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Development, validation and application of a novel LC-MS/MS method for the simultaneous determination of iodinated X-ray contrast media and artificial sweeteners in surface, ground and drinking water

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INTRODUCTION

In recent years, increasing attention has been given to the contamination of the aquatic environment by iodinated X-ray contrast media (**ICM**) and artificial sweeteners (**AS**). In order to be excreted unmetabolized from the body, ICM and AS are designed to be polar and persistent [1,2]. These properties enable them to persist in the aquatic environment. Due to their potential to pass through wastewater treatment plants, they can consequently be detected in surface waters [3,4]. Since surface water is generally used for drinking water production, some of these compounds end up, due to incomplete removal, in produced drinking water.

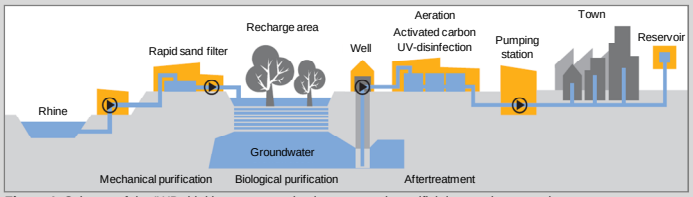


Figure 1: Scheme of the IWB drinking water production process by artificial groundwater recharge

AIMS

- Development, validation and application of a sensitive and robust LC-MS/MS method for the quantification of relevant ICM and AS in order to regularly monitor ICM and AS in the drinking water production process of the IWB (**Fig. 1**)
- If possible, simultaneous determination of ICM and AS down to 10 ng/L without solid phase extraction (SPE)
- Development of a GIS tool (MapChart) for the drinking water production area "Lange Erlen" for geographical analysis and visualization

METHODS

- LC-MS/MS system: Dionex Ultimate 3000 HPLC-System connected to an AB Sciex QTRAP 5500 mass spectrometer (**Fig 2**)
- Electrospray ionization (ESI) operated in positive/negative switching mode
- 10-fold sample enrichment step using a "Genevac" centrifugal vacuum evaporator for sample preparation (**Fig. 3**)
- Scheduled multiple reaction monitoring (sMRM)

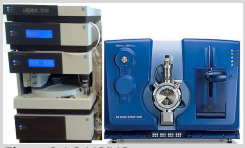


Figure 2: LC-MS/MS system

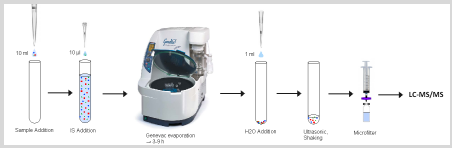


Figure 3: Scheme of the sample preparation procedure

RESULTS

Method development and validation

- Simultaneous determination of 7 ICM and 3 AS by LC-MS/MS in 12 min (**Fig. 4**)
- Compensation of matrix effects (**Fig. 5**) by use of 4 isotopic internal standards
- LOQs < 10 ng/L achieved for all compounds
- Linear working range of 10 - 500 ng/L for ICM and 10 - 2000 ng/L for AS
- Total recoveries between 78 - 113%, covering all three matrix types (**Fig. 6**)

➢ Detailed results of the validation are shown in **Table 1**

Table 1: Validation results

Compound	Linearity R^2	LOQ ng/L	Method precision (CV%) 10ng/L	500/2000 ng/L	SP recovery (n=3)	Total recovery[a] (with IS[b]) (n=5)	Measurement uncertainty (n=4)
Diatrizoic acid (DTZ)	0.9999	1	4%	2%	87 ± 1%	101 ± 4%	18 %
Iopamidol (IOD)	0.9997	5	4%	2%	87 ± 3%	95 ± 5%	27 %
Iomeprol (IOM)	0.9995	5	6%	3%	91 ± 1%	93 ± 10%	24 %
Iopromide (IOP)	0.9995	5	3%	3%	89 ± 2%	103 ± 9%	12 %
Iothalamic acid (IOT)	0.9997	3	6%	2%	88 ± 1%	108 ± 6%	37 %
Ioxithalamic acid (IOX)	0.9998	4	4%	3%	88 ± 1%	86 ± 6%	19 %
Iohexol (IOH)	0.9997	8	5%	3%	86 ± 4%	86 ± 7%	19 %
Acesulfame (ACE)	0.9999	2	3%	1%	95 ± 2%	101 ± 6%	11 %
Saccharin (SAC)	0.9995	7	4%	2%	92 ± 0%	89 ± 7%	23 %
Cyclamate (CYC)	0.9992	1	3%	2%	92 ± 1%	90 ± 10%	17 %

R^2 coefficient of determination, *LOQ* limit of quantification, *CV* coefficient of variation, *SP* sample preparation, *IS* internal standard
[a]avarage recoveries for the three matrix types, [b] IS were taken into account for the calculation of the total recovery

Occurrence and fate of ICM and AS in the drinking water production process

- 7 of the 10 investigated compounds were removed by soil passage and therefore not detected in ground and drinking water (**Table 2**)
- Based on the initial concentration in Rhine water, about 60% of diatrizoic acid and 15-20% of iopamidol and acesulfame passed the whole multi-barrier system of the drinking water production process and were detected in produced drinking water (**Fig. 7**)

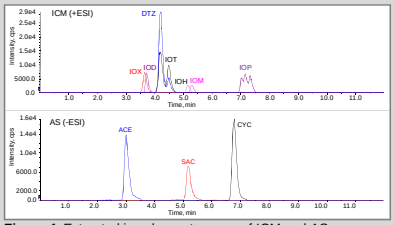


Figure 4: Extracted ion chromatograms of ICM and AS

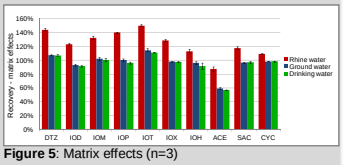


Figure 5: Matrix effects (n=3)

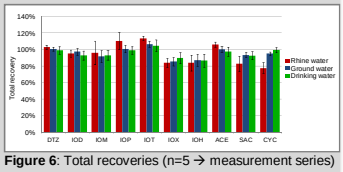


Figure 6: Total recoveries (n=5 → measurement series)

Table 2: Concentrations (ng/L) and relative standard deviations of ICM and AS in Rhine (n=16), ground (n=8) and drinking water (n=18) between March and April 2013

Compound	Rhine water Mean	Rhine water RSD	Ground water Mean	Ground water RSD	Drinking water Mean	Drinking water RSD
Diatrizoic acid	32	25%	27	11%	19	9%
Iopamidol	146	49%	63	28%	28	20%
Iomeprol	153	53%	-	-	-	-
Iopromide	144	36%	-	-	-	-
Iothalamic acid	-	-	-	-	-	-
Ioxithalamic acid	41	23%	-	-	-	-
Iohexol	32	36%	-	-	-	-
Acesulfame	764	11%	415	25%	122	11%
Saccharin	50	21%	-	-	-	-
Cyclamate	33	22%	-	-	-	-

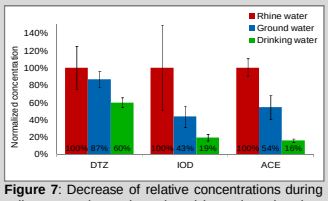
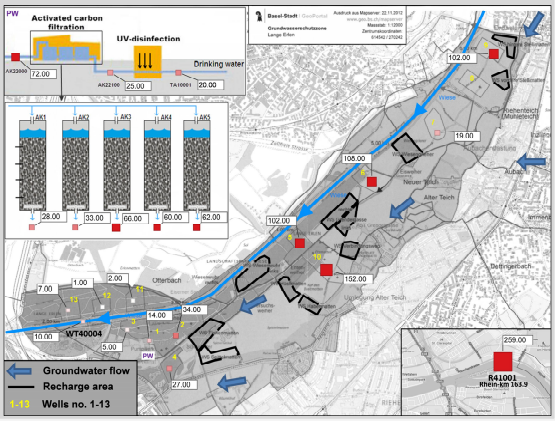


Figure 7: Decrease of relative concentrations during soil passage (groundwater) and by activated carbon filtration/UV-irradiation (drinking water)

Influence of Wiese infiltration and artificial groundwater recharge in the "Lange Erlen"

- Since concentrations of iopamidol and acesulfame differ significantly between Wiese (low) and Rhine water (high), wells that show lower concentrations are mainly influenced by Wiese water infiltration, while wells with higher concentrations are mainly affected by artificial groundwater recharge with Rhine water (see example of iopamidol in **Fig. 7**)

Figure 7: MapChart of the "Lange Erlen" area, showing concentrations of iopamidol in ng/L in groundwater wells.
Concentrations in the different wells differ depending on the location. These differences result from different concentrations of iopamidol in Wiese (WT40004, 10 ng/L) and Rhine water (R41004, 259 ng/L).
Therefore, wells that are located southwest, are due to the lack of recharge areas and their proximity to the Wiese, mainly influenced by Wiese water infiltration. Thus, especially well 3, 11, 12 and 13 show lower concentrations. In contrast, wells 5, 6 and 10 are located close to the main part of recharge areas and are thus mainly influenced by artificial groundwater recharge with Rhine water, which is why they show higher iopamidol concentrations.



CONCLUSION

- A novel, sensitive, fast and easy LC-MS/MS method was developed that allows simultaneous determination of ICM and AS in surface, ground and drinking water by applying a sample enrichment step through centrifugal vacuum evaporation
- The method supports increased sample throughput, is less labor intensive and cheaper than comparable methods using SPE enrichment
- Statements about the fate of ICM and AS during drinking water prod. could be made
- Influences due to Wiese water infiltration and artificial groundwater recharge with Rhine water, which affect the groundwater quality in the "Lange Erlen", could be qualitatively distinguished with the anthropogenic tracer iopamidol and acesulfame

References: [1] Pérez S, Barceló D (2007) Anal Bioanal Chem 387:1235–1246. [2] Lange FT, Scheurer M, Brauch HJ (2012) Anal Bioanal Chem 403:2503-2518. [3] Hirsch R, Ternes TA, Lindart A, Haberer K, Wilken RD, Fresenius J (2000) Fresenius J Anal Chem 366:835-841. [4] Scheurer M, Brauch H-J, Lange FT (2009) Anal Bioanal Chem 394:1585–1594