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ICP-MS multi-element determination – potential applicability in clinical laboratory practice

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PURPOSE / OBJECTIVES

The interest to inductively coupled plasma mass spectrometry (ICP-MS) is steadily increasing, owing to the high analytical potential for simultaneous determination of trace and ultra-trace elements and throughput of the method. However some drawbacks have to be carefully considered, when ICP-MS method is developed, to ensure reliable approach for correction of the possible spectral and non-spectral interferences. The aim of this study was to develop and validate ICP-MS method for multielement determination of Mg, Cu, Zn, Se and Rb in human serum and to verify its applicability by patients with thyroid disorders.

MATERIALS & METHODS

A microwave assisted acid digestion procedure (MW) for human serum samples preparation, as well as an optimized pseudomatrix-matched calibration approach for ICP-MS were used. The MW was performed by Multiwave GO Microwave Digestion system with closed vessels (Anton Paar, Graz, Austria). Multielement determination was carried out by Thermo Scientific iCAP Qc ICP-MS (Thermo Scientific, Germany). The mass spectrometer is equipped with a collision cell, working in Kinetic Energy Discrimination (KED) mode, with helium as collision gas.

The analytical method was validated regarding linearity, instrumental LoDs, method LoQs, selectivity, trueness and precision. The method was tested by quantification of the serum levels of Mg, Cu, Zn, Se and Rb by patients with hypothyroidism (n = 33), hyperthyroidism (n = 41) and age sex matched euthyroid controls (n = 40).

RESULTS

The compensation of the non-spectral interferences, caused by the serum matrix was achieved by specific preanalytical sample preparation, application of the internal standard method, as well as an optimized pseudomatrix-matched calibration. Four microwave assisted digestion methods were tested for compensation of the matrix effects. The chosen method (0.3 mL of sample mixed with 1.5 mL HNO₃ and 1.5 mL water, digested for 25 min at 190°C) provides complete digestion of the serum matrix with acceptable residual carbon content.



ICP-MS iCAP Q Thermo Scientific

Plasma conditions	
RF-power	1550W
Nebulizer Gas Flow	1.03 L min ⁻¹
Auxilliary Gas Flow	0.80 L min ⁻¹
Plasma Gas Flow	14.0 L min ⁻¹
He Gas Flow	4.4 L min ⁻¹
Mass Spectrometer Settings	
Sweeps	15
Replicates	3
Survey run amu	22.39 - 245
Isotops/ Dwell time (s)	
²⁴ Mg	0.02
⁶³ Cu	0.05
⁶⁶ Zn	0.05
⁷⁸ Se	0.2
⁸⁵ Rb	0.05

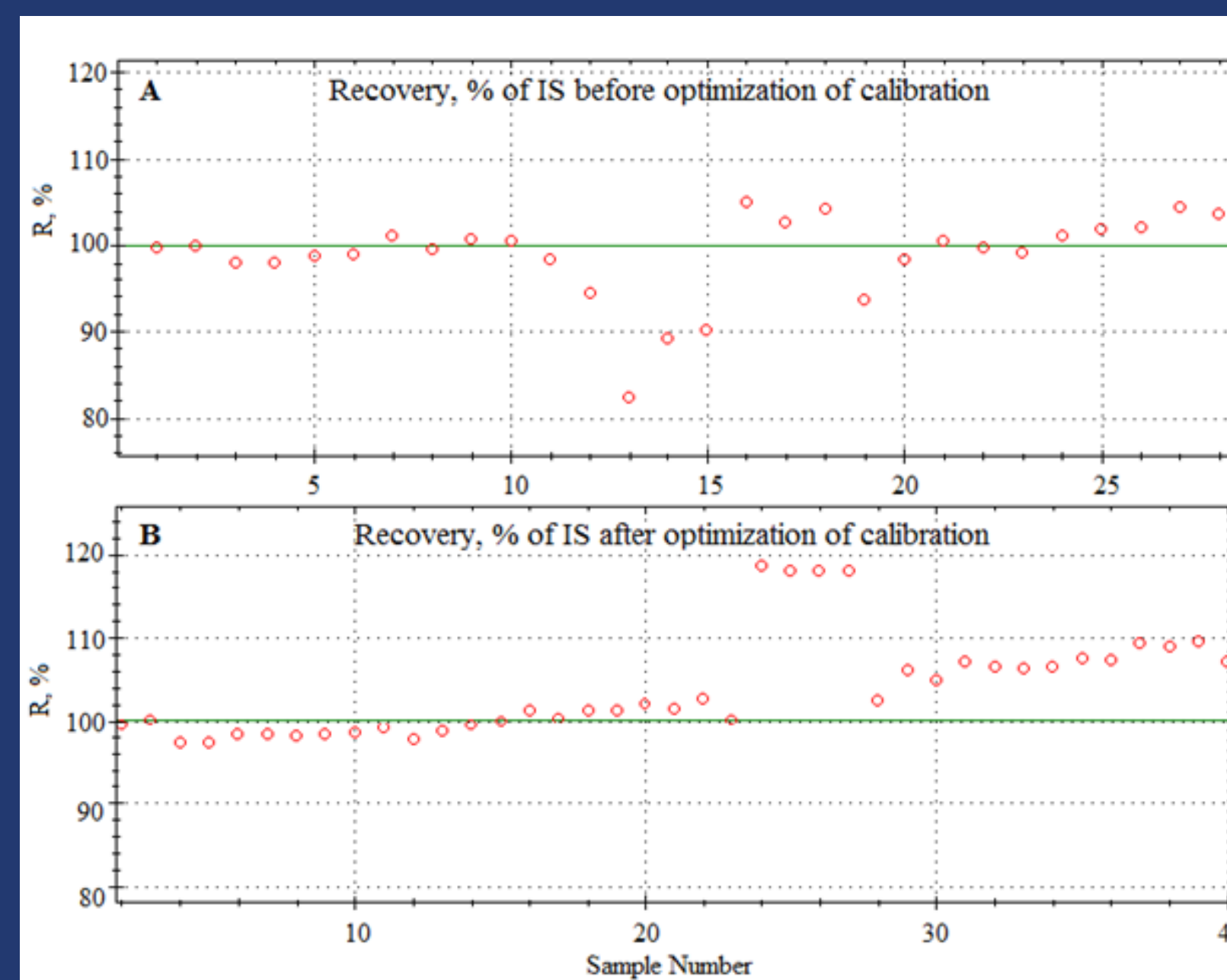


Fig 1. Recovery of Internal standard Rh (2 µg/L) in a consecutive measurements as follows:
A. Sample numbers: (1-10) Calibration standards in 15% HNO₃ with low Na content; (11-15) Calibration standards in 15% HNO₃ with increasing Na content; (16-18) 15% HNO₃; (19-28) serum samples;
B. Sample numbers: (2-23) Calibration standards in 15% HNO₃ with 130 mg/L Na content; (24-27) 15% HNO₃; (28-40) serum samples

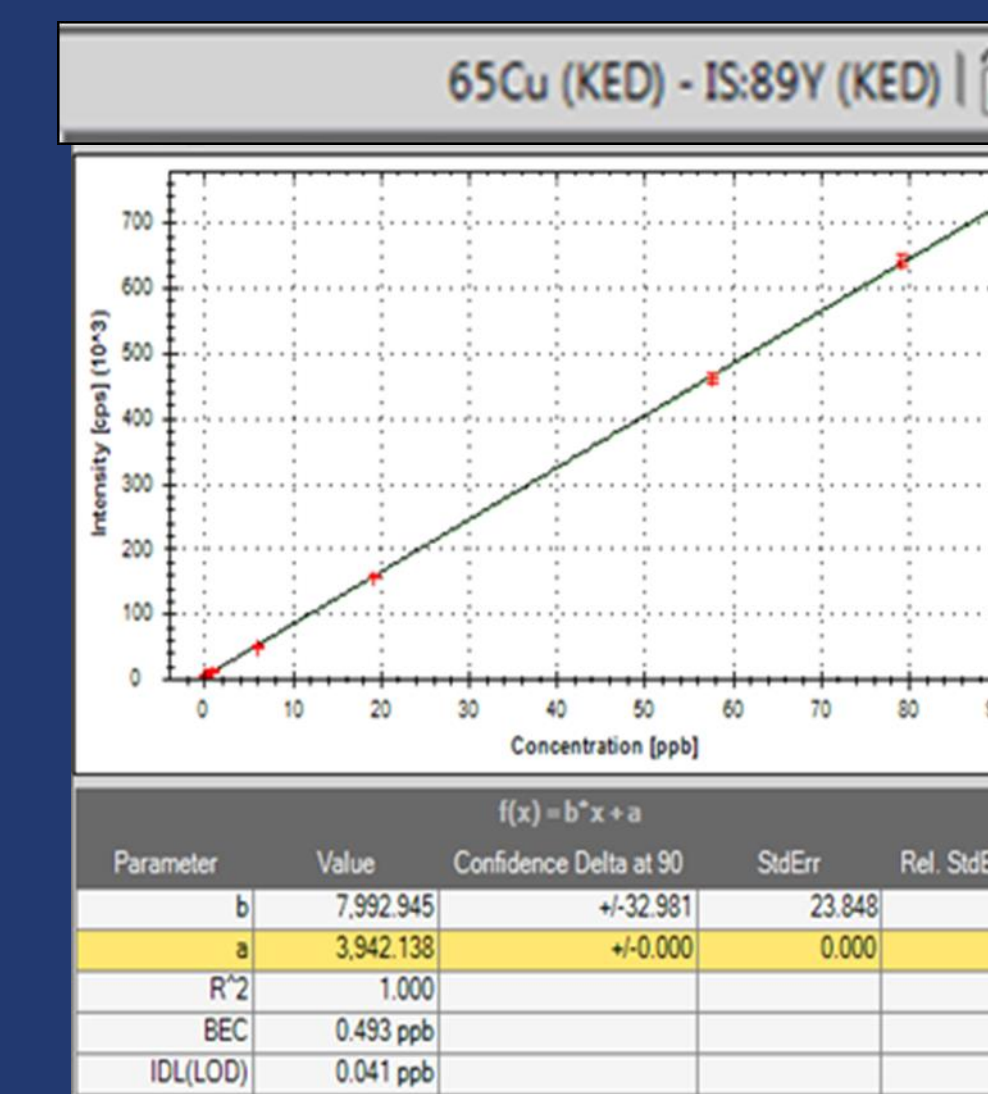


Fig 2. Calibration curve of Cu



Multiwave GO, Anton Paar

RESULTS

Internal Standard (IS) Rh/Y mixture was introduced through an online IS kit. For introduction stability, the acid content in the IS and calibration standard solutions was equalized. It was observed that the high Na content in serum sample solutions causes two opposite effects on the analyte signals: suppression of ionization efficiency into the ICP and gradual enhancement of the ion transmission (**Fig 1A**). For overcoming this matrix interference all calibration solutions and blanks were prepared in 15% v/v HNO₃ with 130 mg/L Na, as a matrix-match component (**Fig 1B**).

The method LoQs achieved for Cu, Zn, Se and Rb were respectively 20, 13, 9.3, 55 nmol/L and 1.9 µmol/L for Mg. The intra-assay CVs, inter-assay CVs and bias% for the different elements ranged respectively 1 ± 2%, 1.9 ± 3.3% and -3.6 ± +1.6, with R² ≥ 0.999 for all elements.

We observed significantly lower serum Mg concentration in both dysthyroidism groups and lower Se levels in the hyperthyroid group (p < 0.05). The serum Cu levels were significantly higher only in hyperthyroid patients (p < 0.001) vs control group.

SUMMARY/CONCLUSION

Simultaneous ICP-MS determination of multiple elements in human biological materials requires specific preanalytical sample preparation, calibration strategies and methodological conditions for overwhelming the spectral and non-spectral interferences.

The proposed ICP-MS method for microwave assisted acid mineralization combined with semi-matrix matched calibration showed to be reliable for Cu, Mg, Se, Zn and Rb simultaneous determination in serum samples and demonstrates a potential feasibility as a good analytical choice in clinical laboratory practice. The approach used is applicable in the development of ICP-MS methods for multielement analysis in other biological materials