(Pre)-analytical pitfalls in urine iodine measurements using the Sandel-Kalthoff method

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Introduction

Iodine is one of the most important trace elements and has a major influence on the development of our brains in childhood and on the supply of thyroid hormones throughout our lives. To determine the current iodine status, urine is the most preferred material, because more than 90 % of the iodine will be excreted by urine. To quantify the iodine status, the WHO recommends the Sandel-Kolthoff method with appropriate sample preparation. However, there are many different sample preparation and measurement techniques used around the world. This makes it difficult to compare iodine concentrations between studies unless compared to a reference method (e.g. ICP-MS), as each method and instrument used has different advantages and disadvantages.

Methods

The methods were derived from an assay established and optimized at the Robert Koch Institute (RKI), variating the amount of sample and addition of sodium hydroxide and ammonium persulfate in compliance with the WHO recommendations (see Table). The measurements were performed in triplicates on a Gallery analyzer (Thermo Scientific), which is UV-VIS based and using the Sandell-Kolthoff method. The results were compared to the RKI (measured on a Cobas Mira analyzer) and ICP-MS as a reference assay. In addition to the WHO recommendations, the kinetic of the reaction was monitored and the reaction constant was determined for each sample instead of the end-point of the reaction. To ensure the quality of all measurements, one pooled urine sample (75 µg/L), two quality controls (QC, Recipe, ClinChek Trace elements, 115, 516 µg/L) and reference material (NIST 3668) with two concentration levels (142, 279 µg/L) were analyzed.

Methods	**RKI**	**Mod 1**	**Mod 2**	**Mod 3**	**WHO**
Sample Volume / µL	500	250	250	250	250
Volume APS / µL	900	450	1000	1000	1000
Volume NaOH / µL	100	50/100	100	-	-
Digestion			Heating Block		
Temperature / °C	85	95	95	95	100
Time / min	60	60	60	60	60
UV-Vis Instruments	Cobas Mira		Gallery (Thermo Scientific)		
Methods	Kinetic		Kinetic		Endpoint
Calibration	Log-Logit4		Kinetic 1st Order		Lin./Quad.
Range / µg/L	13 – 419		13 – 571		13 – 419

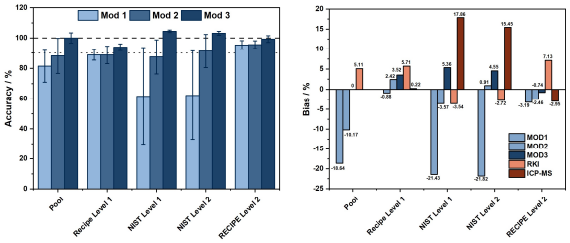
c (APS) = 1 mol/L, **c (NaOH)** = 0.0875 mol/L, **RKI** – Robert-Koch-Institute, **NaOH** – sodium hydroxyde, **APS** – amminoum persulfate

Results

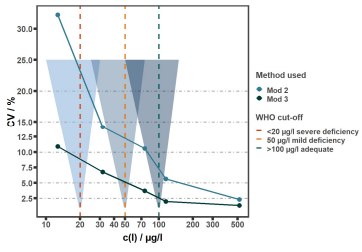
Imprecision – QCs

	n	Method	Within-run Precision / %	Within-run Accuracy /%	Between-run Precision / %	Between-run Accuracy /%
Recipe Level 1	36	Mod 1	2,3	99,15	1,32	99,15
	33	Mod 2	2,72	92,71	2,13	92,4
	15	Mod 3	2,01	101,44	1,9	101,44
Recipe Level 2	36	Mod 1	3,42	96,43	1,73	96,43
	35	Mod 2	1,76	88,59	1,56	88,55
	15	Mod 3	2,72	99,26	1,87	99,26

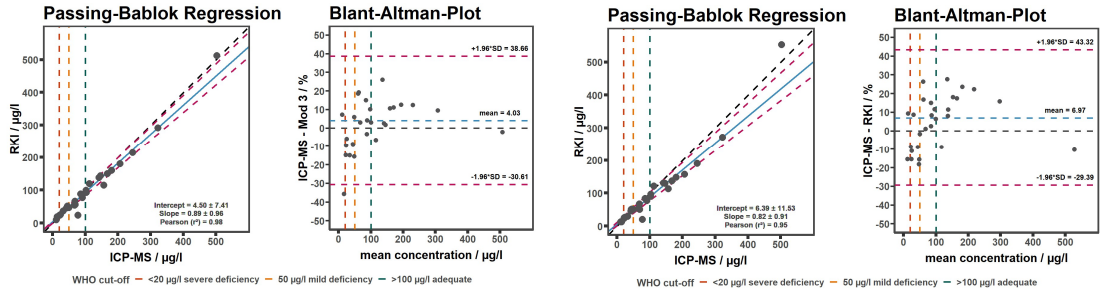
Recovery



Minimal Difference



Method comparison



Discussion and conclusion

The quality assessment samples demonstrated very good correlation with the target values. The bias as well as the precision was less than 10 %, with the exception of one sample preparation method. For ICP-MS, the NIST samples showed a bias of >15 %. Independently, all sample preparation methods compared to ICP-MS show an acceptable values for the Passing-Bablock regression with intercepts in the range of -2.11 – 6.83, a slope between 0.84 – 0.91 and a Pearson correlation of 0.96 – 0.98. However, during the establishment of each method it was observed that the ratio of sample volume to amount of ammonium persulfate, the amount of sodium hydroxide and the quantification strategy have an major impact to the final results.

For urinary iodine methods, the sample preparation strategy should be selected carefully. The different sample preparation methods had an impact on the results and each had its distinct advantages and disadvantages.