Antimony, Lead, Cadmium, Platinum, Mercury, Tellurium, Thallium, Bismuth, Tungsten, Tin

Application	Determination in urine
Analytical principle	Inductively coupled plasma quadrupole mass spectrometry (Quadrupole ICP-MS)
Completed in	August 1998

Summary

Using the quadrupole ICP mass spectrometry (Q-ICP-MS) method described here, antimony, lead, cadmium, platinum, mercury, tellurium, thallium, bismuth, tungsten and tin present in urine due to occupational exposure can be simply, sensitively and specifically determined. With the exception of platinum and bismuth, the ecological concentration range can also be detected. After UV digestion of the urine samples, an internal standard is added and the samples are introduced into the ICP-MS by means of a pneumatic nebulizer. Evaluation is carried out using the standard addition procedure.

Antimony

Within-series imprecision:	Standard deviation (rel. Prognostic range at concentrations of 0.1 or 2.37 µg antimony per litre urine and where n = 10 determinations	s_w = 14.8 or 1.1% u = 26.0 or 2.0%
Between-day imprecision:	Standard deviation (rel.) Prognostic range at a concentration of 1.1 µg antimony per litre urine and where n = 10 days	s = 3.1% u = 5.6%
Accuracy:	Recovery rate	r = 112.7%
Detection limit:	30 ng antimony per litre urine	

Lead

Within-series imprecision:	Standard deviation (rel.)	s_w = 2.0 or 0.4%
	Prognostic range	u = 3.8 or 0.7%
	at concentrations of 0.46 or 2.48 µg lead per litre urine and where n = 10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 3.7%
	Prognostic range	u = 6.0%
	at a concentration of 1.5 µg lead per litre urine and where n = 10 days	
Accuracy:	Recovery rate	r = 100.9%
Detection limit:	30 ng lead per litre urine	

Cadmium

Within-series imprecision:	Standard deviation (rel.)	s_w = 4.8 or 0.9%
	Prognostic range	u = 9.0 or 1.5%
	at concentrations of 0.21 or 2 µg cadmium per litre urine and where n = 10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 2.4%
	Prognostic range	u = 4.2%
	at a concentration of 1 µg cadmium per litre urine and where n= 10 days	
Accuracy:	Recovery rate	r = 95%
Detection limit:	20 ng cadmium per litre urine	

Platinum

Within-series imprecision:	Standard deviation (rel.)	s_w = 0.8%
	Prognostic range	u = 1.5%
	at a concentration of 2 µg platinum per litre urine and where n = 10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 2.4%
	Prognostic range	u = 4.5%
	at a concentration of 1 µg platinum per litre urine and where n= 10 days	
Accuracy:	Recovery rate	r = 93.8%
Detection limit:	10 ng platinum per litre urine	

Mercury

Within-series imprecision:	Standard deviation (rel.)	s_w = 16.2 or 1.5%
	Prognostic range	u = 29.3 or 2.8%
	at concentrations of 0.13 or 2.26 µg mercury per litre urine and where n =10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 8%
	Prognostic range	u =14%
	at a concentration of 1.1 µg mercury per litre urine and where n =10 days	
Accuracy:	Recovery rate	r = 106%
Detection limit:	30 ng mercury per litre urine	

Tellurium

Within-series imprecision:	Standard deviation (rel.)	s_w= 9.1 or 1.6%
	Prognostic range	u =17.2 or 3.0%
	at concentrations of 0.04 or 3.37 µg tellurium per litre urine and where n = 10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 3.6%
	Prognostic range	u =6.5%
	at a concentration of 1.5 µg tellurium per litre urine and where n = 10 days	
Accuracy:	Recovery rate	r = 96.4%
Detection limit:	10 ng tellurium per litre urine	

Thallium

Within-series imprecision:	Standard deviation (rel.)	s_w = 4.4 or 0.8%
	Prognostic range	u = 8.1 or 1.5%
	at concentrations of 0.12 or 2.1 µg thallium per litre urine and where n = 10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 3.7%
	Prognostic range	u =7.0%
	at a concentration of 1.1 µg thallium per litre urine (addition of 1 µg/L thallium) and where n = 10 days	
Accuracy:	Recovery rate	r = 94%
Detection limit:	5 ng thallium per litre urine	

Bismuth

Within-series imprecision:	Standard deviation (rel.)	s_w = 0.5%
	Prognostic range	u = 0.9%
	at a concentration of 2 µg bismuth per litre urine and where n = 10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 1.8%
	Prognostic range	u = 3.2%
	at a concentration of 1.0 µg bismuth per litre urine and where n = 10 days	
Accuracy:	Recovery rate	r = 79.7%
Detection limit:	5 ng bismuth per litre urine	

Tungsten

Within-series imprecision:	Standard deviation (rel.)	s_w = 4.5 or 0.3%
	Prognostic range	u = 8.1 or 0.5%
	at concentrations of 0.18 or 2.54 µg tungsten per litre urine and where n= 10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 3.6%
	Prognostic range	u = 6.8%
	at a concentration of 1.2 µg tungsten per litre urine and where n= 10 days	
Accuracy:	Recovery rate	r = 116.5%
Detection limit:	20 ng tungsten per litre urine	

Tin

Within-series imprecision:	Standard deviation (rel.)	s_w = 9.8 or 0.6%
	Prognostic range	u = 18.1 or 1.0%
	at concentrations of 0.39 or 2.28 µg tin per litre urine and where n = 10 determinations	
Between-day imprecision:	Standard deviation (rel.)	s = 4.2%
	Prognostic range	u = 7.8%
	at a concentration of 1.3 µg tin per litre urine and where n= 10 days	
Accuracy:	Recovery rate	r = 95.5%
Detection limit:	50 ng tin per litre urine	

Antimony

Antimony is a brittle, shiny metal with an atomic mass of 121.75 and an atomic number of 51. It belongs to group Vb in the periodic table, and its chemical, physical and toxicological properties closely resemble those of its neighbour arsenic. It occurs in oxidation states III and V. Antimony is a relatively rare metal with a concentration in the Earth's crust of approximately 0.3 mg/kg. The worldwide production is about 60000 t/a [1].

As antimony alloys are extremely hard and corrosion-resistant, the metal is used industrially together with lead, copper and tin to form alloys for various products such as rechargeable batteries, type-metal, bearings, ammunition, pipes and cables. It is also employed in the ceramics and glassware industry (antimony trioxide as a plaining agent), as a pigment for the manufacture of dyes and paints and in the textile industry (flame-retardant equipment), etc.

Organic compounds of antimony, especially sodium stibogluconate, stibenyl, stibocaptate and stibophen are used to treat parasitic diseases and infections, especially in tropical medicine.

Antimony is released into the environment, especially as a result of the combustion of fossil fuels (approximately 5000–10000 t/a worldwide), and is therefore detectable in low concentrations in practically all environmentally relevant matrices. The toxicity of antimony compounds depends on both the oxidation state and the solubility of the relevant compound. Thus its trivalent compounds are approximately 10 times more toxic than its pentavalent compounds. The lethal dose for organic antimony compounds is about 100 mg/kg body weight.

The toxicology of the various antimony compounds is summarized in Henschler [3], Elinder and Friberg [4] and Merian and Stemmer [5]. Inhalation of dust and vapour containing antimony represents the most important route of intake at the workplace. Its absorption into the blood via the lungs is relatively swift. Once there, it is bound to the erythrocytes and blocks the activity of certain enzymes. For the most part antimony is excreted in the urine (80%) and the faeces (20%) after 1–3 days [6].

A MAK value of 0.5 mg/m^3 (1998) – measured as the inspirable aerosol portion – has been stipulated for metallic antimony [2]. Antimony trioxide has been assigned to group 2 of the carcinogenic working materials [2]. The MAK value for antimony hydride is 0.1 mL/m^3 or 0.52 mg/m^3 (1998) [2]. In some isolated cases, measurements have shown concentrations up to 3 mg/m^3 at workplaces [7]. Knowledge of the concentrations in the blood and urine of exposed persons is very incomplete due to insufficient analytical detection, as the detection limits of approximately 0.5 µg per litre urine achieved by hydride atomic absorption spectrometry [8] or graphite furnace atomic absorption spectrometry [8] are not low enough to include the concentration range of interest to environmental medicine.

ICP-MS opens up new possibilities of investigating these questions by attaining detection limits of 0.03 µg per litre urine (quadrupole ICP-MS: Q-ICP-MS) and approximately 0.005 µg per litre urine (sector field ICP-MS: SF-ICP-MS) [9]. Initial investigations of samples from the general public indicate that a reference value for the antimony concentration in urine could be in the order of 50 ng per litre [9].

Lead

Lead (atomic weight 207.2) is a soft, greyish-blue metal which is extracted from lead ores by smelting. Its melting point is 327 °C, its boiling point 1750 °C and its density is 11.34 kg/L.

In the vaporous state (vaporization from 550 °C) lead is oxidized to lead oxide (PbO) in the air. Lead can form divalent and tetravalent compounds, it is readily soluble in nitric acid and is passivated by orthophosphoric acid, hydrochloric acid and sulphuric acid. The content of lead in the Earth's crust is very low at 16 ppm. The extractable reserves of lead are estimated at approximately 23 million tonnes worldwide [10]. For further information regarding lead the reader is referred to the general toxicological section of the "Lead in blood" method published in volume 2 of "Analyses of Hazardous Substances in Biological Materials" [11].

Cadmium

Cadmium (atomic number 48, relative atomic mass 112.41) is a malleable, relatively soft metal with a melting point of 321 °C and a boiling point of 767 °C. With a content of approximately 5×10^{-5} % in the Earth's crust, cadmium belongs to the rare metals. Sphalerite (ZnS) contains about 0.1–0.5% and smithsonite up to 5% of the metal. Greenockite is the most important mineral.

The most important technical use of cadmium is in the manufacture of batteries. Between 25% and 30% of the total annual cadmium production is employed for the protection of iron and similar metals against corrosion. A similar amount is used in cadmium-containing pigments and cadmium soaps, which function as stabilisers for PVC. In addition, small quantities of cadmium are present in alloys used for making bearings and solder [12]. Among other routes, cadmium is introduced into the environment by means of the combustion of fossil fuels, via waste and sewage sludge, but also through the use of phosphate fertilizers.

Several reviews dealing with the absorption, distribution, retention and excretion of cadmium in the human organism have been published [13–17]. The current state of knowledge of the absorption and kinetics of cadmium can be summarized as follows: Depending on their solubility and particle size, 20 to 30% of the respirable cadmium (particle size <5 µm) are absorbed. The gastro-intestinal absorption rate is less than 10%, but exhibits large inter-individual variation [17]. The individual fluctuation in the level of the iron depot seems to be a significant influencing factor in this case. Iron deficiency can increase the normal absorption rate of cadmium by a factor of more than three [18, 19]. Therefore, the oral absorption rate is higher as a rule for women than men. Cadmium retained in the lungs is released from this site with a half-life of about 5 days while its concentration increases simultaneously in other organs [20]. With regard to the mechanisms which lead to the distribution of absorbed cadmium in the human organism, it is known that the metal becomes bound to the low-molecular protein metallothionein, probably during its first passage through the liver. A certain detoxification is associated with the formation of this cadmium-metallothionein complex, whereby an increased formation of metallothionein can be induced by chronic exposure to cadmium [13].

The target organ for the chronic intake of cadmium is the kidney. The metal accumulates there and initially causes damage to the renal tubuli. In the case of higher internal levels, the function of the glomeruli is also impaired. Enzymuria and proteinuria occur as a consequence of this kidney damage. In the past, early symptoms of a kidney dysfunction appeared as a result of exposure to the then prevailing levels in the environment. Furthermore, the contribution of tobacco smoke to cadmium exposure is not inconsiderable [21]. Cadmium and its compounds cadmium chloride, cadmium oxide, cadmium sulphate, cadmium sulphide and other bioavailable compounds (in the form of inspirable dust/aerosols) have proved carcinogenic in animal studies. Therefore the Deutsche For-schungsgemeinschaft's Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (Commission for Working Materials) has assigned cadmium and the compounds mentioned above to group 2 of the carcinogenic working materials [2].

The technical exposure limit (TRK value) is 0.03 mg/m^3 in areas where batteries are manufactured, for the thermal extraction of zinc, lead and copper, and for the welding of alloys containing cadmium. The TRK value (1998) for other workplaces is 0.015 mg/m^3 – measured as the inspirable aerosol portion in each case [2].

In principle, determination of the cadmium concentration in both blood and urine is suitable for estimating the inner exposure to cadmium. While the cadmium level in blood reflects a recent exposure to cadmium, the determination of the cadmium concentration in urine opens up the possibility of quantifying this metal in the entire organism.

The "Human Biomonitoring" Commission of the Umweltbundesamt (Ministry for the Environment) and the Arbeitsstoffkommission (Commission for Working Materials) have set a reference value (human biomonitoring value: HBM) and a threshold value

Table 1. Reference values and threshold values of cadmium for the general population and for occupationally exposed persons.

Designation	Group of persons	Value
TRK value	Workers	0.03 or 0.015 mg/m^3
Reference value	Children (6–12 years old)	0.5 µg/L whole blood 0.5 µg/g creatinine or 0.5 µg/L urine
	Adults (non-smokers 25–69 years old)	1.0 µg/L whole blood 1.0 µg/g creatinine or 1.0 µg/L urine
HBM I value	Children, adolescents and young adults (<25 years old)	1 µg/g creatinine
	Adults (>25 years old)	2 µg/g creatinine
HBM II value	Children, adolescents and young adults (<25 years old)	3 µg/g creatinine
	Adults (>25 years old)	5 µg/g creatinine
BAT value	Workers	15 µg/L urine 15 µg/L whole blood

(biological tolerance value: BAT) for the evaluation of an inner cadmium stress for the general population and for people exposed to cadmium at the workplace (cf. Tab. 1) [2, 22]:

Platinum

At a concentration of 5 µg/kg in the upper 16 km of the Earth's crust (approximately as much as palladium and gold), platinum is the 76th most abundant element [12]. Platinum can occur in oxidation states from 0 to +VI, whereby bivalent and tetravalent compounds are the most common. In solutions it occurs exclusively in the form of coordination compounds (platinates). The relative atomic masses of the naturally occurring isotopes of platinum are 190 (relative occurrence: 0.01%), 192 (0.79%), 194 (32.9%), 195 (33.8%), 196 (25.3%) and 198 (7.2%) [12].

As finely dispersed platinum exhibits excellent catalytic properties, it is used in large-scale technical processes, such as the manufacture of nitric acid from ammonia, the oxidation of ammonia to produce fertilizers, in petrochemical processes, for example hydrocracking, isomerization, aromatization, hydrogenation, etc., and in catalytic converters to reduce the pollution from the exhaust gases of automobiles [12]. Moreover, certain platinum compounds (cis-platinum, carboplatinum) have been successfully applied in the therapy of cancer. In addition, alloys containing precious metals which are used in dental health can contain a maximum of about 20% platinum according to the manufacturers' declarations [23].

In 1988 125 t of platinum were produced worldwide, of which 31% was used in the western world to manufacture automobile catalytic converters, 29% for the manufacture of jewellery and 14% in the chemical and petrochemical industry [12].

Automobile catalytic converters, such as the three-way catalytic converters commonly mounted on cars in Germany, consist of a ceramic carrier material coated with aluminium oxide, bearing a total amount of about 2–3 g of platinum or palladium and rhodium as well as small proportions of other catalytically active precious metals [24]. Platinum is now increasingly being replaced by palladium for cost reasons. The ratio of platinum to rhodium or palladium to rhodium is approximately 5:1. Under normal running conditions the above-mentioned precious metals are released into the air with the exhaust fumes as suspended particles and vapours as a result of mechanical abrasion and thermal stress. Thus, a distinct rise in the platinum content of dust deposits and in plants compared with its natural occurrence has been observed, particularly in the vicinity of roads carrying high volumes of traffic [25, 26]. According to an investigation carried out by the National Academy of Sciences [27], platinum is emitted from automobile catalytic converters predominantly in its metallic form and as platinum dioxide (PtO_2) bound to the carrier material $A1_2O_3$. In particles with a mean aerodynamic diameter of more than 5 µm, König et al. [28] found platinum concentrations which were equivalent to a concentration of between 3.3 and 39.0 ng/m^3 in the exhaust fumes. In the case of particles with a mean diameter between 0.1 and 20 µm, platinum concentrations between 43 and 88 ng/m^3 were found in exhaust fumes by Innacker and Malessa [29]. The mean platinum emission from an engine with a three-way catalytic converter is given as 15 ng/m^3 at a speed of 100 km/h [24].

According to Alt et al. [30], the total platinum content in suspended dust samples was 0.6 to 130 µg/kg, of which a proportion of 30–43% is soluble in 0.07 mol/L HCl. The platinum content of the air was between 0.02 and 5.1 pg/m^3, i.e. about 4 orders of magnitude below the level in automobile exhaust fumes.

The main route of intake of platinum and its compounds is by inhalation, oral intake is low in comparison. It is excreted in the urine, whereby 20–45% is eliminated within 24 h after its intake [31]. Platinum oxides and soluble platinum compounds can have a sensitizing and allergic effect on humans following dermal exposure and when these compounds are inhaled [31–33]. These effects were observed exclusively in persons who were exposed at the workplace. Workers in platinum refining plants and in the production of catalytic converters are primarily affected. However, elevated internal exposure to platinum was also found in other occupational groups, such as dental technicians and hospital personnel who had contact with cytostatic agents. Table 2 contains the results of platinum determinations in the urine of various groups of people who are exposed to platinum at their workplace. Recent investigations [34–36] have shown that people who are regularly exposed to heavy traffic, such as road construction workers on motorways, workers employed in motorway maintenance as well as bus drivers and taxi drivers do not excrete elevated platinum concentrations in their urine.

At present little is known for sure about the possible effects on humans, animals and plants as a result of the increasing emission of platinum into the environment. Similarly, there is little information on the possible consequences of the release of platinum from dental alloys containing precious metals.

Messerschmidt et al. [40], Begerow et al. [34, 41–43], Schramel et al. [44], Schierl et al. [35, 38], Nygren et al. [45], and Philippeit and Angerer [46] have carried out investigations to determine platinum concentrations in the urine of persons who had not been exposed to platinum at the workplace. The results are summarized in Table 3. As the table demonstrates, there is excellent agreement between the results for the physiological platinum concentrations in urine published by Messerschmidt et al. [40], Schierl et al. [35, 38], Schramel et al. [44], Begerow et al. [41–43], and by Philippeit and Angerer [46]. In the light of the other results, the platinum concentrations published by Nygren et al. [45] must be regarded as distinctly too high.

In contrast to exposure to automobile emissions, the release of platinum from dental alloys can make a considerable contribution to the total exposure of the affected person to the metal. It was shown that the platinum excretion in urine was increased by several hundred percent when a commercially available, frequently used dental alloy with a high proportion of gold (Pt content: 9.0%) was inserted [48]. Before insertion of the dental alloy, the platinum excretion of the three investigated test persons was between 1.0 and 7.4 ng/L, and thus in the range of the background environmental exposure (cf. Tab. 3). After insertion of the artificial denture with a high gold content, a distinct increase in the urinary excretion of platinum was observed in all three test persons, and the elevated levels were maintained throughout the three-month investigation period. In the first few days after insertion the platinum excretion increased on average by a factor of 12 to

Table 2. Results of platinum determination in the urine of people who are occupationally exposed to the metal [ng/L].

Occupation	*n*	Mean value	Range	Reference
Production of catalytic converters	19	950	23–9200	[37]
Recycling of catalytic converters	5	320	20–630	[37]
Handling of platinum nozzles	16	214	10–2900	[37]
Production of catalytic converters	34		16–6270[1]	[38]
Hospital personnel	21		<1.8–34.4	[39]
Dental technicians	27	25.7	0.8–167.8	[34]
Road construction workers	17	0.9	0.2–4.4	[34]
Bus drivers	29	2.8	1.0–40	[35]
MOT testers	13	2.2	0.5–21.0	[35]
Motorway maintenance	18		<1.0–6.6	[36]
Taxi drivers	10	1.3	1.0–28	[35]

[1] ng/g creatinine

Table 3. Results of investigations to determine the platinum content in the urine of the general public [ng/L]

Group of persons	*n*	Mean value	Range	Reference
Adults	14	1.1	0.5–14.3	[40]
Adults	16	1.7	0.5–7.7	[42]
Adults	21	1.8	0.5–7.7[1]	[43]
Children	262	1.8	0.2–19	[43]
Trainees	17	1.1	0.3–2.2	[34]
Adults	10	5.4	1.2–35	[44]
Adults	12	6.3	2.1–17.4	[34]
Adults	12		1–12[1]	[38]
Adults	21	126		[45]
Adults (without gold fillings in their teeth)	20	1.2	0.9–6.6	[46]
Adults (with gold fillings in their teeth)	26	23.1	0.9–151.2	[46]

[1] ng/g creatinine

values between 10.5 and 59.6 ng/L, three months after inserting the artificial denture the mean platinum concentrations in urine were still 7 times higher than the original level. In vitro experiments clearly confirmed the release of platinum from this type of alloy [47]. In this context, Philippeit and Angerer were also able to detect elevated platinum concentrations in the urine of persons with artificial dentures containing a high concentration of gold [46]. In this case the mean platinum excretion in the urine of 26 people was 23.1 ng/L (cf. Tab. 3) [46].

Mercury (Hg)

Mercury is a silvery-white metal which is insoluble in water. It has a high surface tension and its density is 13.6 g/mL. It is the only metal which is liquid at room temperature. Hg and its chemical compounds are of great importance as working materials and also as pollutants of the environment. Among its many uses, mercury is filled into barometers and thermometers, it is employed to extract gold and silver from sand containing these precious metals. It is used in neon tubes and mercury vapour lamps, as a cathode material in chlorine-alkali electrolysis and in the manufacture of dry batteries [12].

The two decisive action mechanisms of mercury poisoning are the denaturization of proteins at the application site, and inhibition of enzymes as a result of divalent mercury ions reacting with free enzymatic thiol groups. The site of action and the toxic effects depend on the differing kinetic behaviour of the individual compounds. It is primarily the central nervous system which exhibits symptoms of poisoning by elemental mercury and its organic compounds, whereas damage to the kidney region (glomeruli, tubuli) is caused by bivalent mercury ions.

It is advisable to determine the mercury levels in various biological matrices, especially in blood and urine, in order to estimate the degree of exposure to mercury at the workplace and in the environment. The concentration of mercury in biological materials depends on its route of intake, on the chemical bonding state of the element and on the duration of the exposure and the degree to which the substance is incorporated. The mercury concentration in the blood and urine is a measure of the dose absorbed during the previous weeks [48–50].

The "Human Biomonitoring" Commission of the Umweltbundesamt (Ministry for the Environment) and the Arbeitsstoffkommission (Commission for Working Materials) have set reference values and threshold values for the evaluation of inner mercury stress for the general population and for people exposed at the workplace [2, 51]. The reference value for children and adults without amalgam fillings is 1.4 µg Hg per litre urine or 1.0 µg Hg per gram creatinine. The value can be up to four times higher when the person has amalgam fillings. The relevant reference value for the determination of mercury in blood is 1.5 µg Hg per litre for children or 2.0 µg Hg per litre blood for adults. The BAT value (Biological Tolerance Value for Working Materials) can be used as a reference for occupational medical and toxicological assessment of the mercury level in the blood and urine of people who are exposed to mercury. The current BAT value (1998) is 25 µg per litre blood or 100 µg per litre urine in the case of exposure to inorganic compounds and metallic mercury [2]. The mercury content of whole blood is measured for the evaluation of occupational exposure to organic mercury compounds, in particular the alkyl mercury compounds. In this case the current BAT value is 100 µg per litre blood [2]. On a collective basis, these BAT values for inorganic compounds or metallic mercury correlate with the current (1998) MAK values of 0.012 mL/m^3 and 0.1 mg/m^3. The Commission for the Investigation of Health Hazards in the Work Area has assigned organic mercury compounds to group 3 of the carcinogenic working materials. This means that, despite justified concern, organic mercury compounds may have a carcinogenic effect on humans, it is impossible make a definitive assessment at present due to lack of information. However, in vitro experiments and animal studies have

provided indications of a carcinogenic effect, but there are insufficient grounds for assigning these compounds to another category [2].

Tellurium

Like sulphur and selenium, tellurium (Te) is a chalcogen. Its atomic number is 52 and it has an atomic mass of 127.61.

Elemental tellurium exists in two polymorphic forms: the silvery-white, shiny hexagonal rhombohedral crystals, and amorphous tellurium which is a fine, black powder. Both elemental tellurium and tellurium dioxide are barely soluble.

Tellurium and selenium are chemically similar, but tellurium has more metallic properties. It occurs in oxidation states II, IV and VI, the tetravalent compounds being the most stable. Tellurium is a very rare element. Its concentration in the Earth's crust is only a few µg/kg.

Tellurium is used as an additive in the steel, chemical, electrical and electronic industries. The worldwide production of tellurium is in the magnitude of 1000 t/a [1]. The degree to which tellurium compounds are absorbed varies to a large extent. While acute poisoning has been observed at the workplace, nothing is known about the chronic effects of small doses.

Tellurium hydride (H_2Te) and tellurium hexafluoride (TeF_6), both of them colourless and extremely toxic gases, are of toxicological interest, as are several other compounds, such as tellurium dioxide (TeO_2) and salts derived from orthotelluric(VI) acid (H_6TeO_6) and telluric(IV) acid (H_2TeO_3).

The MAK value (1998) for tellurium and its compounds has been set at 0.1 mg/m^3. However, this value should not be applied to tellurium hexafluoride and tellurium hydride, as the concentration limits at which these compounds can be regarded as harmless are not known. The concentration of these substances should not exceed 0.01 mg/ m^3 under any circumstances [2].

ICP-MS opens up new possibilities of investigating these questions by achieving detection limits of 0.01 µg/L urine (Q-ICP-MS) and approximately 0.001 µg/L urine (SF-ICP-MS).

Initial investigations of urine samples from the general public indicate that a reference value for the tellurium concentration could be in the order of 50 ng per litre urine [9].

Thallium

Thallium (Tl) has an atomic mass of 204.37 and its atomic number is 81. It is classified as a heavy metal on account of its density (11.83 g/cm^3).

In many ways its chemical behaviour resembles that of lead, its neighbour in the periodic table. The similarity between the ionic radii of Tl(I) ions and potassium ions is of great significance for the physiological characteristics of this element. Thallium occurs in the oxidation states +Iand +VI in its compounds, the former being its more stable form.

Although thallium is employed industrially in small quantities only, it has numerous uses [1]. Thus, its sulphide, arsenide, selenide and telluride are used in semiconductor technology. In the glass industry it is used as an additive in the manufacture of low-melting, extremely durable special glass with a high refractive index. Due to their high transparency in the infrared range, mixed crystals of thallium halides are employed in the manufacture of lenses and prisms.

Products containing thallium, particularly thallium(I) sulphate, are still employed today as pesticides against rats and insects in many countries.

Several review articles presenting the clinic symptoms and pharmacokinetics of thallium have been published [52, 53].

Thallium and its inorganic compounds are absorbed into the human body through the lungs and the gastro-intestinal tract. Intake is rapid and almost complete. It enters the bloodstream through which it is swiftly transported to the interstitial and intracellular spaces in various organs and tissues.

In humans thallium acts as a general cytotoxin and is thus highly poisonous when taken in acute oral doses. At present there is still little knowledge about chronic thallium poisoning in humans.

The MAK value (1998) for soluble thallium compounds is currently 0.1 mg/m^3, based on the inspirable dust fraction [2].

ICP-MS, which achieves detection limits of approximately 0.005 µg per litre urine (Q-ICP-MS) and 0.0005 µg per litre urine (SF-ICP-MS) for thallium, is vastly superior to the previous determination methods (GFAAS, ICP-OES, voltammetry). Initial investigations of urine samples from the general population indicate that a reference value for the thallium concentration could be in the order of 100 ng per litre urine [9]. For further details regarding thallium the reader is referred to the general toxicological section of the "Thallium in Urine" method in Volume 5 of "Analyses of Hazardous Substances in Biological Materials" [54].

Bismuth

Bismuth (Bi) is a greyish-white shiny metal with a melting point of 271 °C, a boiling point of 1560 °C, a density of 9.8 g/cm^3 and an atomic mass of 208.98.

The chemical behaviour of bismuth is similar to that of Pb, As and Sb. As it occurs considerably less frequently (its mean concentration in the Earth's crust is 0.19 mg/ kg), no environmental damage due to bismuth has yet been discovered. Dissolved bismuth compounds are rapidly converted to insoluble compounds.

Bismuth is used for the manufacture of numerous readily fusible alloys, in quenching baths for steel production, for the silvering of mirrors and in dental health. Bi compounds have a multitude of uses in industrial processes and products, such as in the manufacture and reprocessing of nuclear fuel rods, in battery cathodes, in semiconductors and for catalysts in the chemical industry. The *Merck Index* [55] lists 39 bismuth compounds, 17 of which are employed in the pharmaceutical industry and in many cosmetic products. The consequences of intoxication range from stomatitis, local pigmentation, erythema to kidney damage. In addition, cases of bismuth encephalopathy have been described throughout the world. Such cases are probably the result of

intoxication from insoluble Bi salts which are deposited in the brain. In contrast, soluble bismuth salts, which are used in the therapy of various diseases (stomach preparations, syphilis therapy), are rapidly excreted.

Nothing is known about a general risk from bismuth and its compounds. Until now no bismuth compounds have been included in the list of MAK values [2].

Tungsten

Tungsten (atomic mass 183.8) belongs to the transition metals. At 3410 °C it has the highest melting point of all the metals. The most frequently produced radioisotopes are ^{181}W, ^{185}W and ^{187}W. Tungsten can occur in oxidation states from 0 to VI and it is closely related chemically to molybdenum [12].

For further details regarding tungsten the reader is referred to the general toxicological section of the "ICP Collective Method" in Volume 5 of "Analyses of Hazardous Substances in Biological Materials" [56].

Tin

The atomic mass of tin is 118.9, its atomic number is 50 and it exists in 3 allotropic forms (α, β and γ forms). Metallic tin is mainly produced by reduction of its dioxide (SnO_2).

Tin occurs in oxidation states +II and +IV in its compounds. It forms numerous anionic complexes with halides and ligands containing oxygen, especially in its tetravalent state. As its position in group IV of the periodic table would indicate, tin forms organometallic compounds with covalent C-Sn bonds. Pure tin is utilized in the form of tin foil and as a thin coating to prevent the corrosion of iron (tinplate for cans). The most frequent use for elemental tin is for alloys such as bronze, soft solder, letter-type metal, white metal (bearing metal), Wood's alloy etc. Elemental tin is resistant to water and air at room temperature.

$SnCl_2$ is frequently used as a reducing agent. SnO is employed in the manufacture of enamel, SnO_2 is a constituent of opalescent glass, while various inorganic compounds of tin are used for dyeing [1].

The organotin compounds are of particular significance. They are added to paints as fungicides, disinfectants and anti-fouling agents. They function as stabilizers in plastics, catalysts for olefin polymerization and auxiliary reagents in the production of foamed polyurethanes.

The relatively low toxicity of orally ingested metallic and inorganic tin is probably due to the fact that it is not readily absorbable. In contrast, many different organotin compounds are very toxic, compounds containing short-chain alkyl groups being especially dangerous. Toxicity increases with the number of alkyl groups in the compound [57]. Oedema of the white cerebral matter and damage to nerve cells in certain regions of the brain can be caused by exposure to these substances.

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Antimony, Lead, Cadmium, Platinum, Mercury, Tellurium, Thallium, Bismuth, Tungsten, Tin

Application	Determination in urine
Analytical principle	Inductively coupled plasma quadrupole mass spectrometry (Quadrupole ICP-MS)
Completed in	August 1998

Contents

1 General principles

After UV digestion of the urine samples, an internal standard is added and the samples are introduced into the ICP-MS by means of a pneumatic nebulizer. The evaluation is carried out using the standard addition procedure.

2 Equipment, chemicals and solutions

2.1 Equipment

ICP mass spectrometer (quadrupole or SF-ICP-MS) with autosampler, PC and printer

UV digestion device with 20 mL quartz vessels (e.g. UV 1000 from Kiirner)

Microlitre pipette, adjustable between 10 and 100 µL (e.g. from Eppendorf)

Microlitre pipette, adjustable between 100 and 1000 µL (e.g. from Eppendorf)

Millilitre pipette, adjustable between 1 and 5 mL (e.g. from Eppendorf) and/or 1 and 10 mL (e.g. from Rainin)

10, 20, 100 and 1000 mL Volumetric flasks

100 mL Measuring pipettes

Quartz glass or plastic sample vials: approx. 20 mL (depending on the autosampler)

2.2 Chemicals

Antimony standard solution (1 g/L) in the form of Sb_2O_3 in 5% HCl (e.g. from Spex)

Lead standard solution (1 g/L) in the form of $Pb(NO_3)_2$ in 5% HNO_3 (e.g. from Spex)

Cadmium standard solution (1 g/L) in the form of Cd in 5% HNO_3 (e.g. from Spex)

Platinum standard solution (1 g/L) in the form of Pt in 10% HCl (e.g. from Spex)

Mercury standard solution (1 g/L) in the form of Hg in 10% HNO_3 (e.g. from Spex)

Tellurium standard solution (1 g/L) in the form of Te in 5% HNO_3 (e.g. from Spex)

Thallium standard solution (1 g/L) in the form of $TlNO_3$ in 5% HNO_3 (e.g. from Spex)

Bismuth standard solution (1 g/L) in the form of Bi in 10% HNO_3 (e.g. from Spex)

Tungsten standard solution (1 g/L) in the form of $(NH_4)_2WO_4$ in 2% HNO_3+5% HF (e.g. from Spex)

Tin standard solution (1 g/L) in the form of Sn in 20% HCl (e.g. from Spex)

Rhodium standard solution (1 g/L) in the form of Rh in 10% HCl (e.g. from Spex)

Iridium standard solution (1 g/L) in the form of Ir in 2–5% HCl (e.g. from Spex)

Ultrapure water (equivalent to ASTM type 1) or double-distilled water

Argon (welding argon) for ICP

65% HNO_3 (subboiling distilled or "Suprapur" from Merck)

2.3 Solutions

1 M HNO_3 (to clean the glassware):
About 500 mL ultrapure water are placed in a 1000 mL volumetric flask, then 70 mL of the 65% HNO_3 are added with a pipette. The flask is subsequently filled to its nominal volume with ultrapure water while the contents are swirled gently.

1.4 M HNO_3:
About 500 mL ultrapure water are placed in a 1000 mL volumetric flask, then 100 mL of the 65% HNO_3 are added with a pipette. The flask is subsequently filled to its nominal value with ultrapure water while the contents are swirled gently.

These solutions can be stored for several months at 4°C.

2.4 Solution of the internal standard (rhodium and iridium)

1 mL each of the rhodium and iridium standard solutions is pipetted into a 100 mL volumetric flask. The volumetric flask is subsequently filled to its nominal volume with ultrapure water (10 mg/L).

2.5 Standard addition solution

Starting solution:
0.1 mL of the standard solutions of antimony, lead, cadmium, platinum, mercury, tellurium, thallium, bismuth, tungsten and tin are transferred to a 100 mL volumetric flask with a pipette. The flask is then filled to its nominal volume with 1.4 M HNO_3 (1 mg/L).

Standard addition solution:
1 mL of the starting solution is pipetted into a 10 mL volumetric flask. The volumetric flask is subsequently filled to its nominal volume with 1.4 M HNO_3 (0.1 mg/L).

These solutions must be freshly prepared daily.

3 Specimen collection and sample preparation

3.1 Specimen collection

As is the case for all trace element analyses, it is essential to ensure that the reagents are of the highest possible purity and that the vessels are thoroughly clean. This also applies to sample collection.

To prevent a possible exogenous contamination, the plastic vessels for sample collection must be cleaned before use by leaving them filled with 1 M HNO_3 for at least 2 hours, rinsing them thoroughly with ultrapure water and drying them. For determination in the range of the detection limit the cleansing effect can be improved by warming the nitric acid.

The urine should be collected and stored in polyethylene vessels, whereby it is always advisable to collect urine over a 24-hour period. If the determination cannot be carried out immediately, the urine can be stored in the refrigerator for about 1 week at approximately +4°C, but the urine must be acidified (approx. 10 mL HNO_3 per litre urine). If longer storage is necessary, it is advisable to keep the samples in the deep-freezer at –18 °C.

Prior to further processing, the urine samples are thawed and brought to room temperature.

3.2 UV digestion

Before an aliquot is withdrawn for UV digestion, the samples are thoroughly shaken to ensure they are homogeneous.

Then 4 mL urine, 1 mL concentrated HNO_3, 11 mL H_2O and 4 mL H_2O_2 are pipetted into the 20 mL digestion vessels (dilution 1:5). These are placed into the UV digestion device and exposed to UV light for approximately 1 hour. The colourless to slightly yellow solutions are brought to room temperature.

A reagent blank is included in each analytical series. Ultrapure water is used instead of urine in this case.

Between 4.80 and 4.95 mL of the digested sample are pipetted into a 20 mL autosampler vial, then the solution of the internal standard and the standard addition solution are added in accordance with the pipetting scheme shown in Table 4.

Table 4. Pipetting scheme for the standard addition procedure.

Sample		Internal standard	Standard addition solution	Desig-nation	Added metal concentration, based on the urine volume used
Urine	Water				
[mL]	[mL]	[mL]	[mL]		[µg/L]
4.95	–	0.05	–	ADD1	–
4.90	–	0.05	0.05	ADD2	5
4.85	–	0.05	0.1	ADD3	10
4.80	–	0.05	0.15	ADD4	15
–	4.95	0.05	–	Blank value	–

Standard addition solution: 0.1 µg/L

4 Operational parameters for ICP-MS

4.1 Plasma settings

Power supply: 1.2 kW

Sample introduction: peristaltic pump, output <1 mL/min

Nebulizer: cross flow or Meinhard

Nebulizer chamber: Scott type (quartz glass or Rayton®)
Zyklon chamber (advisable - due to less memory effects)

Plasma conditions: combustion gas 15 L/min
nebulizer gas approx. 0.7–0.8 L/min (must be optimized)
plasma gas 0.8 L/min

The given plasma conditions serve only as a guide. The operational parameters must be optimally adjusted for each individual instrument used.

4.2 MS parameters (Q-ICP-MS)

Table 5. ICP-MS parameters.

Sweeps/Reading	20
Reading/Replicate	6
Number of replicates	1
Points across peak	normal
Resolution	peak hop
Scanning mode	0
Baseline time (ms)	replicat
Transfer frequency	+
Polarity	

Table 6. MS program parameters.

Element	Mass	Times [ms]	
		Replicate	Dwell
Rh*	103	2000	100
Cd	111	2000	100
Sn	118	2000	100
Sb	121	2000	100
Te	126		
W	182	2000	100
Ir*	193	2000	100
Pt	195	2000	100
Hg	202	2000	100
Tl	205	2000	100
Pb	208	2000	100
Bi	209	2000	100

*: internal standard

Element equations:
Rh 103 = Rh 103
Cd 111 = Cd 111
Sn 118 = Sn 118
Sb 121 = Sb 121
Te 126 = Te 126–0.003404×Xe 129
W 182 = W 182
Ir 193 = Ir 193
Pt 195 = Pt 195
Hg 202 = Hg 202
Tl 205 = Tl 205
Pb 208 = Pb 208
Bi 209 = Bi 209

Manual settings:

Plasma flow:	15 L/min	RF power:	1200 Watts
Nebulizer flow:	0.75 L/min	CEM voltage:	3.7 kV
Auxiliary flow:	0.8 L/min	Sample uptake:	0.9 mL/min

5 Analytical determination

The ADD1 to ADD4 solutions are introduced into the plasma and analyzed (see Figs. 1 and 2).

The analytical determination is carried out by quadrupole MS. Four measurement points are thus obtained for the evaluation of the analytical result.

6 Calibration and calculation of the analytical result

The concentrations of the metals in the urine sample are obtained from a graph with the aid of the standard addition procedure. The reagent blank value is subtracted from the peak heights of the unspiked and the three spiked samples, which are then divided by the corresponding value for the appropriate internal standard, and the resulting quotients are plotted as a function of the metal concentrations. Linear graphs are obtained and their point of intersection with the concentration axis gives the concentration of the metal in µg per litre urine in each case.

The more modern generation of instruments is equipped with computer-supported evaluation programs which perform the evaluation automatically.

The linear operational range extends to 150 µg of the metals per litre urine. The urine samples must be further diluted when the metal concentrations are not within the linear range of the graph.

7 Standardization and quality control

Quality control of the analytical results is carried out in accordance with the guidelines of the Bundesärztekammer (German Medical Association) [58, 59] and the special preliminary remarks in Volume 1 of the "Analyses of Hazardous Substances in Biological Materials". Material containing antimony, lead, cadmium, mercury and thallium is commercially available for internal quality control, e.g. "Control urine" from Recipe, Munich.

As no control material is commercially available for the remaining metals which can be determined by this method, it must be prepared in-house in the laboratory. For this purpose, urine is spiked with a defined quantity of the metals. Aliquots of this solution can be stored in the deep-freezer for up to a year and used for quality control. The concentration of this control material should lie in the middle of the most frequently occurring concentration range. The theoretical value and the tolerance range for this quality control material is determined in the course of a pre-analytical period (one analysis of the control material on 20 different days) [58, 60].

External quality control can be realized by participation in round-robin experiments. The round-robin experiments carried out to test analysis in occupational and environmental medicine in Germany include antimony, lead, cadmium, mercury and thallium in the concentration range of interest to occupational medicine and cadmium, platinum and mercury in the concentration of interest to environmental medicine in the quality control programme [61, 62].

8 Reliability of the method

8.1 Precision

The precision in the series was checked in 10 analyses of pooled urine from people who had not been exposed to the metals at the workplace. The following relative standard deviations and prognostic ranges were found (cf. Tab. 7).

In addition, the ten metals were added to the same pooled urine so that the concentration of each was 2 µg per litre, and the spiked sample was processed and analyzed 10 times. The following standard deviations and prognostic ranges were obtained (cf. Tab. 8). The precision from day to day was tested using the same pooled urine after adding 1 µg of each of the metals to 1 L urine and the sample was processed and analyzed on 10 different days. The following standard deviations and prognostic ranges were obtained (cf. Tab. 9).

Table 7. Precision in the series.

Element	Concentration [µg/L]	Standard deviation (rel.) [%]	Prognostic range [%]
Cd	0.21	4.8	9.0
Sn	0.39	9.8	18.1
Sb	0.10	14.8	26.0
Te	0.04	9.1	17.2
W	0.18	4.5	8.1
Pt	–	–	–
Hg	0.13	16.2	29.3
Tl	0.12	4.4	8.1
Pb	0.46	2.0	3.8
Bi	–	–	–

Table 8. Precision in the series after addition of 2 µg/L each (n = 10).

Element	Concentration [µg/L]	Standard deviation (rel.) [%]	Prognostic range [%]
Cd	2.10	0.9	1.5
Sn	2.28	0.6	1.0
Sb	2.37	1.1	2.0
Te	3.37	1.6	3.0
W	2.54	0.3	0.5
Pt	2.00	0.8	1.5
Hg	2.26	1.5	2.8
Tl	2.10	0.8	1.5
Pb	2.48	0.4	0.7
Bi	2.00	0.5	0.9

Table 9. Precision from day to day (n = 10 days).

Element	Concentration [µg/L]	Standard deviation (rel.) [%]	Prognostic range [%]
Cd	1.21	2.4	4.2
Sn	1.39	4.2	7.8
Sb	1.10	3.1	5.6
Te	1.04	3.6	6.5
W	1.18	3.6	6.8
Pt	1.00	2.4	4.5
Hg	1.13	8.0	14.0
Tl	1.12	3.7	7.0
Pb	1.46	3.7	6.0
Bi	1.00	1.8	3.2

8.2 Accuracy

Recovery experiments were performed to check the accuracy of the method. For this purpose pooled urine was spiked with 2 µg of each of the metals and analyzed (cf. Tab. 10).

Table 10. Recovery rates.

Element	Concentration (theoretical) [µg/L]	Concentration (found) [µg/L)	Recovery rate [%]
Cd	2.10	1.99	95.0
Sn	2.28	2.17	95.5
Sb	2.37	2.67	112.7
Te	3.37	3.25	96.4
W	2.54	2.96	116.5
Pt	2.00	1.90	94.9
Hg	2.26	2.39	106.0
Tl	2.10	1.97	93.8
Pb	2.48	2.50	100.9
Bi	2.00	1.59	79.7

Furthermore, the method described here was checked with the aid of commercially available control material. The following results were obtained (cf. Tab. 11).

Table 11. Results obtained using commercially available control material. (Note: the control material had different concentration levels, i.e. level I and II).

Element/level	Unit	Reference value	Range	Found (n = 5)
Sb/I	µg/L	12.2	9.5–14.9	12.3±0.6
Sb/II		45.5	36.1–51.9	45.5±1.0
Pb/I	µg/L	37.5	30.2–44.6	39.2±1.2
Pb/II		64.5	53.7–75.3	66.1±2.0
Cd/I	µg/L	11.1	9.0–13.2	11.1±0.4
Cd/II		21.7	17.8–25.7	20.9±1.0
Hg/I	µg/L	12.3	9.8–14.9	14.5±1.5
Hg/II		120	92–147	122±5
Tl/I	µg/L	3.1	1.8–4.6	3.6±0.3
Tl/II		17.9	13.5–22.3	21.1±1.5

8.3 Detection limits

Under the analytical conditions given here the detection limits in urine samples were calculated as three times the standard deviation of the background signal at the mass of the given isotope (cf. Tab. 12).

Table 12. Calculated detection limits.

Element	Isotope m/e [amu]	Detection limit Urine [µg/L]
Sb	121	0.03
Pb	208	0.03
Cd	111	0.02
Pt	195	0.01
Hg	202	0.03
Te	126	0.01
Tl	205	0.005
Bi	209	0.005
W	182	0.02
Sn	118	0.05

8.4 Sources of error

Interferences due to overlapping masses ("polyatomic interferences") were not observed for the mass/charge ratios (m/e) measured in this case. Depending on the origin of the lead standard and the exogenous lead exposure, erroneous results of up to ±15% can

occur when determining the metal because of local variations in the isotope frequency of lead (final product of a chain of radioactive decay).

When human biological samples are to be determined, sample digestion to destroy the organic matrix is strongly recommended. Thus spectral and non-spectral interferences are distinctly reduced and the long-term stability of the ICP-MS is considerably improved.

The demands placed on sample digestion are normally not very stringent, as there is sufficient thermal energy in the ICP to ensure complete destruction of the organic matrix if this has not already been achieved by sample digestion. UV digestion of the urine samples has proved very practicable for this purpose [42, 63]. In this method, relatively small quantities of acid are added, as H_2O_2 (or rather the OH radicals it generates) represents the real digestion agent. This results in distinctly lower blank values and dispenses with the necessity of sample dilution.

Alternatively, an oxidative digestion with acid, generally with HNO_3 in a closed system (pressure digestion) [64, 65], can achieve satisfactory digestion for analysis. However, limitations are imposed by the relatively high acid concentrations present after an acidic digestion, as they must be lowered by dilution.

The use of two different internal standards (rhodium and iridium) is advisable because of the large range of masses of the elements to be analyzed. However, the precondition for the use of rhodium and iridium is that these elements are not to be subsequently analyzed in other samples in the ultratrace range (risk of memory effects).

It is strongly advisable to shake the samples vigorously after they have been stored, as sedimentation occurring in the urine samples can lead to absorption of the analytes on the surface of the sediment, and thus cause erroneous results [66].

9 Discussion of the method

The method presented here permits the simultaneous analysis of antimony, lead, cadmium, platinum, mercury, tellurium, thallium, bismuth, tungsten and tin in urine.

Apart from bismuth and platinum, the ecological concentration range can be detected. In order to achieve the detection of bismuth and platinum at ecological concentrations, a sector field ICP-MS instrument must be employed.

In this method standard addition was used to evaluate the results. While checking the method it was shown that external aqueous standards can be used for calibration when the metal concentrations of the urine samples are in the concentration range of interest to occupational medicine. However, in this case the accuracy of the calibration must always be checked by means of the standard addition procedure (cf. Appendix).

The examiners of the method carried out the analysis using urine samples which had not been digested. This resulted in a large proportion of the matrix reaching the ICP-MS. This type of test represents the “worst-case scenario”. UV digestion of the urine samples minimizes the interfering constituents of the matrix, thus improving the analytical reliability criteria. This was confirmed by comparison with the results for undigested samples obtained by the examiners.

UV digestion of the urine samples is strongly recommended for the investigation of larger series of samples, otherwise clogging of the sample introduction system and the cones is caused by the high salt concentration in the samples, and the removal of such blockages is extremely time-consuming.

According to the examiners, the amount of acid used for digestion can be further reduced if necessary, without reducing the effectiveness of the digestion.

In addition to the isotopes mass spectrometrically evaluated by the author, i.e. ^{111}Cd, ^{202}Hg, ^{208}Pb, ^{121}Sb, ^{118}Sn, ^{205}Tl and ^{182}W, one of the examiners evaluated ^{114}Cd, ^{200}Hg, ^{207}Pb, ^{120}Sn, ^{203}Tl and ^{184}W for comparison. The results of the author were confirmed.

Besides great sensitivity, the use of mass spectrometry for the analysis described here ensures a high degree of specificity with relatively little effort. Thus, this method is superior to the procedures for the analysis of metals such as AAS or ICP-OES which have been available until now.

Instruments used:
ICP mass spectrometer ELAN 5000 (from Perkin Elmer Sciex, Canada)
Autosampler AS-90 (from Perkin Elmer, Germany), PC and printer

UV digestion device UV 1000 (from Kürner)

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11 Appendix

Comparison of the results achieved by the standard addition method with those of an aqueous calibration curve.

Element	Urine A Measurement 1 Cal. curve [µg/L]	Urine A Measurement 2 Cal. curve [µg/L]	Standard addition [µg/L]	Urine B Measurement 1 Cal. curve [µg/L]	Urine B Measurement 2 Cal. curve [µg/L]	Standard addition [µg/L]
Sb	0.023	0.025	0.017	0.058	0.060	0.047
Pb	0.56	0.58	0.54	0.83	0.81	0.86
Cd	0.067	0.067	0.054	0.316	0.366	0.316
Pt	0.011	0.028	0.0004	0.013	0.028	0.001
Hg	0.030	0.048	0.020	0.51	0.63	0.44
Te	0.023	0.028	0.012	0.018	0.035	0.011
Tl	0.29	0.28	0.28	0.43	0.38	0.41
Bi	<0.010	<0.010	<0.010	<0.010	<0.010	<0.010
W	0.042	0.063	0.020	0.065	0.12	0.040
Sn	0.33	0.36	0.30	2.8	2.7	3.3

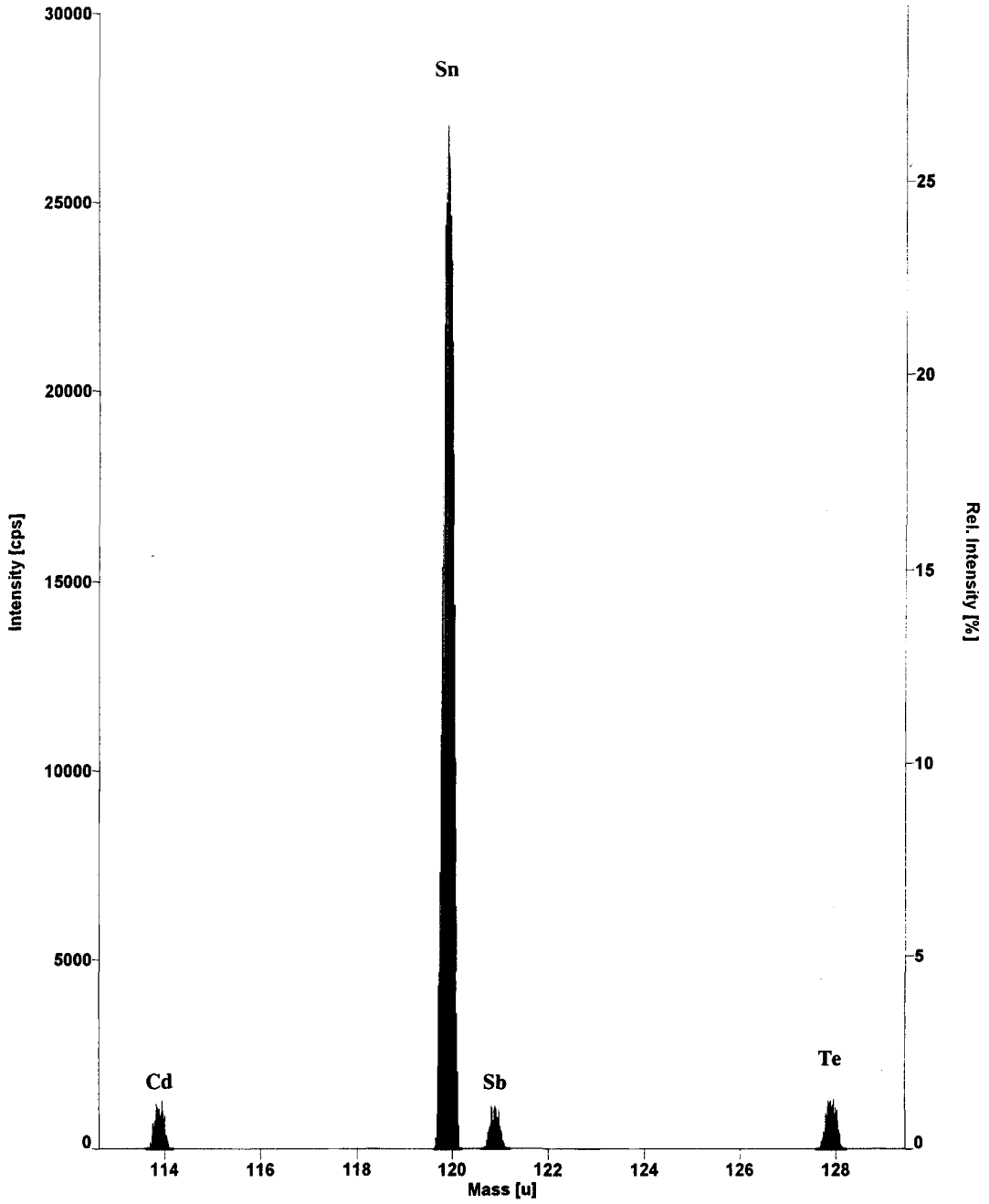

Fig. 1. Q-ICP-MS determination of cadmium, tin, antimony and tellurium in urine.

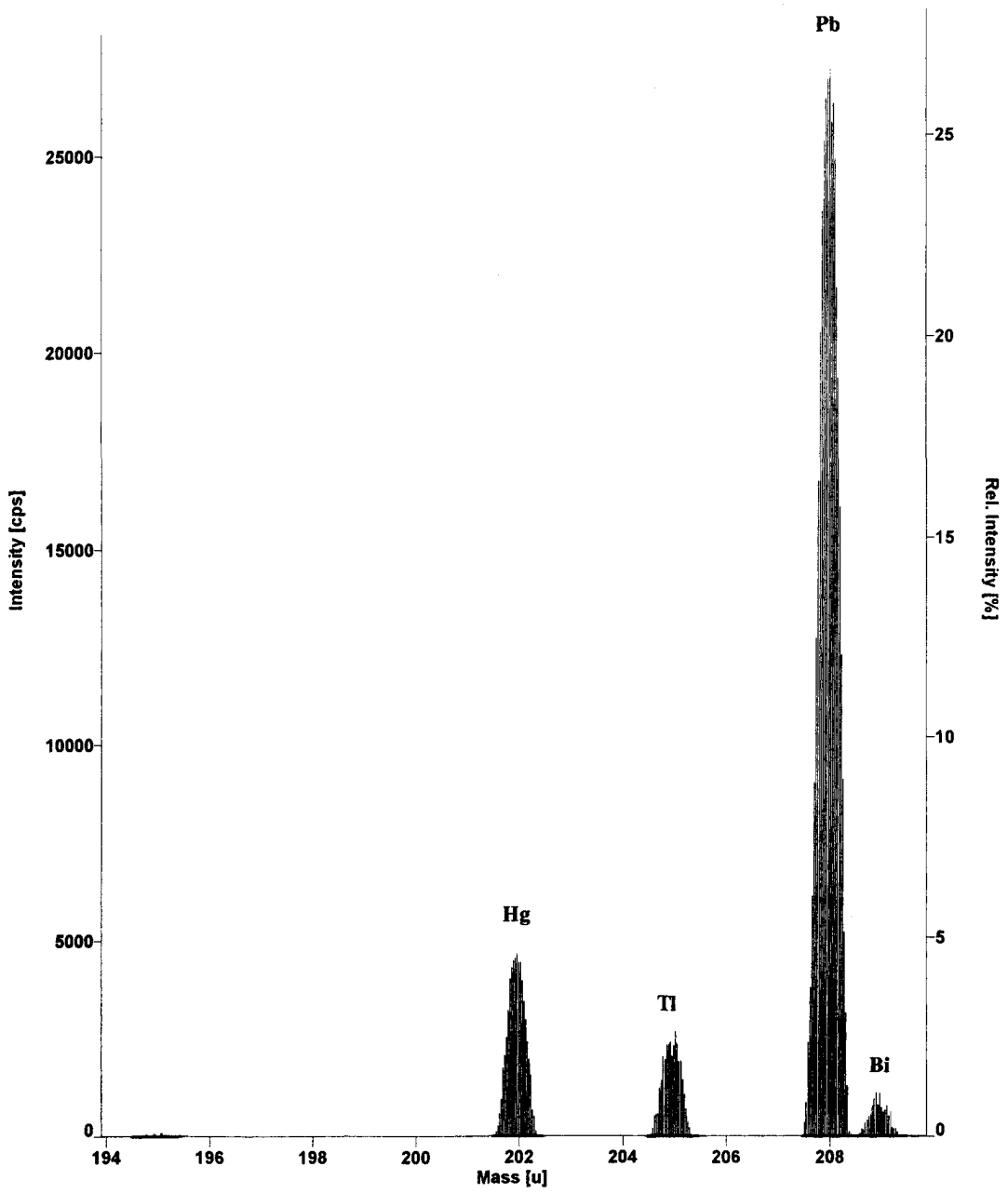

Fig. 2. Q-ICP-MS determination of mercury, thallium, lead and bismuth in urine.