www.analytic-news.com Publication Date: 15.10.2015

Direct Determination of Trace Elements in Body Fluids Using ICP-Mass Spectrometry

Dr. René Chemnitzer

Analytik Jena AG

Introduction

The better understanding of the relevance of various elements in metabolic and other processes in organisms leads to increased interest in the analysis of biological samples like body fluids. Here, the focus is on supply of essential elements and detection of toxic elements. Fast and more sensitive analytical techniques are necessary to satisfy these demands.

Inductively Coupled Plasma Mass Spectrometry offers low detection limits, multi-element capabilities, simplified sample preparation and low sample consumption. It is very useful for the determination of trace and ultra-trace elements in various biological samples.

Analysis of various matrices

The analysis of biological samples allows a variety of conclusions about the current status of an organism.

Different matrices can be investigated (Table 1). The individual properties of the body fluids are related to specific functions in the organism. Therefore the selection of the right matrix is crucial to get the correct answer for a specific question.

Tab. 1: Sample matrix body fluids

Research area	Appropriate sample matrix
Medicine	
• Monitoring of the mineral balance	Urine
• Detection of medicines and additive drugs	Plasma
• Exposition to harmful substances	Serum
• Detection of toxins	Whole blood
• Historical samples	Hair
Therapeutic medicine	
• Pharmacodynamics	

Blood is a transport medium. The trace element concentration depends on short term uptake. Since an insufficient mineral uptake is balanced with body's own reserves e.g. serum cannot indicate mineral deficiencies.

Heavily discussed is the value of hair analyses. Results are highly dependent on age, sex, length and color as well as care products and environmental factors. The endogenous and exogenous portions cannot be distinguished and a correlation of elemental concentrations in hair and blood/urine is not proven [1]. Generally accepted is the analysis of hair samples for the detection of addictive drugs and the analysis of ancient samples. [2]

Analytical methods

Traditionally the characterization of body fluids was performed using atomic absorption techniques. The combination of flame (F-AAS) and graphite furnace AAS (GF-ASS) is able to cover a large concentration range. Since AAS is a single element technique and needs an individual excitation source the analysis is time consuming and the number of elements, that can be characterized, is limited.

With ICP-MS a multi-element technique is nowadays used since it offers the low detection limits of GF-AAS and a large dynamic range of 10 orders of magnitude. A characterization that took between 30 sec and 5 min for just one element is now possible for >20 elements in less than 5min.

ICP-MS, with its capability to detect individual isotopes, can be furthermore applied for long term studies with isotopic enriched medical drugs.

Method development

For the analysis of whole blood the challenges are the sample matrix and interferences that influence the analysis for elements of interest. The primary focus is on essential but also on toxic elements like Selenium, Arsenic, Cadmium, Lead and Chromium.

Interferences that are formed by the sample matrix and e.g. Argon or Oxygen can be removed with interference management systems. These systems use Hydrogen and Helium to generate collisions and reactions with the molecular interferences. As a result, new and non-interfering species are formed or the kinetic energy of the interfering molecules is decreased so that they do not reach the mass filter.

The sample preparation is very simple. All liquid matrices can be diluted and directly analyzed with the ICP-MS. The calibration of the method can be performed using an external calibration with different calibration levels or by using a standard addition calibration on a real sample. The standard addition calibration is useful if matrix effects will influence the sample introduction and excitation in the plasma.

Instrumentation

Direct multi-element analysis of plasma and whole blood control materials was carried out using an Analytik Jena PlasmaQuant® MS, ICP-MS. All work was done under routine analytical laboratory conditions, not "clean room" conditions.

Materials and reagents

High purity nitric acid (Baseline®, Seastar Chemicals), Triton-X 100 (Sigma Aldrich) and deionized water (18 MΩ cm^{-1}) were used in the preparation of sample and calibration solutions. All labware, new or used, was thoroughly cleaned by acid washing and rinsing, and then the clean containers were left filled with 2% v/v HNO_3 until use. Three multi-element calibration solutions are prepared from a multi-element solution in 2% v/v HNO_3. An internal standard solution was prepared with 1% v/v HNO_3. The internal standard was added to the nebulizer through a "Y-piece".

Sample analysis

All certified materials were prepared according to the manufactures instructions. After carefully dissolving the materials the samples were diluted with a diluent of 0.5% v/v HNO_3 und 0.005% v/v TritonX-100.

The measured values shown are the average of two repeat measurements.

The reference material ClinChek-plasma control Level 1 and 2 (Recipe®) was dissolved in 3 mL deionized water and subsequently diluted 1:10 using the diluent solution. The obtained results (Table 2) are in perfect match with the certified concentrations.

The reference material "trace elements in whole blood" (Seronorm) was diluted 1:20 after carefully dissolving it in 5mL deionized water. As seen from Table 3, excellent agreement between the measured and the certified values is observed.

Fig. 1: PlasmaQuant® MS Elite

Conclusion

This work has successfully demonstrated that the ICP-MS PlasmaQuant® MS provides a simple and very effective solution for the direct determination of trace elements in complex samples such as plasma and whole blood. The fast multi-element capability and low detection limits will increase the use of ICP-MS in the characterization of body fluids. Easy handling and straightforward software solutions have increased the use of this method in the past years.

References

[1] Dtsch Arztebl 2002, 99: A3026-3029 [Heft 45]

[2] Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz 2005, 48, 246-250

Tab. 2: Results for the analysis of ClinChek®-plasma control Level 1 and 2 (Ch.-B.: 417)

Element		Plasma Level 1		Plasma Level 2	
		Measured	Certified	Measured	Certified
Cd	µg/L	2,2	2,0 – 3,4	9,8	9 – 15
Cr	µg/L	3,5	2,6 – 4,2	14	11 – 16
Co	µg/L	5	4,1 – 6,7	16,6	14 – 22
Cu	µg/L	850	634 – 1056	1290	1050 – 1750
Fe	µg/L	756	563 – 937	964	859 – 1431
Li	mg/l	2,4	1,9 – 3,1	5,2	3,9 – 6,5
Mg	mg/l	26	23 – 37	33	32 – 37
Mn	µg/L	4,9	3,8 – 6,2	14,6	11 – 17
Mo	µg/L	1,1	0,7 – 1,2	6,6	4,5 – 7,5
Ni	µg/L	7,4	5,9 – 9,7	18	16 – 26
Tl	µg/L	0,03	<1	2,5	2,1 – 3,5
Zn	µg/L	1113	823 – 1371	1338	1133 – 1887

Tab. 3: Results for the reference material Seronorm™ Trace Elements Whole Blood Level 1 and 2

Element		Seronorm Level 1 LOT 404107		Seronorm Level 2 LOT MR9067	
		Measured	Certified	Measured	Certified
Cd	µg/L	0,72	0,67 – 0,76	5,77	5,4 – 7,2
Co	µg/L	0,13	<1	5,3	5,2
Cr	µg/L	1,3	1,2	7,2	7,1
Mn	µg/L	9,5	9	13,9	12,8 – 15,1
Ni	µg/L	1,6	2	5,2	5
Pb	µg/L	33	31 – 39	364	353 – 443