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Hydrogen sulfide – Determination of thiosulfate in urine by GC-MS

Biomonitoring Method – Translation of the German version from 2022

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thiosulfate; hydrogen sulfide; biomonitoring; urine; GC-MS

Abstract

The working group "Analyses in Biological Materials" of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area developed and verified the presented biomonitoring method. The method described herein allows for the sensitive and sufficiently precise determination of thiosulfate in human urine as a marker of hydrogen sulfide exposure. Samples are derivatised using pentafluorobenzyl bromide and extracted into iodine ethyl acetate solution. Analysis is conducted by gas chromatography-mass spectrometry. Calibration is carried out with calibration standards prepared in pooled urine from individuals with no known exposure to hydrogen sulfide. The calibration standards are processed analogously to the samples to be analysed. The method is specific and sensitive, and its quantitation limit of 0.22 mg/l is sufficient to determine both occupational and background exposure to hydrogen sulfide.

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1 Characteristics of the method

Matrix	Urine
Analytical principle	Gas chromatography-mass spectrometry (GC-MS)

Parameter and corresponding hazardous substance			
Hazardous substance	**CAS No.**	**Parameter**	**CAS No.**
Hydrogen sulfide	7783-06-4	Thiosulfate	14383-50-7

Reliability criteria

Thiosulfate

Within-day precision:	Standard deviation (rel.) Prognostic range at a spiked concentration of 2.80 mg or 22.4 mg thiosulfate per litre of urine and n = 10 determinations	s_w = 16.3% or 8.1% u = 36.9% or 18.3%
Day-to-day precision:	Standard deviation (rel.) Prognostic range at a spiked concentration of 2.80 mg or 22.4 mg thiosulfate per litre of urine and n = 5 determinations	s_w = 23.1% or 20.1% u = 64.1% or 55.8%
Accuracy:	Recovery rate (rel.) at a spiked concentration of 22.4 mg thiosulfate per litre of urine and using n = 10 individual urine samples	r = 106–148%
Detection limit:	0.08 mg thiosulfate per litre of urine	
Quantitation limit:	0.22 mg thiosulfate per litre of urine	

2 General information on hydrogen sulfide

Hydrogen sulfide (H_2S; molar mass: 34.08 g/mol) is a toxic gas generated by non-specific and anaerobic bacterial reduction of sulfates and sulfur-containing organic compounds. Natural sources include crude petroleum, natural gas, volcanic gases, and hot springs (ATSDR 2016). It can also be found in groundwater and may be released from stagnant or polluted waters and manure or coal pits. The principal industrial source of hydrogen sulfide is recovery as a by-product in the purification of natural and refinery gases. It is also a by-product of pulp and paper manufacturing as well as of carbon disulfide production and is used as an intermediate in certain manufacturing processes (e. g. sulfuric acid) (Jones 2014; WHO and IPCS 2003).

Human exposure to exogenous hydrogen sulfide is principally via inhalation with rapid absorption. Hydrogen sulfide is metabolised through three pathways: oxidation to sulfate, methylation to methanethiol and dimethylsulfide, and reactions with metalloproteins and disulfide-containing proteins. Oxidation in the liver is the major detoxification pathway, forming thiosulfate, which is then converted to sulfate and excreted in the urine (Hartwig 2013). Only incomplete data are available on the excretion kinetics of thiosulfate. Thiosulfate is completely excreted 24 hours after the end of exposure, with the highest urinary concentrations at 5 to 15 hours after exposure (Jones 2014; Kangas and Savolainen 1987). The methylation pathway also serves as a detoxification route.

The toxicity of hydrogen sulfide is a result of its reaction with key metabolic metalloenzymes (ATSDR 2016; WHO and IPCS 2003). In the mitochondria, cytochrome oxidase (the final enzyme in the respiratory chain) is inhibited by hydrogen sulfide. This disrupts the electron transport chain and impairs oxidative metabolism which particularly

impacts nervous and cardiac tissues (both are tissues with high oxygen demand and rely on oxidative metabolism). In the central nervous system, this effect may result in unconsciousness or even death from respiratory arrest (WHO and IPCS 2003).

Hydrogen sulfide has a very low odour threshold (0.008 ml/m^3), but odour perception is lost at concentrations of 150–250 ml/m^3 (WHO 2000), adding to the danger of high level exposures as they may not be recognised by the individual by smell. The Commission has derived a MAK Value for thiosulfate of 5 ml/m^3 (5 ppm; peak limitation category I; excursion factor 2). Details on the toxicological evaluation can be found in the corresponding MAK Value Documentations published by the Commission (Hartwig 2013, 2015).

The method described herein enables the measurement of both occupational exposure and background levels in the general population. Urinary thiosulfate concentrations are in the single-digit mg/l range for individuals with no known exposure to hydrogen sulfide (Chwatko and Bald 2009; Kangas and Savolainen 1987). In cases of acute poisoning with immediate fatality, no thiosulfate is generally detectable in the urine. For these cases, however, thiosulfate in blood can be used as a biomarker (see Section 12). In cases of delayed fatality, thiosulfate values of up to 137 mg/l can be measured in urine (Kage et al. 2002).

Representative data on urinary thiosulfate concentrations from the occupationally non-exposed general population as well as in workers following occupational exposure (resulting in death in some cases) are given in Table 1.

Tab. 1 Thiosulfate concentrations in urine

Collective (Number of persons)	Sampling time	Thiosulfate concentration	Reference
Background exposure, Finland (29)	–	2.9 ± 2.5 mg/g creatinine[a)]	Kangas and Savolainen 1987
Volunteer study, Finland (1)	15 h after exposure	29.7 mg/g creatinine	
H_2S exposure; wastewater treatment in a pelt-processing plant, Finland (4)	15 h after exposure	5–60 mg/g creatinine[b)]	
Background exposure, Poland (13)	–	1.35–4.85 mg/g creatinine	Chwatko and Bald 2009
H_2S exposure; cleaning activities in a fish hatchery, USA (1)	Day 1 after arrival in hospital	78 mg/g creatinine (surviving worker)	Nikkanen and Burns 2004
H_2S exposure; seepage-water pit at an industrial waste site, Japan (2)	2 h after exposure	29.4 mg/l (surviving worker)	Kage et al. 2002
	2 h after exposure	137 mg/l (death after 22 d)	
H_2S exposure; seepage-water pit at an industrial waste site, Japan (2)	–	< LOQ–0.90 mg/l (immediate death)	
H_2S exposure; paper regeneration, Japan (2)	6 h after exposure	13.5–48.2 mg/l (surviving workers)	Kage et al. 1997
H_2S exposure; paper regeneration, Japan (2)	15 h after exposure	< LOQ–43.7 mg/l (surviving workers)	
H_2S exposure; animal-rendering plant, UK (2)	9 h after exposure	36.6 mg/l (surviving worker)	Jones 2014
	unknown	11.2 mg/l (surviving worker)	
H_2S exposure; biodigester facility, UK (1)	–	< LOQ (immediate death)	Jones 2014

LOQ: limit of quantitation
[a)] mean ± SD
[b)] interpreted from diagram

3 General principles

The method for the determination of thiosulfate in urine is based on a method by Kage et al. (1991). Urine samples are derivatised using pentafluorobenzyl bromide, extracted into iodine ethyl acetate solution, and washed with water. Thereby thiosulfate is converted to bis(pentafluorobenzyl) disulfide by alkylation and oxidation. Analysis is by gas chromatography-mass spectrometry. Calibration is carried out with calibration standards prepared in pooled urine

from individuals with no known exposure to hydrogen sulfide and are treated in the same manner as the samples to be analysed.

4 Equipment, chemicals, and solutions

4.1 Equipment

- Gas chromatograph with a mass spectrometer (e. g. Agilent 6890 with Agilent 5973, Agilent Technologies Germany GmbH & Co. KG, Waldbronn, Germany)
- Capillary GC column: Zebron™ ZB-WAXplus™, 30 m × 0.32 mm × 1.0 µm (e. g. Phenomenex Ltd. Deutschland, Aschaffenburg, Germany)
- Freeze-dry system (e. g. Cole-Parmer Instrument Company, LLC, Saint Neots, United Kingdom)
- Centrifuge (e. g. Heraeus Deutschland GmbH & Co. KG, Hanau, Germany)
- Vortex mixer (e. g. Whirlimixer™, Fisher Scientific UK Ltd, Loughborough, United Kingdom)
- Rotary tumbler (e. g. Adelab Scientific, Thebarton, Australia)
- Analytical balance (e. g. No. AA-200DS, BDH Prolabo, VWR International GmbH, Darmstadt, Germany)
- Various Multipettes® with matching CombiTips® (e. g. Eppendorf UK Limited, Stevenage, United Kingdom)
- Displacement pipette with 200-µl tips (e. g. Eppendorf UK Limited, Stevenage, United Kingdom)
- Various beakers (e. g. Cole-Parmer Instrument Company, LLC, Saint Neots, United Kingdom)
- 5-ml, 10-ml, 20-ml, and 100-ml glass volumetric flasks, Grade A (e. g. BRAND GMBH + CO KG, Wertheim, Germany)
- Pyrex culture tubes (100 × 16 mm) with Bakelite screw caps, PTFE-lined (e. g. Fisher Scientific UK Ltd, Loughborough, United Kingdom)
- 10-ml glass vials with rubber bungs and aluminium crimp-seal tops for quality-control samples (e. g. Fisher Scientific UK Ltd, Loughborough, United Kingdom)
- 12-mm crimp-cap vials with inserts and aluminium crimp-seal tops with rubber septa (e. g. Chromatography Direct Ltd, Runcorn, United Kingdom)
- Polypropylene urine containers (e. g. Sarstedt AG & Co. KG, Nümbrecht, Germany)

4.2 Chemicals

Unless otherwise specified, all chemicals must be a minimum of *pro analysi* grade.

- Acetone, HPLC-grade (e. g. No. 103725, Merck KGaA, Darmstadt, Germany)
- L(+)-Ascorbic acid (e. g. No. 100468, Merck KGaA, Darmstadt, Germany)
- Ethyl acetate for gas chromatography (e. g. No. 100789, Merck KGaA, Darmstadt, Germany)
- Iodine, sublimated for analysis, EMSURE® (e. g. No. 104761, Merck KGaA, Darmstadt, Germany)
- 2,3,4,5,6-Pentafluorobenzyl bromide (PFBBr) (e. g. No. 841643, Merck KGaA, Darmstadt, Germany)
- Sodium chloride for analysis (e. g. No. 10092740, Fisher Scientific GmbH, Schwerte, Germany)
- Sodium thiosulfate solution (0.1 mol/l ≙ 15.8 g/l; 11.2 g thiosulfate/l) (e. g. No. 109147, Merck KGaA, Darmstadt, Germany)
- Ultra-pure water (e. g. Milli-Q Direct Water Purification System, Merck KGaA, Darmstadt, Germany)

- Urine from individuals with no known exposure to hydrogen sulfide
- Helium 5.0 (e. g. Linde GmbH, Pullach, Germany)

4.3 Solutions

- Ascorbic acid solution (35.2 g/l; 200 mmol/l)

  Using a weighing boat, weigh out 352 mg of ascorbic acid and transfer quantitatively, using ultra-pure water, to a 10-ml Grade-A volumetric flask. Make up to volume with ultra-pure water.

  The ascorbic acid solution can be stored at room temperature for six months.

- Iodine solution (3.17 g/l; 25 mmol/l)

  Using a weighing boat, weigh out 317 mg of iodine chips and transfer quantitatively, using ethyl acetate, to a 100-ml Grade-A volumetric flask. Make up to volume with ethyl acetate.

  The iodine solution should be prepared fresh each time.

- Sodium chloride solution (50 g/l; 5 wt%)

  Using a weighing boat, weigh out 500 mg of sodium chloride and transfer quantitatively, using ultra-pure water, to a 10-ml Grade-A volumetric flask. Make up to volume with ultra-pure water.

  The sodium chloride solution can be stored at room temperature for six months.

- PFBBr solution (5.22 g/l; 20 mmol/l)

  In a fume cupboard, add 60 µl of PFBBr (~104 mg) to a 20-ml Grade-A volumetric flask. Make up to volume with acetone.

  This solution should be prepared fresh each time.

4.4 Calibration standards

- Sodium thiosulfate spiking solution (79.05 mg/l ≙ 56.1 mg thiosulfate/l; 500 µmol/l)

  25 µl of the sodium thiosulfate solution (0.1 mol/l) are pipetted into a 5-ml volumetric flask, which is then made up to volume with pooled urine.

  The sodium thiosulfate spiking solution should be prepared fresh each time.

Calibration standards are prepared by spiking pooled blank urine from individuals with no known exposure to hydrogen sulfide. For this purpose, the sodium thiosulfate spiking solution and the blank urine are pipetted into Pyrex culture tubes according to the pipetting scheme given in Table 2. The calibration standards thus prepared are processed and analysed analogously to the urine samples as described in Sections 5 and 6.

Tab. 2 Pipetting scheme for the preparation of calibration standards for the determination of thiosulfate in urine

Calibration standard	Spiking solution [µl]	Urine [µl]	Thiosulfate [mg/l]
1	0	200	0
2	20	180	5.61
3	40	160	11.2
4	80	120	22.4

Tab. 2 *(continued)*

Calibration standard	Spiking solution [µl]	Urine [µl]	Thiosulfate [mg/l]
5	120	80	33.6
6	160	40	44.9
7	200	0	56.1

5 Specimen collection and sample preparation

5.1 Specimen collection

The urine samples are collected in sealable plastic containers. Samples should preferably be frozen at –80 °C immediately after collection and analysed within two weeks.

5.2 Sample preparation

The urine samples are brought to room temperature and mixed. 200 µl of urine are pipetted into Pyrex culture tubes and mixed with 50 µl of ascorbic acid solution (35.2 g/l) and 50 µl of 5% sodium chloride solution. In the fume cupboard, 500 µl of PFBBr solution are pipetted to each sample. The tubes are closed tightly and the samples are mixed on a vortex mixer. In the fume cupboard, 2 ml of iodine solution (3.17 g/l) is pipetted into the tubes, which are then resealed and mixed on a vortex mixer. The samples are centrifuged at 1260 × *g* for 5 minutes. The samples are then left at room temperature for one hour for derivatisation. After derivatisation, 2 ml of ultra-pure water is added to each sample and the samples are mixed on a rotary tumbler for 20 min and centrifuged again (1260 × *g*, 5 minutes). Then, 200 µl of the supernatant are pipetted into crimp-cap vials with inserts, which are finally sealed.

6 Operational parameters

Analytical determination was carried out using a device configuration consisting of a gas chromatograph with a mass spectrometer.

6.1 Gas chromatography

Capillary column:	Stationary phase:	100% polyethylene glycol
	Length:	30 m
	Inner diameter:	0.32 mm
	Film thickness:	1.0 µm
Temperatures:	Column:	Initial temperature of 100 °C, hold for 1 min, increase at a rate of 12 °C/min to 240 °C, 3 min at final temperature
	Injector:	220 °C
	Transfer line:	230 °C
Carrier gas:	Helium	
	Flow rate:	1.2 ml/min, constant
Injection:	Injection volume:	1 µl, splitless

6.2 Mass spectrometry

Ionisation:	Positive electron-impact ionisation (EI+)
Ionisation energy:	70 eV
Source temperature:	230 °C
Quadrupole temperature:	150 °C
Solvent delay:	2 min
Detection mode:	Single Ion Monitoring (SIM)
Ion trace:	*m/z* 426
Retention time:	13.1 min

All settings are instrument-specific and must be individually adjusted by the user. The parameters given can therefore only be used as a guide.

7 Analytical determination

1 µl of the processed urine sample (see Section 5.2) is injected into the GC-MS system. All samples are analysed in duplicate and the mean value is used for data output. The analyte is identified by its specific ion trace and retention time. The retention time given in Section 6.2 can only serve as a point of reference. The user must ensure the separation performance of the column used and the resulting retention behaviour of the analyte. Representative chromatograms are shown in Figure 1.

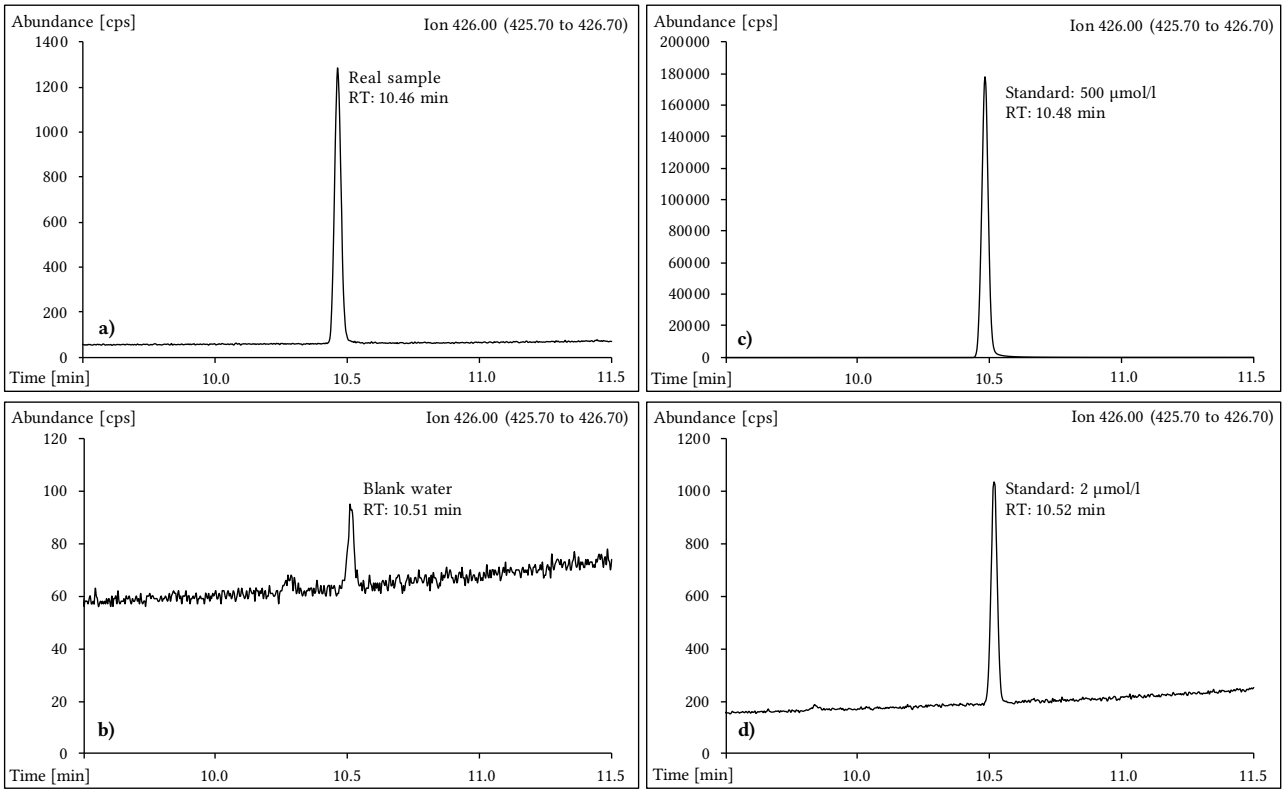

Fig. 1 Chromatogram of a) a native urine sample, b) a water blank, c) a standard spiked with 500 µmol thiosulfate/l, and d) a standard spiked with 2 µmol thiosulfate/l

8 Calibration

Calibration standards are prepared at the start of each run as described in Section 4.4, processed the same way as all samples (see Section 5.2) and analysed (see Section 6). The calibration curve is generated by plotting the peak height of the analyte against the concentration of the corresponding calibration standard. Figure 2 shows a representative calibration curve for the determination of thiosulfate in urine.

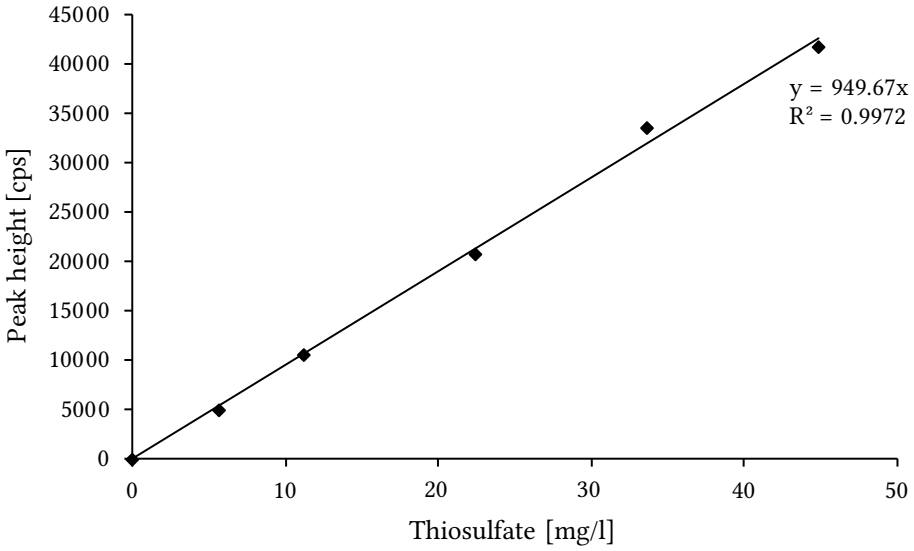

Fig. 2 Calibration curve for the determination of thiosulfate in urine

9 Calculation of the analytical results

Calculation of the analytical results is determined by calibration. The height of the analyte peak is inserted into the calibration function of the respective analytical run to calculate the analyte concentration in mg/l urine. If any result exceeds the maximum calibration range (56.1 mg/l), the sample must be diluted with ultra-pure water, reprocessed, and newly analysed. The dilution factor must be taken into account when calculating the final result.

10 Standardisation and quality control

Quality control of the analytical results is carried out as stipulated in the guidelines of the *Bundesärztekammer* (German Medical Association) and in a general chapter published by the Commission (Bader et al. 2010; Bundesärztekammer 2014).

For quality assurance of the analytical results, quality-control samples are processed and analysed in parallel with the samples in each analytical run. Since control material is not currently commercially available, the material must be prepared in the in-house laboratory. For this purpose, pooled urine from individuals with no known exposure to hydrogen sulfide is spiked with 22.4 mg thiosulfate/l. 5-ml aliquots of the quality-control sample are pipetted into 10-ml vials. For method development, the aliquots were freeze-dried and stored at –20 °C. Before use, the lyophilisates are resuspended in 5 ml of ultra-pure water. Two quality-control samples are each measured after the standard-curve samples and after every fifth sample.

11 Evaluation of the method

The reliability of this method was confirmed by comprehensive validation as well as by replication and verification in a second, independent laboratory.

11.1 Precision

For the determination of the precision, ten urine samples from individuals with no known exposure to hydrogen sulfide were spiked at a nominal 22.4 mg/l (200 µmol/l) of thiosulfate and ten quality-control samples were spiked at a nominal 2.8 mg/l (25 µmol/l) of thiosulfate.

Within-day precision

For the determination of the within-day precision, these samples were processed and analysed in parallel. The results are shown in Table 3.

Tab. 3 Within-day precision for the determination of thiosulfate in urine (n = 10)

Spiked concentration [mg/l]	Determined concentration [mg/l]	Standard deviation (rel.) s_w [%]	Prognostic range u [%]
2.80 (frozen at –20 °C)	1.15	16.3	36.9
22.4 (freeze-dried)	17.1	8.1	18.3

Day-to-day precision

For the determination of day-to-day precision, five analytical runs (ten samples per run on five different days) were processed and analysed. The results are shown in Table 4.

Tab. 4 Day-to-day precision for the determination of thiosulfate in urine (n = 5)

Spiked concentration [mg/l]	Determined concentration [mg/l]	Standard deviation (rel.) s_w [%]	Prognostic range u [%]
2.80 (frozen at –20 °C)	1.38	23.1	64.1
22.4 (freeze-dried)	19.8	20.1	55.8

11.2 Accuracy

To determine accuracy, ten urine samples from individuals with no known exposure to hydrogen sulfide were used. Three aliquots of each urine were spiked with thiosulfate at 22.4 mg/l (200 µmol/l) (see Table 5). Then, the samples were processed and analysed. The mean recovery rates were between 106% and 148% (after subtraction of blank values).

Tab. 5 Relative recovery of thiosulfate in individual urine samples (n = 3)

Urine sample	Creatinine [g/l]	Relative recovery r [%]	
		Mean	Range of mean values
1	0.252	121	113–126
2	0.630	112	107–115
3	0.943	106	101–113
4	1.222	134	129–139
5	1.455	106	103–112

Tab. 5 *(continued)*

Urine sample	Creatinine [g/l]	Relative recovery *r* [%]	
		Mean	Range of mean values
6	1.710	148	132–160
7	2.114	147	140–159
8	2.523	120	90–153
9	2.811	124	77–150
10	3.546	114	95–123

11.3 Matrix effects

To check for matrix influences, calibration was conducted in both water and urine (Figure 3) during external method verification. Here, the area of the thiosulfate peaks was used for quantification. As the calibration curves in water and in urine showed different slopes, a calibration in matrix is considered necessary for a correct quantification of thiosulfate in urine.

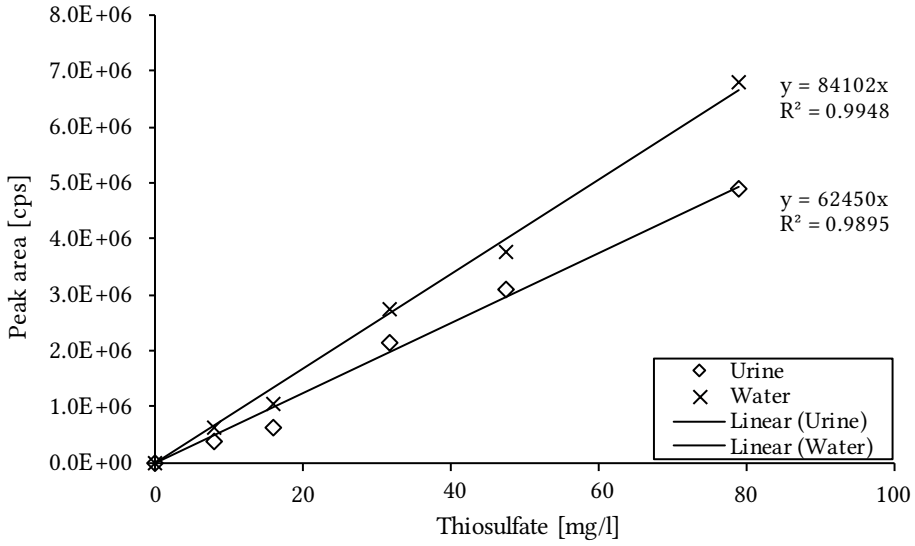

Fig. 3 Calibration curves in water and urine

11.4 Limits of detection and quantitation

The detection limit was determined on the basis of a signal-to-noise ratio of 3 : 1. The limit of quantitation was similarly ascertained from the tenfold signal-to-noise ratio. The calculated values are shown in Table 6.

Tab. 6 Limits of detection and quantitation for the determination of thiosulfate in urine

Analyte	Detection limit [mg/l]	Quantitation limit [mg/l]
Thiosulfate	0.08	0.22

11.5 Sources of error

The stability of thiosulfate in real samples was not tested. During method development, spiked samples were frozen at −80 °C. Under these conditions, thiosulfate was found to be stable for a period of two weeks. It is therefore recommended to store the urine samples immediately at −80 °C and to analyse the samples within two weeks. The lyophilised quality-control samples (see Section 10) were shown to be stable for at least three weeks at −20° C.

For external method verification thiosulfate standards were freshly prepared, stored in the refrigerator at 4 °C, and used within a week. This approach yielded lower relative standard deviations for within-day precision; these values lied at 8.66% and 4.36% for spiked concentrations of 11.2 mg/l and 44.8 mg/l, respectively.

12 Discussion of the method

The method described here allows for the selective and sensitive quantitation of thiosulfate in urine. The method exhibits a linear working range of up to 56.1 mg (500 µmol/l) thiosulfate/l urine. Compared with the method published by Jones (2014), the method hereby presented includes the addition of water after derivatisation, enabling the neutralisation of excess derivatisation reagent and extending the service lifetime of the column. Moreover, this method allows for the analysis of higher sample throughput and is more sensitive.

The precision data of the method may be improved by the use of a suitable internal standard. The use of 1,3,5-tribromobenzene, as described by Kage et al. (1997) and tested by the developers of this method (Jones 2014), did not turn out to be optimal since the substance does not reflect influences during the processes of extraction or derivatisation. Moreover, the use of 1,3,5-tribromobenzene did not improve the precision data. Sodium thiosulfate-^{34}S-pentahydrate has also been tested as an internal standard, but it was decided not to use this standard due to problems with stability.

According to the developers of the method, it is suitable for the determination of thiosulfate in blood as well, whereby blood samples have primarily been taken in cases of fatal poisoning. In order to ensure the stability of the analyte, the blood samples should be cooled until processing. The determination of thiosulfate in blood has not been externally verified.

Notes

Competing interests

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

References

ATSDR (Agency for Toxic Substances and Disease Registry) (2016) Toxicological profile for hydrogen sulfide and carbonyl sulfide. Atlanta, GA: ATSDR. https://www.atsdr.cdc.gov/toxprofiles/tp114.pdf, accessed 27 Sep 2022

Bader M, Barr D, Göen T, Schaller KH, Scherer G, Angerer J (2010) Reliability criteria for analytical methods. Biomonitoring Method, 2010. In: Angerer J, Hartwig A, editors. The MAK-Collection for Occupational Health and Safety. Part IV: Biomonitoring Methods. Volume 12. Weinheim: Wiley-VCH. p. 55–101. Also available from https://doi.org/10.1002/3527600418.bireliabe0012

Bundesärztekammer (2014) Richtlinie der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen. Dtsch Ärztebl 111(38): A1583–A1618

Chwatko G, Bald E (2009) Determination of thiosulfate in human urine by high performance liquid chromatography. Talanta 79(2): 229–234. https://doi.org/10.1016/j.talanta.2009.03.040

Hartwig A, editor (2013) Hydrogen sulfide. MAK Value Documentations, 2007. In: The MAK-Collection of Occupational Health and Safety. Part I: MAK Value Documentations. Weinheim: Wiley-VCH. https://doi.org/10.1002/3527600418.mb778306e4313

Hartwig A, editor (2015) Hydrogen sulfide. MAK Value Documentation, 2010. In: The MAK-Collection of Occupational Health and Safety. Part I: MAK Value Documentations. Weinheim: Wiley-VCH. https://doi.org/10.1002/3527600418.mb778306e4815

Jones K (2014) Case studies of hydrogen sulphide occupational exposure incidents in the UK. Toxicol Lett 231(3): 374–377. https://doi.org/10.1016/j.toxlet.2014.08.005

Kage S, Nagata T, Kudo K (1991) Determination of thiosulfate in body fluids by GC and GC/MS. J Anal Toxicol 15(3): 148–150. https://doi.org/10.1093/jat/15.3.148

Kage S, Takekawa K, Kurosaki K, Imamura T, Kudo K (1997) The usefulness of thiosulfate as an indicator of hydrogen sulfide poisoning: three cases. Int J Legal Med 110(4): 220–222. https://doi.org/10.1007/s004140050071

Kage S, Kashimura S, Ikeda H, Kudo K, Ikeda N (2002) Fatal and nonfatal poisoning by hydrogen sulfide at an industrial waste site. J Forensic Sci 47(3): 652–655. https://doi.org/10.1520/jfs2001216

Kangas J, Savolainen H (1987) Urinary thiosulphate as an indicator of exposure to hydrogen sulphide vapour. Clin Chim Acta 164(1): 7–10. https://doi.org/10.1016/0009-8981(87)90101-X

Nikkanen HE, Burns MM (2004) Severe hydrogen sulfide exposure in a working adolescent. Pediatrics 113(4): 927–929. https://doi.org/10.1542/peds.113.4.927

WHO (World Health Organization) (2000) Air quality guidelines for Europe. WHO Regional Publications, European Series, No. 91, 2nd ed. Copenhagen: WHO Regional Office for Europe. https://apps.who.int/iris/bitstream/handle/10665/107335/9789289013581-eng.pdf, accessed 07 Feb 2022

WHO (World Health Organization), IPCS (International Programme on Chemical Safety) (2003) Hydrogen sulfide: human health aspects. Concise International Chemical Assessment Document, No. 53. Geneva: WHO. https://apps.who.int/iris/bitstream/handle/10665/42638/9241530537.pdf, accessed 25 Apr 2022