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Determination of trace elements in serum by dynamic reaction cell inductively coupled plasma mass spectrometry Developing of a method with a desolvating system nebulizer

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Abstract

An inductively coupled plasma mass spectrometer (ICP-MS), equipped with a dynamic reaction cell (DRC) and coupled with a desolvating nebulizing system (Apex-ACM) to reduce the oxide formation, was used in the determination of Al, Co, Cr, Mn, Ni and Se in serum samples. The effect of the operating conditions of the DRC system was studied to get the best signal-to-background (S/B) ratio. The potentially interfering molecular ions at the masses m/z ^{27}Al, ^{59}Co, ^{52}Cr, ^{55}Mn, ^{60}Ni and ^{78}Se, were significantly reduced in intensity by using NH_3 and H_2, as the reaction cell gases in the DRC, while a proper Dynamic Bandpass Tuning parameter q (RPq) value was optimized. The detection limits for ^{27}Al, ^{59}Co, ^{52}Cr, ^{55}Mn, ^{60}Ni and ^{78}Se, estimated with 3-σ method, resulted to be 0.14, 0.003, 0.002, 0.01, 0.01 and 1.8 μg L^{-1}, respectively. This analytical method was developed on both a human serum certified reference material and a lyophilized animal serum produced and proposed in an intercomparison study. The results obtained for the reference samples agreed satisfactorily with the certified values. Precision (expressed as CV%) between sample replicates was better than 10% for elements determination, with the only exception of aluminium (14%).

Keywords: Trace elements; Dynamic reaction cell inductively coupled plasma mass spectrometry; Serum; Desolvating system

1. Introduction

In the biological monitoring, the quantification of trace elements, such as Al, Co, Cr, Mn, Ni and Se in serum, as indicators of the exposure level, is rather challenging. The role of these metals in living organisms and their potential toxicity are well known and widely taken into account by several authors [1–5]. In fact, Co, Cr, Mn and Se are nutrients that play a role in human physiological functions (such as bone mineralization, protein and energy metabolism, metabolic regulation, cellular protection from damaging, free radical species), while Ni is considered to be essential for animal species, but its essentiality for the human being has not yet been proven. However, exposure to high levels of Ni can cause adverse health effects. Aluminium, due to its chemical nature, is normally excluded from biochemical and metabolic processes. Nevertheless, the analysis of trace elements at low concentrations still pose a challenge, in terms of accurate and precise multi-elemental determination, to most of the analytical techniques.

The difficulties encountered in the analysis of human fluids are mainly ascribable to the very low concentration of the elements, frequently found below the detection capabilities of the techniques routinely used. Furthermore, the risk of contamination of samples, especially for Al and Cr during their manipulation represented another drawback.

Inductively coupled plasma mass spectrometry (ICP-MS), equipped with quadrupole (Q) or sector field (SF) technology, is a powerful technique for multielemental analysis in biological matrices, because of its capability of detection at very low concentrations [6–16]. However, one of the major disadvantages of ICP-MS is the occurrence of mass interferences, caused by atomic or polyatomic species having the same mass/charge ratio of the analyte [17]. In order to avoid this, SF high resolution mass spectrometry was widely used, operating at medium or high resolving power [9,18–20]. Nevertheless, for some isotopes, the use of the highest resolution settings to eliminate spectral interferences, leads to a lowering in sensitivity, thus compromising the determination of physiological levels of elements. Moreover,

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it should be noted that only a few laboratories use the SF technique for routine biomedical analyses, due to its complexity and high cost of the instrumentation and maintenance.

Chemical resolution by means of ion–molecule reactions, offers an interesting alternative compared to high mass resolution instrumentation. In fact, the selectivity of a chemical reaction can often be utilized to avoid significant losses in sensitivity, typical of SF operating in high resolution mode. Collision and reaction cells have been widely used as an implementation in mass spectrometry to reduce interferences in multielemental analysis [21–30]. In serum, since it is a more complex matrix than urine and water (due to higher presence of mass interferences), the dynamic reaction cell (DRC) technology offers a more versatile approach in the utilization of ion–molecule reactions, thanks to the opportunity of choosing a variety of reaction gases. Charge transfer or even atom transfer reactions can be utilized because discrimination against unwanted reaction products is based on the band-pass setting of the DRC. The onset and width of the band-pass can be dynamically adjusted so that precursor ions of undesired reaction products are rejected when a given analyte ion is being detected. This work is in advance since its aim is to quantify trace elements in serum by DRC-ICP-MS with band-pass correction coupled with a desolvating system nebulization. With this method, it was possible to eliminate all the potential mass interferences present in serum, among which the oxygen-based molecular ions are the most difficult to eliminate by means of DRC technology. In fact, the oxides formation was strongly reduced before sample ionization in the torch by using the desolvating system.

Analyses were performed on both a human serum certified reference material and a lyophilized animal serum.

Furthermore, some analytical parameters were determined such as detection limits, precision, sensitivity and accuracy.

2. Experimental

2.1. Reagents and sample treatment

All calibrant solutions were daily prepared from 1000 mg L^{-1} stock solutions (Spex Industries Inc., Edison, NJ, USA) after subsequent dilution, with high-purity deionized water (<0.3 μS cm^{-1}, Water Purification Systems, Labconco Corp., Kansas City, MO, USA). Super-pure concentrated HNO_3 (Merck, Darmstadt, Germany) was diluted up to 2% with deionized water and used to rinse the Apex nebulizer.

The addition calibration approach was chosen to quantify the content of elements. Gallium was added at the concentration of 1 μg L^{-1} as the internal standard.

For the accuracy, the Human Serum Certified Reference Material ClinChek Serum Control Level I (Recipe Chemicals Instruments, Münich, Germany, with two different lot numbers) was employed.

The lyophilized equine serum was in-house produced and proposed in a proficiency test (PT), organized with some Italian public laboratories as a part of a Research Programme focused on the determination of potentially neurotoxic elements in body fluids. The freeze-dried animal serum, after reconstitution by adding 5 mL of deionized water, was simply diluted 1 + 19 (v/v) with high-purity deionized water and analyzed without any digestion procedure on the same day.

2.2. Instrumentation

Measurements were performed by means of a quadrupole-based ICP mass spectrometer, Elan DRC II (Perkin-Elmer SCIEX, Norwalk, CT, USA). A desolvating system (Apex IR, Omaha, NE, USA) was combined with DRC-ICP-MS, as the sample introduction method, in order to minimize the oxides contribution. In this system, the liquid samples are dispersed by a micro-flow PFA nebulizer into a heated cyclonic spray chamber and then into a Peltier-cooled desolvation apparatus with a multipass condenser, where the sample aerosol is efficiently conditioned to produce an intense and uniform dry aerosol. The residual solvent vapour, in the sample aerosol stream, is removed by a Nafion® fluoropolymer membrane desolvation module (ACM) in conjunction to the ICP torch injector. In particular, the solvent vapour passes into the Nafion® membrane and is removed by a counter current sweep flow of a dry gas (argon), which does not pass through the membrane or enter the sample aerosol stream. The use of the ACM membrane further reduces the oxides percentage and other interferences produced by the solvent.

The instrumental settings and operative conditions are reported in Table 1.

3. Results and discussion

3.1. Interferences correction

Mass interferences can be a major restriction in a quadrupole mass analyzer that restricts the resolution to approximately one mass unit. Therefore, ions with the same nominal mass of the analyte (single, doubly charged and polyatomic ions) cannot be

Table 1
Instrument settings and data acquisition parameters for DRC-ICP-MS

Instrumentation	Elan DRC II (Perkin-Elmer SCIEX, Norwalk, CT, USA)
Sample uptake rate	400 μL min^{-1}
Sample introduction	Apex IR (ESI, Elemental Scientific Inc., Omaha, NE, USA): condenser, −5 °C, heater 140 °C, N_2 flow 10 mL min^{-1}
Internal standard	^{71}Ga
Radio frequency power	1500 W
Gas flow rates (L min^{-1})	Plasma, 15; auxiliary, 1.0; nebulizer, 0.8
Interface	Ni cones
Extraction lens voltage	Optimized for maximum I (^{56}Fe)
Reaction gases	NH_3 and H_2
Reaction gas flow rates	Optimized for maximum S/B ratio
RPq	^{27}Al, 0.65; ^{59}Co, 0.70; ^{52}Cr, 0.70; ^{55}Mn, 0.70; ^{60}Ni, 0.75; ^{78}Se, 0.65
Scanning mode	Peak hopping
Dwell time (ms)	100
Number of replicates	5