Committee of the Berlin Chamber of Physicians approved the project (Eth-31/18). 43 adults were female, 34 were male. The participant's age was in the range of 19–78 years (arithmetic mean: 45.8 a).

Urine samples were collected in polyethylene containers which were cleaned with 2% (v/v) nitric acid prior collection. Complete amounts of first-morning void urine were collected by the participants themselves at their homes. Furthermore, 15 field blanks (polyethylene containers filled with ultrapure water) were opened for a short period of time at selected participant's homes.

All samples were, aliquoted in polypropylene tubes (Sarstedt, Germany), frozen (−20 °C) and kept frozen until analysis.

2.6. Statistical analysis

Generated concentration data were analysed descriptively using MS Excel. Biomarker concentrations below the LOQ were assigned with the value half of the LOQ. Following the US EPA recommendation (US EPA, 1998), this substitution approach was used solely for the calculation of mean values when less than 15 percent of the measured values were below the LOQ. Percentiles were calculated using the quantile function of MS Excel.

3. Result and discussion

3.1. Method validation

In human urine samples the elements As, Be, Bi, Cd, Co, Cr, In, Mn, Mo, Ni, Pb, Sn, Tl, V, and Zn can occur in ranges from a few ng/L to mg/L. Our aim was to determine all of these elements in a single method and thereby keep this method as simple as possible. In general, the determination of element concentrations in biological samples using ICP-MS is compromised by polyatomic ions having the same mass-to-charge ratio as the analyte ions. However, several polyatomic interferences described for urine analyses such as $^{43}Ca^{16}O^{+}$ on $^{59}Co^{+}$, $^{44}Ca^{16}O^{+}$ on $^{60}Ni^{+}$ and $^{40}Ar^{12}C^{+}$ on $^{52}Cr^{+}$ could already be resolved sufficiently using ICP-CRC-QMS and helium as collision gas (Heitland and Köster, 2004; Morton et al., 2014). Some elements exhibit no relevant interferences. Therefore, the determination of cobalt, chromium, indium, manganese, nickel, and tin was conducted in the single-quadrupole mode of the ICP-MS/MS using helium as collision gas and beryllium, bismuth, lead, and thallium were analysed without a collision gas.

Molybdenum-based polyatomic interferences such as $^{98}Mo^{16}O^{+}$ or $^{97}Mo^{16}O^{1}H^{+}$ can result in an overestimation of cadmium (Jarrett et al., 2008). Neither sf-ICP-MS, nor helium as collision gas in ICP-CRC-QMS enable a cadmium determination without mathematical molybdenum correction (Vrijens et al., 2011). However, with oxygen MoO^{+} can be quantitatively converted into MoO_2^{+}. Since the reaction of $^{114}Cd^{+}$ and oxygen is not favourable, a determination on mass is possible. Thereby, the tandem mode of the ICP-MS/MS enables full control of the reaction. The addition of molybdenum to a native urine sample, did not affect the measured cadmium concentration (0.21 μg/L (no Mo added) *vs.* 0.21 μg/L (added Mo concentration: 1 mg/L)). There are further isotopes that can interfere on Cd isotopes. For that reason a mathematical interference correction was applied for ^{114}Sn a low abundance tin isotope: $I(^{114}Cd) = I(^{114}Cd+^{114}Sn)-0.027\cdot I(^{118}Sn)$. Another mathematical interference correction was necessary for indium: $I(^{115}In) = I(^{115}In+^{115}Sn)-0.016\cdot I(^{118}Sn)$.

As^{+} and V^{+} react readily with oxygen (Balcaen et al., 2015; Bolea-Fernandez et al., 2017) and therefore were determined interference-free in the mass shift mode. The most common interfering ions such as $^{40}Ar^{35}Cl^{+}$ on $^{75}As^{+}$ and $^{35}Cl^{16}O^{+}$ on $^{51}V^{+}$ are removed completely. The addition of sodium chloride (added chloride concentration: 0.5 g/L) to a urine sample did not affect the measured arsenic (15.88 μg/L *vs.* 15.87) and vanadium (19.00 μg/L *vs.* 18.96 μg/L) concentrations. In addition, considerably lower LOQs are reached in comparison to Heitland and Köster (As: 0,02 vs. 0.26 μg/L, V: 0.005 vs. 0.056 μg/L) (Heitland and Köster, 2004). The method was validated regarding method LOQ, accuracy and precision.

The LOQ was determined by $LOQ = 10\cdot CV_b\cdot c/SBR$ using the SBR-RSDB approach (signal-to-background ratio - relative standard deviation of the background) (Boumans, 1991). CV_b is the coefficient of variation of the background intensity of 12 measurements, c is the concentration of the element in solution and SBR is the signal to background ratio.

For internal quality assurance and to evaluate accuracy and precision of the method, control materials in different concentration levels were used. Values were not certified for indium and bismuth. Therefore, a native urine sample was spiked using single element standards. Measured and certified values of the control materials are compared in Table 3. Measured values are average values of ten individual measurements plus-minus the standard deviation. All measured values are within the certified range.

For intraday precision, the same sample was prepared separately ten times on one day. The sample preparation was repeated on nine further days to determine interday precision. For a bioanalytical methods, the European Medical Agency recommends a coefficient of variation (CV) below 15% for intra- and interday precision (EMA, 2011). Intraday CVs ranges from 0.4% for vanadium to 3.7% for beryllium. For interday precision slightly higher CVs were observed in a range from 0.9% (cadmium, manganese, and lead) to 4.8% (nickel).

A native urine sample exhibiting a low burden was spiked to evaluate recoveries of lower concentrations than given in the control materials. Spike recoveries for added concentrations of 15 μg/L for arsenic, molybdenum and zinc, and 0.6 μg/L for chromium and nickel, and 0.15 μg/L for all other trace elements were in the range of 94–106%.

External quality control was assured by participating in international interlaboratory comparison programs performed by the Clinic for Occupational, Social and Environmental Medicine of the Friedrich-Alexander-University Erlangen-Nuremberg (German External Quality Assessment Scheme, G-EQUAS) and the Institut National De Santé Publique Du Québec (Quebec Multielement External Quality Assessment Scheme, QMEQAS). Participation in both programs allows external quality assessment for all measured elements in this study. Table 4 summarises the results. All measured values are within the acceptable range and the deviation of measured and the target values is less than 10%.

Reference materials were diluted with ultrapure water to evaluate the effect of different matrix concentrations on the determined metal and metalloid concentrations. The results are summarised in table S1

Table 3
Validation parameters.

Isotope	LOQ/(µg/L)	Spike recovery[a] (spiked concentration)/% (µg/L)	Control material	Concentration/(µg/L)		CV/%	
				Certified	Measured	Intra-day	Inter-day
^{75}As	0.02	102 (15)	ClinChek 1	43.5 ± 8.7	43.9 ± 0.3	0.7	1.9
			ClinChek 2	82.3 ± 16.4	80.5 ± 0.56	0.7	1.6
^{9}Be	0.003	102 (0.15)	ClinChek 1	0.057 ± 0.016	0.062 ± 0.003	3.7	4.5
			ClinChek 2	0.246 ± 0.062	0.208 ± 0.004	1.8	2.0
^{209}Bi	0.006	97 (0.15)	spiked Pool	0,3[b]	0.301 ± 0.006	0.9	2.0
			spiked Pool	0,6[b]	0.592 ± 0.013	1.5	2.2
^{114}Cd	0.005	94 (0.15)	ClinChek 1	2.47 ± 0.49	2.39 ± 0.025	0.8	1.1
			ClinChek 2	14.3 ± 2.9	14.1 ± 0,12	0.9	0.9
^{59}Co	0.003	95 (0.15)	ClinChek 1	2.03 ± 0.40	1.94 ± 0.029	0.9	1.5
			ClinChek 2	34.3 ± 6.8	33.5 ± 0.55	0.5	1.6
^{52}Cr	0.1	98 (0.6)	ClinChek 1	4.0 ± 0.81	3.8 ± 0.12	0.7	3.1
			ClinChek 2	19.9 ± 4.0	18.8 ± 0.57	0.6	3.0
^{115}In	0.001	94 (0.15)	spiked Pool	0,3[b]	0.308 ± 0.06	1.4	2.0
			spiked Pool	0,6[b]	0.608 ± 0.02	1.4	3.4
^{55}Mn	0.07	103 (0.15)	Seronorm 1	1.38 ± 0.28	1.28 ± 0.04	2.9	3.1
			Seronorm 2	9.3 ± 1.9	9.7 ± 0.08	0.5	0.9
^{98}Mo	0.009	102 (15)	ClinChek 1	23.9 ± 4.8	23.8 ± 0.33	0.5	1.4
			ClinChek 2	99.3 ± 19.8	97.9 ± 1.8	0.6	1.8
^{60}Ni	0.15	102 (0.6)	ClinChek 1	3.24 ± 0.65	3.30 ± 0.16	2.1	4.8
			ClinChek 2	29.6 ± 5.9	28.7 ± 0.44	0.5	1.5
$^{206+207+208}Pb$	0.004	97 (0.15)	ClinChek 1	27.5 ± 5.5	28.4 ± 0.67	0.9	2.4
			ClinChek 2	54.4 ± 10.9	52.2 ± 0.49	1.2	0.9
^{118}Sn	0.03	105 (0.15)	ClinChek 1	5.14 ± 1.02	4.8 ± 0.06	1.1	1.2
			ClinChek 2	10.0 ± 2.0	8.8 ± 0.17	0.9	2.0
^{205}Tl	0.002	104 (0.15)	ClinChek 1	6.8 ± 1.36	7.2 ± 0.11	1.0	1.5
			ClinChek 2	17.7 ± 3.5	18.2 ± 0.19	1.0	1.0
^{51}V	0.005	106 (0.15)	ClinChek 1	20.8 ± 4.2	20.4 ± 0.32	0.4	1.6
			ClinChek 2	50.6 ± 10.2	48.7 ± 0.99	0.8	2.0
^{66}Zn	0.75	102 (15)	ClinChek 1	206 ± 42	197 ± 3.3	0.7	1.7
			ClinChek 2	531 ± 106	523 ± 8.6	0.5	1.6

[a] Spike recoveries were determined using a low burdened native urine sample.
[b] Spiked concentration.

Table 4
External Quality assessment.

Element	Concentration/(µg/L)					
	QMEQAS		64th G-EQUAS		65th G-EQUAS	
	Result	Target	Result	Target	Result	Target
As_{total}	33	32 ± 7.8	21	22 ± 4.9	21.7	20.8 ± 3.6
Be	3.5	3.6 ± 0.8	0.069	0.071 ± 0.012	0.125	0.119 ± 0.033
Bi	0.59	0.60 ± 0.24	–	–	–	–
Cd	2.3	2.4 ± 0.48	0.15	0.15 ± 0.06	0.40	0.42 ± 0.12
Cr	5.0	5.1 ± 1.3	0.64	0.70 ± 0.15	0.33	0.33 ± 0.09
Co	1.4	1.3 ± 0.28	8.8	8.7 ± 1.5	14.4	14.1 ± 1.8
In	–	–	0.82	0.78 ± 0.15	0.62	0.60 ± 0.12
Mn	2.7	2.9 ± 1.4	8.1	8.1 ± 1.5	2.6	2.8 ± 0.6
Mo	89	91 ± 13	13	13 ± 1.8	37.9	36.5 ± 5.7
Ni	5.3	4.9 ± 1.8	0.62	0.64 ± 0.18	0.74	0.73 ± 0.21
Pb	120	110 ± 16	6.6	6.0 ± 0.9	8.7	8.1 ± 1.5
Sn	8.5	8.7 ± 1.5	0.65	0.68 ± 0.27	0.52	0.52 ± 0.15
Tl	3.9	3.7 ± 0.56	2.3	2.1 ± 0.3	1.7	1.6 ± 0.3
V	1.5	1.5 ± 0.93	6.4	6.5 ± 1.2	17.2	16.6 ± 2.1
Zn	610	600 ± 100	279	272 ± 34	111	106 ± 17

(see supplementary information). Compared to the 1/10 (v/v) dilution described above, no effects on the determined metal and metalloid concentrations were observed in the dilution range of 1/40 (v/v) to 1/5 (v/v). The recoveries were in the range of 93–106%.

3.2. Analysis of native urine samples

In total, 77 first morning void urine samples of non-specifically occupationally exposed persons and 15 field blanks have been collected. Metal and metalloid concentrations as well as creatinine levels were determined in these samples. In the field blanks, all metal and metalloid concentrations were below the respective LOQs indicating no contamination of the urine samples from the sampling site. According to the German MAK commission's recommendation (Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area) (Weihrauch et al., 2000), only urine samples with creatinine concentrations of 0.5–2.5 g/L were regarded as valid and used for further statistical analysis.

The results of the 65 urine samples meeting this criterion are summarised in Table 5, which describes the percentage equal to or above the LOQ, concentration ranges, mean concentrations, and percentiles. Values are given volume based and corrected for creatinine to adjust effects of urinary dilution. Due to limited number of participants no stratification by age and sex has been done. Moreover, the samples are not population-representative.

With the exception of indium, all elements were found in urine samples above the LOQ which demonstrates the suitability of the presented method to measure the general population's exposure to metals, metalloids, and their compounds. Arsenic, cadmium, cobalt, molybdenum, nickel, lead, tin, thallium, vanadium, and zinc could be quantified in 100% of the samples.

Since the general population's exposure to elements is influenced by factors that may differ between countries such as lifestyle (e.g. smoking behaviour, use of consumer products), diet (food preferences), and the environment, we focus on German human biomonitoring data generated through multi-element ICP-MS analyses for comparison. Multi-element analysis of 87 adult urine samples collected in western and northern Germany has been undertaken by Heitland and Köster (2006). The

Table 5
Urinary element concentrations.

Element	% ≥ LOQ	Range (μg/L)	GM (μg/L)	AM (μg/L)	P90 (μg/L)	Range (μg/$g_{creatinine}$)	GM (μg/$g_{creatinine}$)	AM (μg/$g_{creatinine}$)	P90 (μg/$g_{creatinine}$)
As	100	1.5–174	9,2	17.6	39	1.4–140	8.7	16	34
Be	2	<LOQ – 0.005	–	–	<LOQ	0.0006[1]–0.005	–	–	0.0026[1]
Bi	38	<LOQ – 0.14	–	–	0.027	0.001[1]–0.14	–	–	0.024
Cd	100	0.021–0.91	0.16	0.21	0.38	0.036–0.59	0.15	0.18	0.35
Co	100	0.049–3.5	0.35	0.62	1.6	0.078–5.9	0.33	0.58	1.3
Cr	68	<LOQ – 1.1	–	–	0.23	0.037–0.78	–	–	0.21
In	0	<LOQ	–	–	–	–	–	–	–
Mn	11	<LOQ – 1.7	–	–	<LOQ	0.014[1]–1.1	–	–	0.082[1]
Mo	100	3–135	32	43	85	3–126	30	38	72
Ni	100	0.39–4.6	1.4	1.7	3.1	0.40–4.0	1.4	1.6	2.7
Pb	100	0.10–3.4	0.59	0.75	1.3	0.12–2.6	0.56	0.68	1.4
Sn	100	0.07–13.6	0.41	0.80	1.2	0.06–8.7	0.39	0.65	1.3
Tl	100	0.06–0.85	0.21	0.24	0.40	0.09–0.61	0.19	0.21	0.31
V	100	0.010–0.27	0.040	0.051	0.079	0.013–0.34	0.038	0.049	0.11
Zn	100	65–1330	308	401	821	48–1490	288	355	675

LOQ (limit of quantification); GM = geometric mean; AM = arithmetic mean; P90 = 90th percentile;[1] = corresponding volume based value is < LOQ.

obtained results in our study are comparable to those reported by them. Similar geometric means (GMs) were obtained for cadmium (0.16 *vs.* 0.17 μg/L) and lead (0.59 *vs.* 0.60 μg/L). However, lower GMs were obtained for total arsenic (9.2 *vs.* 13 μg/L), tin (0.41 *vs.* 0.84 μg/L), and vanadium (0.040 *vs.* 0.057 μg/L), and higher GMs were obtained for cobalt (0.35 *vs.* 0.18 μg/L), nickel (1.4 *vs.* 0.3 μg/L), thallium (0.21 *vs.* 0.069 μg/L) and zinc (308 *vs.* 207 μg/L). Differences in the total arsenic levels could be explained by diet as dietary factors, especially the consumption of sea food (Becker et al., 2003), highly influences the arsenic uptake, which was not taken into consideration neither by Heitland and Köster, nor by us. An even lower arsenic GM of 3.6 μg/L is reported by German Environmental Specimen Bank (ESB, 2021) for urine samples of young not specifically exposed volunteers.

For cadmium and thallium, toxicologically derived health-based guidance values have been derived by the German Human Biomonitoring Commission. The Human Biomonitoring Values (HBM-I values) are 1 μg/L, and 5 μg/L respectively (Schulz et al., 2012; Apel et al., 2017). All measured concentrations were below these HBM-I values.

The general population's exposure to beryllium is expected to be low. Beryllium is usually found solely in individual cases. For Belgium, Hoet and coworkers (2013) report beryllium concentrations below the LOD of 7 ng/L for 99% of all samples. In Heitland's and Köster's study (N = 87) all samples were below the LOQ of 9 ng/L respectively.

Our results are in line with those studies. Although our method possesses an even lower LOQ of 3 ng/L, beryllium was found solely in a single sample above the LOQ. For beryllium, the German MAK commission determined a Biological Reference Values for Chemical Compounds in the Work Area (BAR) of 50 ng/L representing the upper reference concentration in the general adult population without occupational exposure to this metal (Schaller, 2009). Our results, although they are not population-representative, and the results of the studies mentioned support that the general's population exposure to beryllium might be substantially lower. Therefore, it is recommended to reconsider the BAR value.

4. Conclusion

We presented a method that allows the simple determination of 15 metals and metalloids in urine samples in ng/L ranges. Spectral interferences are resolved using ICP-MS/MS.

Furthermore, the application for biomonitoring of the general population's exposure has been demonstrated by analysing native urine samples.

These data are the base for planning multi-element analysis of samples of the full-scale study GerES VI.

Credit author statement

Andy Schmied Formal analysis, Writing – original draft, Investigation, Aline Murawski Writing – original draft, Writing – review & editing, Marike Kolossa-Gehring Funding acquisition, Supervision, Writing – review & editing, Peter Kujath Funding acquisition, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2021.131425.

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