HANDBOOK OF ICP-QQQ APPLICATIONS USING THE AGILENT 8800 AND 8900

3RD EDITION

Primer

Agilent Technologies

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Foreword

Five years have passed since Agilent Technologies launched its 8800 Triple Quadrupole ICP-MS (ICP-QQQ) at the 2012 Winter Conference on Plasma Spectrochemistry in Tucson, Arizona, USA. At that time, ICP-MS had already been around for almost three decades and was widely praised for its low limits of detection. In fact, it was considered as the technique-par-excellence for multi-element (ultra-)trace analysis in a wide variety of fields. However, spectral interferences were still causing concern in some applications. Significant progress had been made in providing ICP-MS users with adequate tools to cope with spectral overlaps compared to the early commercial instruments introduced in 1983. By using a double-focusing sector-field mass spectrometer instead of a quadrupole filter for mass analysis, many spectral interferences can be resolved, but this approach requires expensive instrumentation. Quadrupole-based instruments could be equipped with a multipole-based collision/reaction cell (CRC), which alleviated spectral interferences to a significant extent, for instance, by using a non-reactive collision gas such as helium to slow down polyatomic interfering ions to a larger extent than the atomic analyte ions, such that the former could be selectively discriminated against on the basis of their lower kinetic energy. The analytical community first saw Agilent's 8800 ICP-QQQ instrumentation as an improved version of a quadrupole-based ICP-MS equipped with a CRC. But 5 years later, the conclusion has to be that it is much more than that.

In Agilent's ICP-QQQ, an octopole CRC is preceded by an additional quadrupole, enabling double mass selection, i.e. before the ions enter the CRC and afterwards. When the first quadrupole is used as an ion guide only, the ICP-QQQ system can be used as a "traditional" quadrupole-based ICP-MS instrument. This mode could be useful for carrying out routine analysis not significantly challenged by spectral interferences. When operated in tandem or MS/MS mode, however, the double mass selection only allows the analyte ion and the interfering ion(s) with the same mass-to-charge ratio to enter the CRC; all ions with a different mass-to-charge ratio are removed at this stage. Consequently, the control over the processes in the cell is greatly improved as the reaction of other (e.g. matrix) ions with the cell gas no longer hinders the desired reaction process. In case of a mass shift reaction – i.e. chemical conversion of the analyte ion into a reaction product ion that can be measured interference-free at another mass-to-charge ratio – the absence of other ions at the new "location" of the product ion in the mass spectrum is guaranteed. As a result, interesting but challenging elements, such as S and P in biochemical applications, As and Se in environmental and food applications, or Si in nanoparticle applications can be easily assayed, interference-free.

Profiting from the analytical advantages offered by MS/MS functionality, some ICP-QQQ users have demonstrated a larger degree of creativity by using very reactive gases such as NH_3 or CH_3F in the CRC and monitoring reaction product ions at much higher mass-to-charge ratios than could be adequately exploited previously. Although this might initially sound complicated, the ICP-QQQ's software offers tools like product ion scanning, precursor ion scanning and differential mass scanning that provide the user with a clear insight into the reactions proceeding in the cell and allow the product ion that will provide the best, often unprecedented limits of detection to be easily identified. This level of freedom and ease of use leads to a situation in which every type of spectral overlap – whether caused by a polyatomic ion, doubly charged ion or isobaric nuclide – can be successfully overcome. Moreover, ICP-QQQ users have also been charmed by the additional advantages provided by this type of instrumentation, such as the unparalleled abundance sensitivity, which is an added benefit of double mass selection.

In 2016, the 8800 ICP-QQQ was replaced by the Agilent 8900 ICP-QQQ series. While maintaining the performance to resolve spectral interferences, this second generation ICP-QQQ instrument provides enhanced sensitivity and a faster detector system with a 100 µs minimum dwell time. The latter feature is of specific importance in single-nanoparticle analysis, a rapidly emerging type of application, and in handling fast transient signals, such as those generated via laser ablation systems equipped with ultra-fast ablation cells.

In my opinion, ICP-QQQ has not only fulfilled its initial promises, but has greatly surpassed the anticipations of the diverse community of ICP-MS users.

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Introduction to Agilent Triple Quadrupole ICP-MS

Agilent introduced the world's first triple quadrupole ICP-MS (ICP-QQQ) in 2012. The Agilent 8800 ICP-QQQ signaled a major advance in ICP-MS technology and redefined performance for trace element analysis. Compared to existing quadrupole ICP-MS instruments, the 8800 offered significant analytical benefits across many applications in both industry and academic research laboratories. Building on this success, the Agilent 8900 ICP-QQQ was launched four years later, in 2016.

Configuration of Agilent's ICP-QQQ instrumentation

According to IUPAC (term 538 from the 2013 Recommendations), a triple quadrupole mass spectrometer is a *"Tandem mass spectrometer comprising two transmission quadrupole mass spectrometers in series, with a (non-selecting) RF-only quadrupole (or other multipole) between them to act as a collision cell."*

The cell containing the ion guide—the Octopole Reaction System (ORS) in the case of Agilent ICP-QQQ—can be pressurized with a collision or reaction gas to allow the selective attenuation of potential interfering ions.

In MS/MS operation, where both quadrupoles are operated as unit mass filters, ions at the target analyte mass are selected by the first quadrupole (Q1) and passed to the ORS cell, where the analyte ions are separated from overlapping interfering ions. The resulting product ions that emerge from the cell are then filtered by the second quadrupole (Q2) before being passed to the detector. This configuration releases the full potential of reaction cell gas methods to resolve spectroscopic interferences including isobaric and doubly-charged interferences, as well as polyatomic ion overlaps.

As a result, ICP-QQQ can determine a wider range of analytes at much lower concentrations with greater reliability and higher confidence.

Figure 1. Cutaway diagram of the Agilent 8900 ICP-QQQ

ICP-MS/MS technology

The tandem MS configuration of Agilent ICP-QQQ instruments – with two fully functioning mass filters, one either side of the ORS cell – allows unprecedented control over the ions that enter the collision/reaction cell (CRC). Q1 rejects all non-target masses/elements, ensuring more consistent reaction processes in the CRC, even when the sample composition varies. Precise ion control by the first quadrupole Q1 is crucial therefore to the accurate analytical performance in MS/MS mode. For reliable, consistent control of reaction processes, Q1 must allow only ions at the target mass-to-charge ratio (*m/z*) to pass into the cell. Inefficient mass filtering would cause results to be compromised by interferences arising from non-target ions entering the cell. To ensure the most effective mass filtering and the best quality data, Agilent ICP-QQQ instruments use the same hyperbolic quadrupole mass spectrometer for Q1 and Q2. Both quadrupoles are placed in the high vacuum region to ensure optimum mass filtering. This arrangement allows both quadrupoles to operate at unit mass resolution and low abundance sensitivity without a significant loss of sensitivity.

The impact of varying Q1 mass filter performance is illustrated in the comparison of product ion spectra for Ti–NH$_3$ cluster ions shown in Figure 2. The product ion spectrum on the left was obtained using Q1 settings that provide compromised mass resolution, with Q1 passing all masses in a 2.1 amu window. This wider Q1 mass window allowed non-target ions to enter the cell, so the reaction processes and product ions formed were not under control. In this case, the overlapping ions were derived from different NH$_3$ clusters formed from the other Ti isotopes. For example, when ^{49}Ti is the target analyte but Q1 fails to exclude ^{48}Ti from the cell, ^{48}Ti(NH$_2$)(NH$_3$)$_4^+$ overlaps ^{49}Ti$^+$(NH)(NH$_3$)$_4^+$ at *m/z* 132. In contrast, the Ti isotopic pattern on the right was obtained with Q1 set to operate with mass resolution of 0.7 amu; i.e. as a true mass filter providing genuine MS/MS operation. The Ti-NH$_3$ product ions fit the expected Ti isotopic pattern perfectly, confirming that each Ti isotope entered the cell in isolation to react with the NH$_3$ cell gas, i.e. ^{48}Ti+ + NH$_3$ → ^{48}Ti+(NH)(NH$_3$)$_4^+$. The results show that if the mass resolution of Q1 is greater than 0.7 amu, precise analysis of the specific target analyte ion/isotope is impossible. Without true MS/MS operation (both quadrupoles operating with unit mass resolution), analytical results acquired for any analyte could be compromised because unexpected reaction product ions can be formed and cause overlap on target ions.

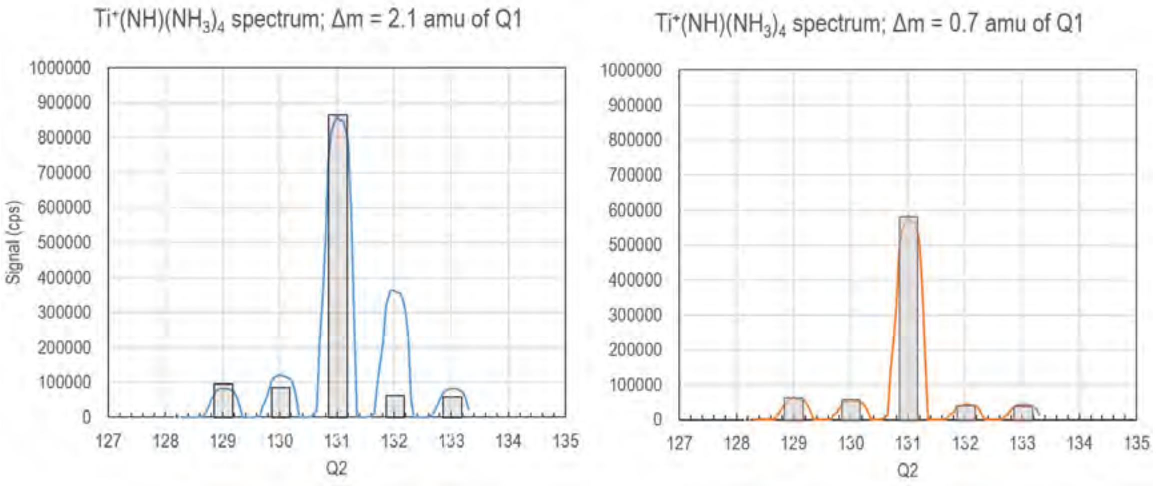

Figure 2. Ti$^+$(NH)(NH$_3$)$_4$ product ion spectrum of five Ti isotopes obtained with NH$_3$ cell gas mode: ^{46}Ti (8.25%), ^{47}Ti (7.44%), ^{48}Ti (73.72), ^{49}Ti (5.41%), and ^{50}Ti (4.29%). A Ti standard solution was analyzed using ICP-QQQ with NH$_3$ cell gas. Left: Q1 was set at Δm = 2.1 amu. Right: spectrum was acquired with Q1 set at Δm = 0.7 amu.

Second-generation triple quadrupole ICP-MS: the Agilent 8900 ICP-QQQ

Building on the success of the 8800, the 8900 ICP-QQQ provides performance and productivity improvements for a wider range of applications:

- **Double the sensitivity of the 8800:** users of the 8900 can achieve lower detection limits or improve matrix robustness by diluting samples, without degrading detection capability. Note that the sensitivity of the Agilent 8900 Semiconductor configuration ICP-QQQ now exceeds 1Gcps/ppm.
- **Axial Acceleration** accelerates ions in the cell, which increases the sensitivity in reaction cell mode and reduces potential product ion overlaps due to slow moving ions.
- **Lower contribution from instrumental background:** the 8900 ICP-QQQ is designed and manufactured to control background signals arising from the instrument itself. This attention to detail allows users to achieve even lower BECs than the 8800. The DL specification of the 8900 for sulfur and silicon is < 50 ppt.
- **0.1 ms dwell time:** the 8900 ICP-QQQ uses a new fast detector with fast time resolved analysis (TRA) capability suitable for the accurate analysis of single nanoparticles (sNPs). High speed is combined with effective interference removal and specialized software to process the signals and reveal the particle size and size distribution.

With true triple quadrupole performance, the advanced features and the robustness of the 8900 ICP-QQQ make it the world's most powerful and flexible multi-element analyzer. Agilent's Triple Quadrupole ICP-MS instruments will continue to open up new possibilities for analysts, especially for the most challenging applications.

Semiconductor

Ultratrace Measurement of Calcium in Ultrapure Water

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Keywords

semiconductor, process chemicals, ultra pure water, UPW, calcium, method of standard additions, hydrogen on-mass

Introduction

In the semiconductor industry, the control of metal impurities in the process chemicals used in the manufacture of semiconductor devices is critical to achieve the required product performance and yield. As device performance is continually increasing, the required impurity control becomes ever more stringent. For example, metal content of the ultra-pure water (UPW) used in the manufacturing process must be at the sub-ppt level. ICP-MS is the standard technique used for the trace metals analysis of semiconductor chemicals and devices. The most common instrument and measurement technique used in the semiconductor industry is single quadrupole ICP-MS (ICP-QMS) with cool plasma. The cool plasma technique [1], developed in the mid 1990's, enables the quantification of key contaminant elements at the single ppt level. Collision and reaction cell ICP-QMS, developed from 2000 onwards, enabled the direct analysis of more complex semiconductor matrices, but did not improve on the DLs or BECs of cool plasma for low-matrix samples. To achieve measurement at the sub-ppt level, reduction of the BEC is required. As outlined in this paper, the Agilent 8800 ICP-QQQ provides new reaction cell technology that enables a significant reduction in the BEC that can be achieved for Ca, to 100 ppq.

Table 1. Cool plasma operating conditions

Parameter	Unit	Tuning value
RF	W	600
Sampling depth	mm	18
Carrier gas flow	L/min	0.7
Makeup gas flow	L/min	1.0
Spray chamber temp.	°C	2

Experimental

Instrumentation: Agilent 8800 #200.

Plasma conditions: For the ultra-trace measurement of Ca, cool plasma operating conditions were used (Table 1). The sample was self-aspirated at a carrier gas flow rate of 0.7 L/min.

Reagents and sample preparation: A Ca standard was prepared in UPW acidified with 0.1% high purity HNO_3. This was used to make 50 ppt and 100 ppt additions to a UPW blank acidified with 0.1% high purity HNO_3.

Results and discussion

Ultra-low BEC for Ca using MS/MS mode

Figure 1 shows the BECs obtained for Ca, measured at its major isotope of ^{40}Ca, using the method of standard additions (MSA) under three different operating conditions on the 8800 ICP-QQQ: Single Quad mode with no cell gas, MS/MS mode with no cell gas, and finally MS/MS mode with a H_2 cell gas flow of 1 mL/min. The Single Quad mode uses operating conditions with Q1 acting as an ion guide, to emulate the Agilent 7700 ICP-QMS. The obtained BEC of 6.8 ppt is similar to that routinely achieved with the Agilent 7700 operated in cool plasma mode.

Using MS/MS mode (without cell gas) improved the Ca BEC to 1.4 ppt. MS/MS mode with H_2 at 1 mL/min in the cell further improved the BEC down to 0.041 ppt (41 ppq). The obtained MSA plot is shown in Figure 2. The Agilent 8800 ICP-QQQ in MS/MS mode with H_2 cell gas achieved a BEC for Ca in UPW two orders of magnitude lower than the BEC obtained using conventional ICP-QMS.

Figure 3 shows the spectrum obtained for UPW using cool plasma conditions in Single Quad mode with no cell gas. As can be seen, Ar^+ (m/z 40) is suppressed under the lower temperature plasma conditions, but two intense background peaks are observed at $m/z = 19$ and 30. These are $(H_2O)H^+$ and NO^+ respectively. In Single Quad mode, all ions formed in the plasma, including these two intense ions, pass through to the cell. Even with no gas added to the cell, a reaction occurs in the cell which causes a new interfering ion at *m/z* = 40. The likely reaction occurring in the cell is: $NO^+ + Ar \rightarrow Ar^+ + NO$ (charge transfer reaction), which increases the BEC for Ca by several ppt. Although the ionization potential (IP) of NO (IP = 9.26 eV) is lower than that of Ar (IP = 15.7 eV), a metastable ion, NO^+, exists close to the ionization potential of Ar [2]. So it is reasonable to assume that the charge transfer reaction shown occurs in the cell.

With MS/MS mode on the 8800 ICP-QQQ, Q1 rejects all non-target ions such as NO^+ and $(H_2O)H^+$, preventing unwanted reactions from occurring in the cell, which lowers the Ca BEC. The addition of H_2 in the cell also removes any residual $^{40}Ar^+$ that is formed even under cool plasma conditions.

References

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2. R. Marx, Y.M. Yang, G. Mauclaire, M. Heninger, and S. Fenistein, Radioactive lifetimes and reactivity of metastable $NO^+(a^3\Sigma^+,v)$ and $O_2^+(a^4\ II,v)$, J.Chem. Phys., Vol. 95, No. 4, 2259-2264, 1991.

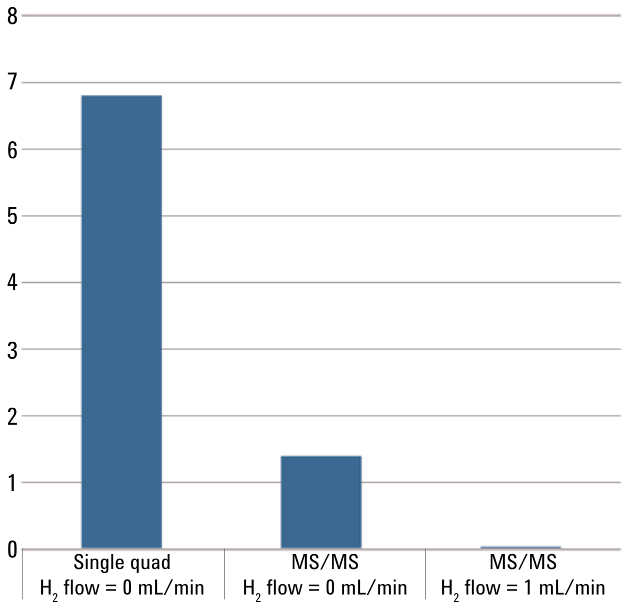

Figure 1. BECs for Ca obtained using Single Quad mode with no cell gas [6.8 ppt], MS/MS mode with no cell gas [1.4 ppt], and MS/MS mode with an H_2 cell gas flow of 1 mL/min [0.041 ppt].

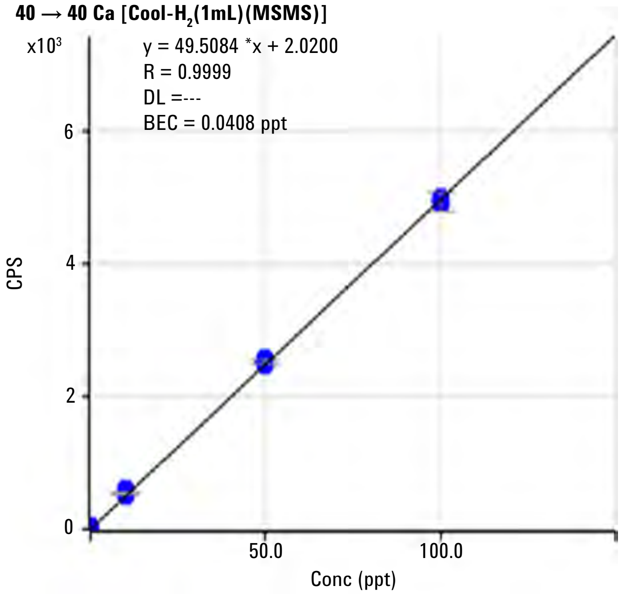

Figure 2. MSA calibration plot for Ca using MS/MS mode with H_2 flow of 1 mL/min.

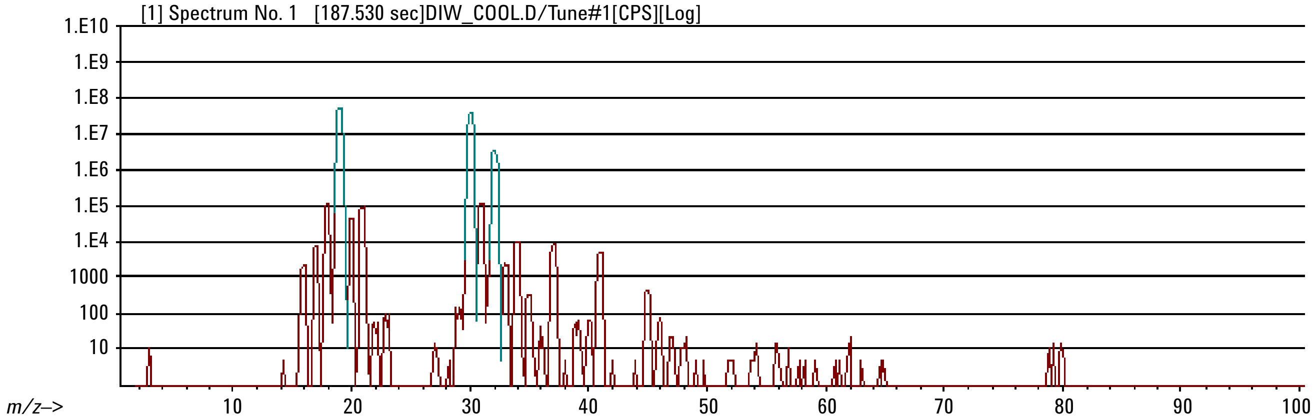

Figure 3. Spectrum of UPW acquired using cool plasma conditions in Single Quad mode with no gas mode.

Determination of Ti, V and Cr in 9.8% Sulfuric Acid

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Keywords

semiconductor, process chemicals, sulfuric acid, H_2SO_4*, titanium, vanadium, chromium, ammonia mass-shift, oxygen mass-shift*

Introduction

High purity H_2SO_4 is frequently used in the manufacturing of semiconductor devices, in processes such as the removal of organic substances from the surface of silicon wafers. The required metallic impurity level is lower than 100 ppt in the concentrated (usually 98%) acid. ICP-MS is the technique of choice for the measurement of trace metal impurities in semiconductor process chemicals. There are, however, some limitations for the measurement of elements such as Ti, V and Cr in H_2SO_4. Because of its high viscosity of 27 cP, it is not possible to introduce H_2SO_4 directly into the ICP without dilution. A 10 times dilution in UPW is normally applied, thus the BEC of the calibration curve must be lower than 10 ppt in the 9.8% H_2SO_4 solution measured. In addition, spectral interferences from SO^+, S_2^+ and ArS^+ originating from H_2SO_4 make it difficult to determine elements such as Ti and Cr at low concentration even by quadrupole ICP-MS (ICP-QMS) equipped with collision/reaction cell (CRC). As outlined in this report, the Agilent 8800 ICP-QQQ with MS/MS mode allows the successful determination of the most problematic elements including Ti, V and Cr in H_2SO_4.

Table 1. ICP-QQQ operating conditions

		O_2 MS/MS[1]	NH_3 MS/MS[2]
RF power	W	1600	
Sampling depth	mm	8	
CRGS flow rate	L/min	0.8	
MUGS flow rate	L/min	0.41	
Octopole bias V	V	-20	
KED	V	-20	
He	mL/min	3	1
O_2	mL/min	0.4	0
NH_3	mL/min	0	3

1) 100% O_2 (purity 99.995%)

2) 10% NH_3 balanced with 90% He (purity 99.995%)

Experimental

Instrumentation: Agilent 8800 #200. Operating parameters are given in Table 1.

Reagents and sample preparation: Highly purified H_2SO_4, TAMAPURE-AA-100 (98% H_2SO_4) was purchased from Tama Chemicals Co., Ltd. (Kanagawa, Japan). 5 g of H_2SO_4 was diluted by a factor of 10 in a chilled PFA bottle.

Results and discussion

Of the potential polyatomic interferences formed from the H_2SO_4 matrix, the SO^+ ion is very stable and difficult to eliminate because its dissociation energy is as high as 5.44 eV. In addition, its ionization potential is 10.3 eV, which is almost the same as that of S, 10.36 eV. The spectral interferences caused by SO^+ and SOH^+ overlap with ^{48}Ti ($^{32}S^{16}O$), ^{51}V ($^{33}S^{18}O$, $^{34}S^{16}OH$ and $^{32}S^{18}OH$) and ^{52}Cr ($^{34}S^{18}O$). Quadrupole ICP-MS operating in He collision mode provides BECs of 60 ppt for ^{47}Ti (the BEC for the preferred isotope ^{48}Ti is much higher), 3 ppt for V and 8 ppt for Cr in 9.8% H_2SO_4. The BEC of Ti, in particular, is not acceptable for producers and users of semiconductor grade H_2SO_4.

Appropriate reaction gases to remove SO^+ successfully in ICP-QMS are difficult to find. NH_3 can reduce SO^+ by two orders of magnitude but the background signal remains too high for this application. Additionally, cluster ions of NH_3 such as N_mH_n produced by the reaction between Ar^+ and the NH_3 cell gas lead to new reaction product ion interferences that increase the background at m/z 51, for example.

The 8800 ICP-QQQ operating in MS/MS mass-shift mode with NH_3 or O_2 reaction gas provides reliable and consistent measurement of Ti as $^{48}Ti^{14}NH(^{14}NH_3)_3$ (Figure 1) and Cr as $^{52}Cr^{16}O$ in H_2SO_4. Furthermore, in MS/MS mode, the Ar^+ ion is removed by Q1, preventing it from reacting with NH_3 to form new product ion interferences in the cell. This reduces the background at *m/z* 51 improving the BEC for V, as shown in Figure 2. The final BECs obtained by ICP-QQQ in 9.8% high purity H_2SO_4 are summarized in Table 2.

Table 2. BECs of Ti, V and Cr in 10x diluted 98% H_2SO_4, measured by ICP-QQQ

Element	Ti	V	Cr
Mode (cell gas)	MS/MS (NH_3)	MS/MS (NH_3)	MS/MS (O_2)
Measured ion	$^{48}Ti^{14}NH(^{14}NH_3)_3^+$	$^{51}V^+$	$^{52}Cr^{16}O^+$
Mass pair	Q1 = 48, Q2 = 114	Q1 = Q2 = 51	Q1 = 52, Q2 = 68
BEC - ppt	0.72	0.07	3.70

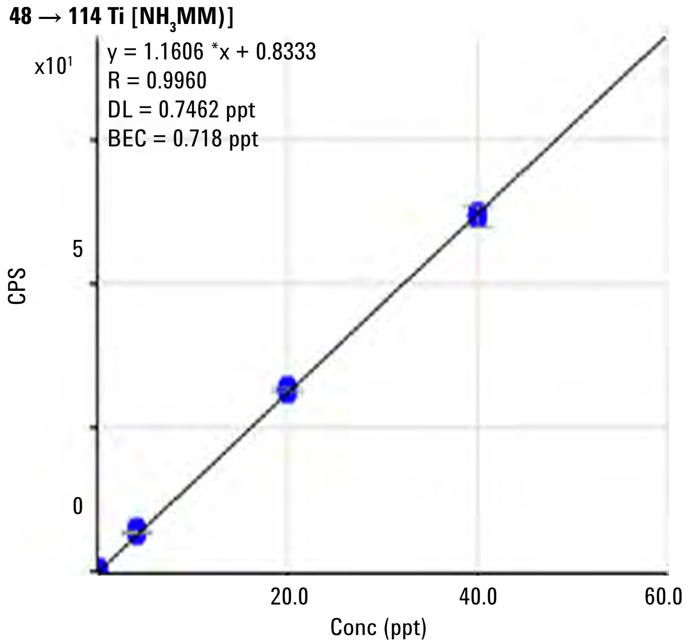

Figure 1. Calibration curve of Ti in 9.8% H_2SO_4

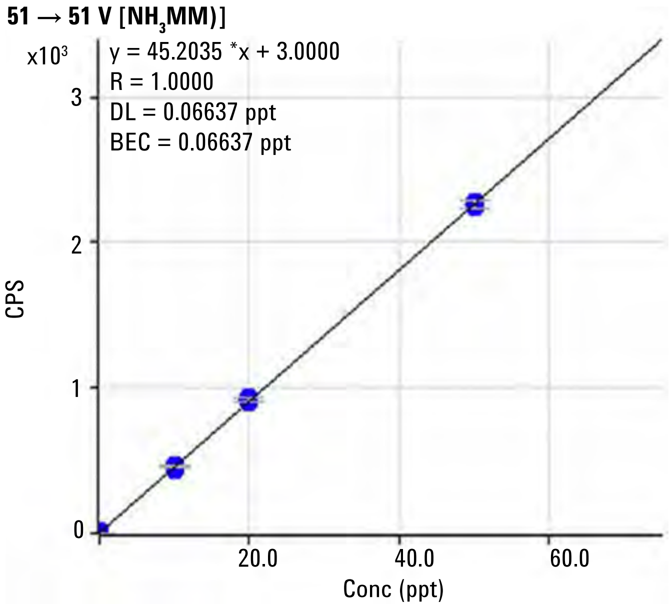

Figure 2. Calibration curve of V in 9.8% H_2SO_4

Conclusions

ICP-QQQ operating in MS/MS mode provides a reliable means for manufacturers of high purity H_2SO_4 to guarantee all metallic impurity concentrations at less than 100 ppt in the concentrated acid.

More information

Determination of challenging elements in ultrapure semiconductor grade sulfuric acid by Triple Quadrupole ICP-MS, Agilent application note, 5991-2819EN.

Direct Determination of V, Cr, Ge and As in High-Purity 20% Hydrochloric Acid

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Keywords

semiconductor, RCA Standard Clean, silicon wafer, hydrochloric acid, vanadium, chromium, germanium, arsenic, ammonia on-mass, ammonia mass-shift, oxygen mass-shift

Introduction

Since the 1970s, the RCA Standard Clean (SC) method has been used extensively in many countries for cleaning silicon wafer surfaces. SC-2 refers to a mixture of HCl and H_2O_2 that is used to remove ionic and metallic contaminants from the surface of silicon wafers. Because cleaning solutions are in direct contact with semiconductor devices, ultra high purity is required for these solutions. The SEMI standard Tier-D protocol for HCl defines the contaminant level to be <10 ppt for each element. Some elements have been very difficult to determine at ppt level by quadrupole ICP-MS (ICP-QMS) due to significant spectral interferences arising from the Cl matrix, even when analyzed by ICP-MS equipped with a collision/reaction cell (CRC). Consequently, some methods for the analysis of high purity HCl by ICP-MS have recommended sample pre-treatment steps to remove the chloride matrix, which can lead to analyte loss and sample contamination. In this study, ICP-QQQ was used to analyze undiluted HCl directly. Using MS/MS mode with mass-shift to remove polyatomic ions, the most problematic elements, such as V, Cr, Ge and As could be determined in HCl at single-figure ppt detection limits.

Table 1. ICP-QQQ operating conditions

		O_2 MS/MS 1)	NH_3 MS/MS 2)
RF power	W	1600	
Sampling depth	mm	8	
CRGS flow rate	L/min	0.8	
MUGS flow rate	L/min	0.41	
Octopole bias V	V	-20	
KED	V	-20	
He	mL/min	3	1
O_2	mL/min	0.4	0
NH_3	mL/min	0	3

1) 100% O_2 (purity 99.995%)

2) 10% NH_3 balanced with 90% He (purity 99.995%)

Experimental

Instrumentation: Agilent 8800 #200. Operating parameters are given in Table 1.

Reagents: 20% TAMAPURE-AA-100 HCl (metallic impurities are guaranteed to be below 100 ppt) was purchased from Tama Chemicals Co., Ltd. (Kanagawa, Japan). The undiluted HCl was introduced directly into the ICP-QQQ.

Results and discussion

Determination of BECs of V, Cr, Ge and As in high purity HCl

ICP-QMS with a CRC using He collision mode can successfully eliminate some polyatomic ions such as ArCl [1], and the use of NH_3 as a reaction gas also works to remove the ClO^+ ion for the determination of V. However, ICP-QMS has some serious limitations when highly reactive cell gases (such as NH_3) are used in the CRC. Principal among these limitations is the fact that all ions enter the CRC, so predicted reaction pathways can be disrupted and new reaction product ion overlaps can be formed if the analyte levels in the sample change. ICP-QQQ with MS/MS removes this limitation, as the first quadrupole mass filter (Q1) allows precise selection of the ions that are allowed to enter the cell. This ensures that reaction processes and product ions are strictly controlled, dramatically improving detectability of the analyte ions shown in Table 2.

Table 2. Spectral interferences arising from the Cl matrix on some key elements

Polyatomic interference	*m/z*	Analyte ion
ClO^+	51, 53	$^{51}V^+$
$ClOH^+$	52, 54	$^{52}Cr^+$, $(^{54}Fe^+)$*
$ClCl^+$	70, 72, 74	$^{70}Ge^+$, $^{72}Ge^+$, $^{74}Ge^+$
$ArCl^+$	75, 77	$^{75}As^+$, $(^{77}Se^+)$*

*Alternative isotopes can be chosen to avoid spectral interferences on Fe and Se.

The MS/MS acquisition mode using O_2 or NH_3 as the reaction gas enables the determination of trace ^{51}V (measured directly as V^+ using NH_3 cell gas), Cr as $^{52}Cr^{16}O^+$ (using O_2), Ge as $^{74}Ge^{14}NH_2^+$ (using NH_3) and As as $^{75}As^{16}O^+$ (using O_2). In the case of As, the $^{91}Zr^+$ ion is removed by Q1 (which is set to the As^+ precursor ion mass of *m/z* 75), so the potential overlap from Zr on the AsO^+ product ion at *m/z* 91 is also removed. The complete cut-off of cluster ions by Q1 also eliminates the possibility that $^{14}NH_2^{35}Cl$ is created in the cell, so the potential new product ion interference on ^{51}V is avoided. Representative calibration curves for V and Ge are shown in Figure 1. BECs and DLs determined by the ICP-QQQ for V, Cr, Ge and As are given in Table 3.

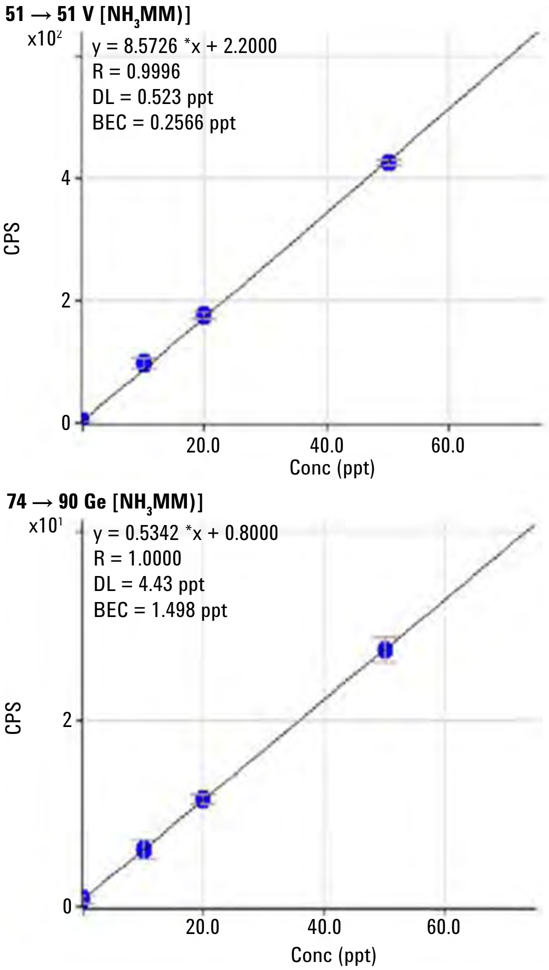

Figure 1. Calibration curves of V (NH_3 on-mass mode) and Ge (NH_3 mass-shift mode) in 20% HCl

Table 3. BECs and DLs for V, Cr, Ge and As in 20% HCl

Element	V	Cr	Ge	As
Mode (cell gas)	MS/MS (NH_3)	MS/MS (O_2)	MS/MS (NH_3)	MS/MS (O_2)
Measured ion	$^{51}V^+$	$^{52}Cr^{16}O^+$	$^{74}Ge^{14}NH2^+$	$^{52}Cr^{16}O^+$
Mass pair	Q1 = Q2 = 51	Q1 = 52, Q2 = 68	Q1 = 74, Q2 = 90	Q1 = 75, Q2 = 91
BEC - ppt	0.3	8.0	1.5	19.7
DL - ppt	0.5	1.1	4.4	3.4

Investigation of arsenic contamination

As the BEC for arsenic in high purity HCl was relatively high (Table 3), the signal count at *m/z* 91 was investigated further. The signals of the mass-pairs 75/75, 77/77, 75/91 and 77/91 were measured by ICP-QQQ with MS/MS, the mass pair number represents the set mass of Q1 followed by the set mass of Q2, so an MS/MS mode acquisition of mass pair 75/91 represents a mass-shift mode with Q1 = 75 and Q2 = 91, for example. The four mass pairs were measured in HCl blanks from three different lots, and the results are shown in Table 4. The following observations were made:

1. The ratio of the signal of 75/75 to 77/77 is around four, which is close to the ratio of the abundance of ^{35}Cl to ^{37}Cl, i.e. 3.13.

2. The ratio of the signal of 75/91 to 77/93 is 200–1000, which is far in excess of the ratio of ^{35}Cl to ^{37}Cl.

3. While the signals of 75/75 and 77/77 are similar for the three HCl blanks, those of 75/91 and 77/93 vary.

Table 4. Comparison of background counts (cps) in 3 different lots of 20% HCl*

Mass pair	75->75	77->77	75->91	77->93
Sample A	509.3	133.5	584.4	2.5
Sample B	508.4	126.0	1172.6	1.9
Sample C	612.7	130.0	3175.6	2.6

*All the samples were obtained from the new bottles of high purity HCl

Finding #1 suggests that the remaining signal on 75/75 and 77/77 was mostly from $ArCl^+$. This is a reasonable assumption since $ArCl^+$ doesn't react with O_2 very efficiently so most $ArCl^+$ remains at the original masses of 75 and 77. Finding #2 suggests that the signal of 75/91 is not due to $ArCl^+$. Assuming that all counts of 77/93 arise from $^{40}Ar^{37}Cl$, the contribution of $^{40}Ar^{35}Cl$ to the signal of 75/91 in the HCl blank is estimated to be just 7-8 cps, which is two orders of magnitude lower than the signal that is actually observed. Observation #3, together with #1 and #2, suggests the high count obtained for 75/91 in HCl is due to As impurity in the acid.

Reference

1. Direct analysis of trace metallic impurities in high purity hydrochloric acid by Agilent 7700s ICP-MS, Agilent application note, 5990-7354EN.

Silicon Wafer Analysis by ICP-QQQ: Determination of Phosphorus and Titanium in a High Silicon Matrix

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Keywords

semiconductor, silicon wafer, phosphorus, titanium, Vapor Phase Decomposition, VPD, oxygen mass-shift

Introduction

The semiconductor industry first used ICP-MS for trace element analysis in the early 1980s. Nowadays the technique is widely used for control of trace impurities in materials and chemicals, particularly by silicon device manufacturers. The major challenge for quadrupole ICP-MS (ICP-QMS) is the presence of spectroscopic interferences on key contaminant elements, although performance has been gradually improved through developments such as cool plasma and collision/reaction cells (CRC), and improved performance has also been provided by high resolution ICP-MS. Consequently metallic impurity control of silicon wafers can be successfully monitored by ICP-MS in the case of low silicon samples such as Vapor Phase Decomposition (VPD) of native silicon wafers. However, difficulties of Si-based spectral interferences, particularly on P and Ti, still affect the analysis of samples that contain high concentrations of Si, such as VPD samples of thermally oxidized wafers and samples relating to bulk silicon wafers. These interferences cannot be reduced adequately by ICP-QMS and have required HR-ICP-MS. In this paper, we evaluate triple quadrupole ICP-MS with MS/MS technology for the determination of ultratrace P and Ti in a high Si matrix.

Table 1. Robust tuning conditions

		O_2 MS/MS	H_2 MS/MS
RF power	W	1600	
Sampling depth	mm	8	
CRGS flow rate	L/min	0.6	
MUGS flow rate	L/min	0.6	
He	mL/min	3	0
O_2	mL/min	0.4	0
H_2	mL/min	0	10

Experimental

Instrumentation: Agilent 8800 #200 with an inert sample introduction kit including a low flow nebulizer (PFA-20) and a Pt/Ni skimmer cone. The actual sample uptake rate was 36 µL/min. The sample was self-aspirated from an Agilent I-AS autosampler.

Plasma conditions: Robust tuning conditions were applied as summarized in Table 1.

Ion lens tune: Extract 1 = 0 V was used and other lens voltages were optimized using Auto tune.

Sample preparation: Silicon wafer samples were dissolved in TAMAPURE HF/HNO_3 and the final Si concentration was adjusted to 2000 ppm.

Results and discussion

Phosphorus is monoisotopic at *m/z* 31, and suffers an interference from ^{30}SiH. While P^+ can be detected as PO^+ under cool plasma conditions, it is difficult to maintain cool plasma when the matrix concentration is high. Si sample solutions always contain HF, so Si will form SiF (IP: 7.54 eV) that also interferes with Ti. Table 2 shows the Si-based spectral interferences on P and Ti. Using the 8800 ICP-QQQ operating in MS/MS mode with O_2 mass-shift, P and Ti can be determined as their oxide ions, avoiding the Si-based interferences.

Table 2. Spectral interferences of Si on P and Ti

Polyatomic interference	*m/z*	Analyte ion
$^{30}SiH^+$	31	$^{31}P^+$
$^{30}Si^{16}O^+$	46	$^{46}Ti^+$
$^{28}Si^{19}F^+$, $^{30}Si^{16}OH^+$	47	$^{47}Ti^+$, $^{31}P^{16}O^+$
$^{29}Si^{19}F^+$, $^{30}Si^{18}O^+$	48	$^{48}Ti^+$
$^{30}Si^{19}F^+$	49	$^{49}Ti^+$

For Ti analysis, Q1 is set to *m/z* 48, and so will transmit $^{48}Ti^+$ and any other interfering ions at mass 48, such as $^{29}Si^{19}F^+$ and $^{30}Si^{18}O^+$. But only ^{48}Ti reacts with oxygen in the CRC, producing the product ion $^{48}Ti^{16}O^+$, which is transmitted by setting Q2 to *m/z* 64. NH_3 can be used as an alternative reaction gas, as it produces $^{48}Ti^{14}NH^+$ that can be detected at *m/z* 63.

$^{31}P^+$ reacts readily with O_2 to form $^{31}P^{16}O^+$. The selection of ions at *m/z* 31 by Q1 eliminates the spectral interference of $^{28}Si^{19}F$. However, ^{30}SiH passes through Q1 and reacts with O_2 to create $^{30}Si^{16}OH$. In order to determine P in a high Si matrix, H_2 mass-shift is a preferred option, despite the relatively low efficiency of production of PH_3^+ or PH_4^+ ions. The MSA calibration curves for P and Ti in a matrix of 2000 ppm Si are shown in Figure 1. The calculated BECs are summarized in Table 3. A long term stability test was carried out by analyzing a spiked sample repeatedly over five hours (Figure 2).

Table 3. BECs of P and Ti in 2000 ppm Si

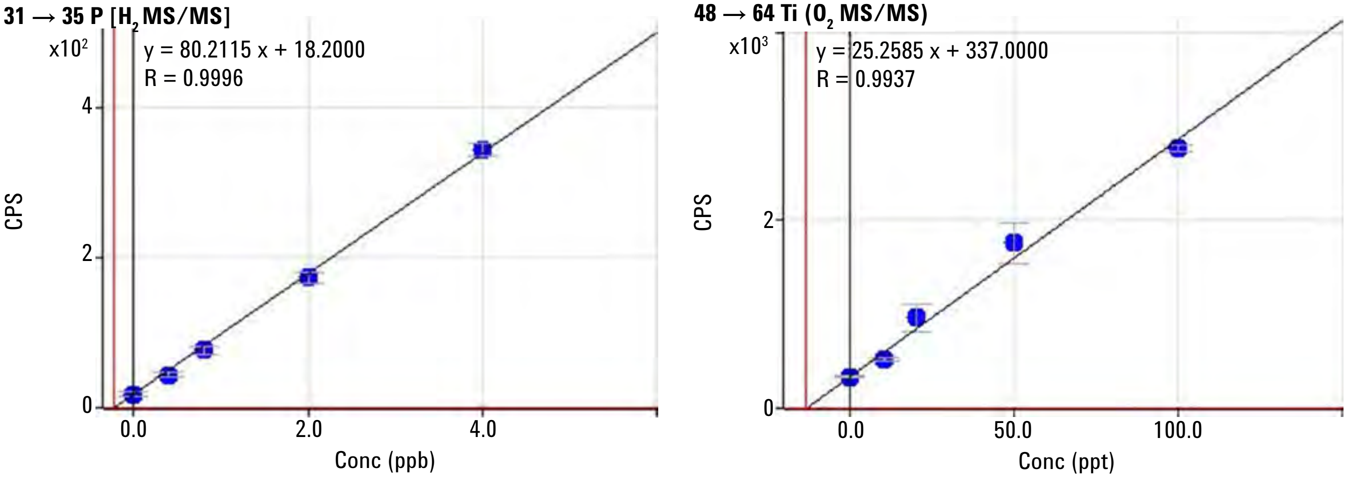
Element	P	Ti
Mode (cell gas)	MS/MS (H_2)	MS/MS (O_2)
Measured ion	$^{31}PH_4^+$	$^{48}Ti^{16}O^+$
Mass pair	Q1 = 31, Q2 = 35	Q1 = 48, Q2 = 64
BEC - ppt	227	13

Conclusions

The MS/MS mass-shift mode of the ICP-QQQ is effective for the determination of P, Ti and other trace elements in high purity silicon matrices, providing effective removal of the potential Si-based polyatomic interferences.

More information

Improvement of ICP-MS detectability of phosphorus and titanium in high purity silicon samples using the Agilent 8800 Triple Quadrupole ICP-MS, Agilent application note, 5991-2466EN.


31 → 35 P [H_2 MS/MS]

48 → 64 Ti (O_2 MS/MS)

Figure 1. MSA curves of P and Ti in 2000 ppm Si

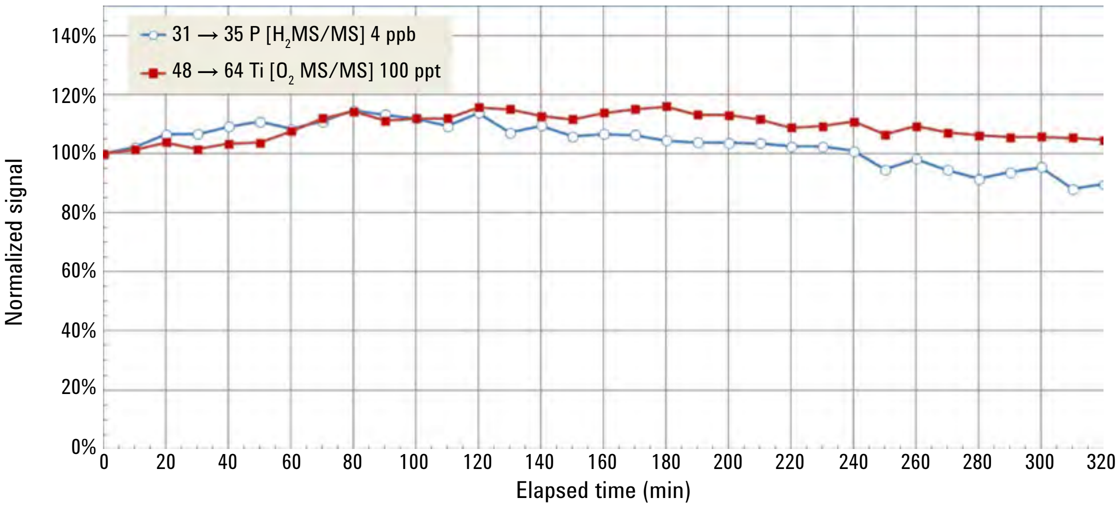


Figure 2. Five-hours test of P and Ti spiked in 2000 ppm Si

Analysis of Sulfur, Phosphorus, Silicon and Chlorine in N-methyl-2-pyrrolidone

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Keywords

N-methyl-2-pyrrolidone, NMP, semiconductor, process chemicals, sulfur, phosphorus, silicon, chlorine, method of standard additions, oxygen mass-shift

Introduction

N-Methyl-2-Pyrrolidone (NMP), chemical formula: C_5H_9NO, is a stable, water-soluble organic solvent that is widely used in the pharmaceutical, petrochemical, polymer science and especially semiconductor industries. Electronic grade NMP is used by semiconductor manufacturers as a wafer cleaner and photo resist stripper and as such the solvent comes into direct contact with wafer surfaces. This requires NMP with the lowest possible trace metal (and non-metal) contaminant levels. ICP-MS is the technique of choice for the measurement of trace metal impurities in semiconductor process chemicals. It is a challenge, however for ICP-MS to measure non-metallic impurities such as sulfur, phosphorus, silicon, and chlorine in NMP. The low ionization efficiency of these elements greatly reduces analyte signal, while the elevated background signal (measured as background equivalent concentration, BEC) due to N-, O-, and C-based polyatomic ions formed from the NMP matrix makes low-level analysis even more difficult (Table 1).

Table 1. ICP-QMS BECs obtained in no gas mode for selected analytes in NMP

Element	*m/z*	Ion-ization potential (eV)	Ion-ization ratio (%)	BEC without cell (ppm)	Interference
Si	28	8.152	87.9	>100	$^{14}N_2^+$, $^{12}C^{16}O^+$
P	31	10.487	28.8	0.39	$^{14}N^{16}OH^+$, COH_3^+
S	32	10.360	11.5	9.5	$^{16}O_2^+$, NOH_2^+
Cl	35	12.967	0.46	0.26	$^{16}O^{18}OH^+$

Experimental

Instrumentation: Agilent 8800 #200 with narrow injector (id =1.5 mm) torch (G3280-80080) typically used for the analysis of organic solvents. A C-flow 200 PFA nebulizer (G3285-80000) was used in self-aspiration mode. An option gas flow of 20% O_2 in Ar was added to the carrier gas to prevent carbon build up on the interface cones.

Plasma conditions: NMP analysis requires hotter plasma conditions than normal. This was achieved by reducing Makeup Gas (MUGS) by 0.2 L/min. Plasma tuning conditions are summarized in Table 2.

Table 2. Plasma conditions for NMP analysis

Parameter	Unit	Tuning value
RF	W	1550
Sampling depth	mm	8.0
Carrier gas flow	L/min	0.50
Makeup gas flow	L/min	0.10
Option gas flow	L/min	0.12 (12% of full scale)
Spray chamber temperature	°C	0

CRC conditions: Table 3 summarizes the cell tuning parameters (gas flow rate and voltages) used.

Reagents and sample preparation: Electronic industry grade NMP was distilled at 120 °C and acidified by adding high purity HNO_3 to a concentration of 1% w/w.

Table 3. CRC operating conditions

Parameter	Unit	O_2 reaction cell		H_2 reaction cell	
Method	-	On-mass	Mass-shift	On-mass	Mass-shift
Cell gas	-	O_2		H_2	
Gas flow rate	mL/min	0.30		4.0	
Octopole bias	V	-14		-10	
KED	V	-5	-5	0	-5

Results and discussion

NMP was analyzed directly using the method of standard additions (MSA). Three replicate measurements (ten replicates for the blank) were acquired for S, P, Si and Cl using an integration time of 1 s per isotope.

P and S measurement in NMP

The mass-shift method using O_2 worked well for P and S measurement in NMP. The reactions of P and S with O_2 are exothermic, indicated by the negative value for ΔH, as shown below; therefore P^+ and S^+ are efficiently converted to their oxide ions, PO^+ and SO^+. P and S can be measured as the product ions, avoiding the original spectroscopic interferences on their elemental masses, *m/z* 31 and *m/z* 32.

$$P^+ + O_2 \rightarrow PO^+ + O \quad \Delta Hr = -3.17\ eV$$

$$S^+ + O_2 \rightarrow SO^+ + O \quad \Delta Hr = -0.34\ eV$$

In MS/MS mode, Q1 rejects $^{36}ArC^+$ before it can enter the cell, preventing it from overlapping SO^+. This allows ICP-QQQ to control the reaction chemistry pathways and reaction product ions, ensuring that the analyte product ion is measured free from overlap, regardless of the levels of other co-existing analyte (or matrix) elements.

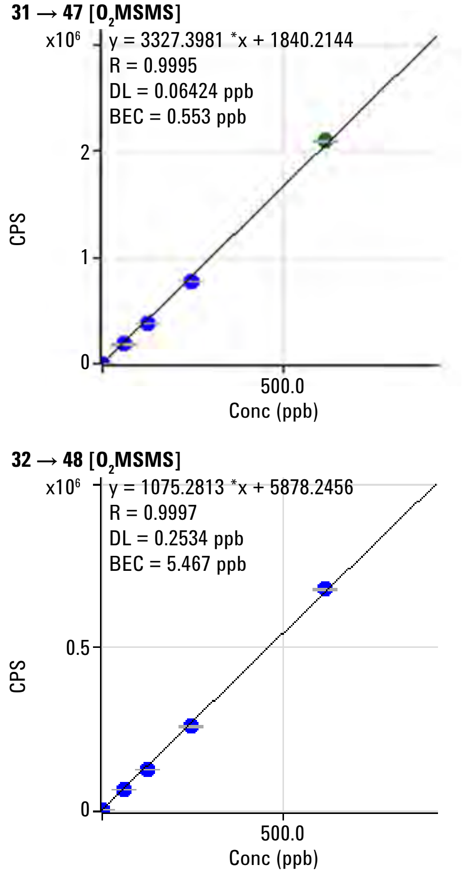

Figure 1. Calibration curve using MS/MS with O_2 mass-shift for P (top) and S (bottom) in NMP

MS/MS mode with the O_2 mass-shift method achieved BECs of 0.55 ppb and 5.5 ppb for P and S respectively in NMP. The low BECs and linear calibration plots achieved in MS/MS mode also prove that the matrix-based interferences do not react with O_2, allowing the analytes to be separated from the interferences.

Si measurement in NMP

H_2 cell gas was applied to the measurement of Si in NMP. The reaction kinetics for Si and its major interferences with H_2 cell gas are shown below. The reaction rate data suggests that Si does not react with H_2 cell gas (endothermic reaction indicated by the positive value for ΔH), and so could be measured in NMP using the direct, on-mass method. While the reaction of Si^+ with H_2 is endothermic, the reactions of the major interfering ions on Si at mass 28 (N_2^+ and CO^+) are exothermic, and these interferences are therefore neutralized or reacted away.

$$Si^+ + H_2 \rightarrow SiH^+ + H \quad \Delta Hr = 1.30\ eV$$

$$N_2^+ + H_2 \rightarrow HN_2^+ + H \quad \Delta Hr = -\ 0.60\ eV$$

$$CO^+ + H_2 \rightarrow COH^+ + H \quad \Delta Hr = -\ 1.63 eV$$

The results obtained are shown in Figure 2 (top). The H_2 on-mass method achieved a BEC of 15.8 ppb for Si in NMP.

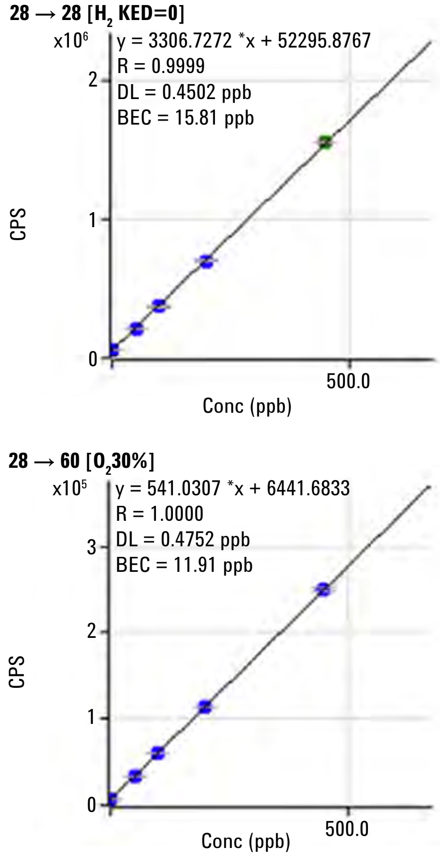

Figure 2. Calibration plots for Si in NMP. Top: H_2 on-mass method (Q1=Q2=28). Bottom: O_2 mass-shift method (Q1=28, Q2=60)

Oxygen cell gas was also tested of the measurement of Si in NMP. As shown below, the reaction of Si^+ with O_2 to form SiO^+ is endothermic. However, collisional processes in the cell provide additional energy which promotes the reaction, enabling the O_2 mass-shift method to be applied.

$Si^+ + O_2 \rightarrow SiO^+ + O \quad \Delta Hr = 0.11\ eV$

Unfortunately a major interference on Si at *m/z* 28 (CO^+) also reacts with O_2, so the BEC achieved using the O_2 mass-shift method to measure Si as SiO^+ (Q1 = 28, Q2 = 44) was not satisfactory. Fortunately, another Si reaction product ion (SiO_2^+) also forms and this can be measured at *m/z* 60 (Q1 = 28, Q2 = 60) giving a BEC of 11.9 ppb for Si in NMP (Figure 2, bottom).

Cl in NMP

Cl^+ reacts exothermically with H_2 to form HCl^+ as shown below. HCl^+ continues to react via a chain reaction to form H_2Cl^+.

$Cl^+ + H_2 \rightarrow HCl^+ + H \quad \Delta Hr = -0.17eV$

$HCl^+ + H_2 \rightarrow H_2Cl^+ + H \quad \Delta Hr = -0.39eV$

Figure 3 (left) shows calibration plots obtained for Cl in NMP using the H_2 mass-shift method. The plot obtained using the O_2 mass-shift method (Figure 3, below) is also shown for comparison. A slightly better BEC of 34.2 ppb was achieved with much higher sensitivity for Cl in NMP using the H_2 mass-shift method.

More information

Trace level analysis of sulfur, phosphorus, silicon and chlorine in NMP using the Agilent 8800 Triple Quadrupole ICP-MS, 2013, Agilent application note, 5991-2303EN.

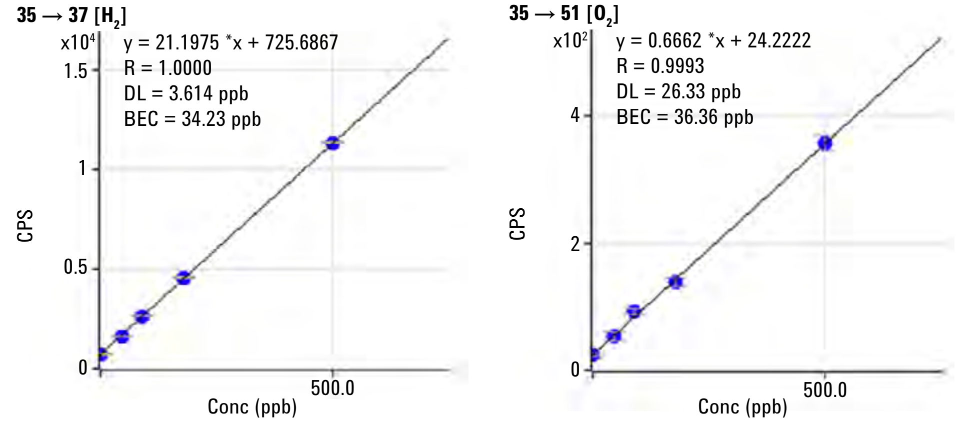

Figure 3. Calibration plots for Cl in NMP. Left: H_2 mass-shift method (Q1 = 35, Q2 = 37). Right: O_2 mass-shift method (Q1=35, Q2=51)

Analysis of Silicon, Phosphorus and Sulfur in 20% Methanol

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Keywords

organic solvents, methanol, silicon, phosphorus, sulfur, hydrogen on-mass, oxygen mass-shift

Introduction

Analysis of organic solvents for trace metals presents a number of challenges to ICP-MS, many of which have been overcome to varying degrees on Agilent's 7700 Series quadrupole ICP-MS systems. However, even with these advances, several elements remain challenging in organic solvents, particularly silicon, phosphorus and sulfur. All three elements are subject to intense interferences from polyatomic ions based on carbon, nitrogen and oxygen, which are difficult to completely remove using conventional quadrupole ICP-MS (ICP-QMS). Examples include CO^+, COH^+, N_2^+ and NO^+ on silicon 28, 29 and 30; COH^+, NOH^+, N_2H^+, NO^+ and CO^+ on phosphorus 31 and O_2^+, NO^+, NOH^+ and NOH_2^+ on sulfur 32 and 34. Additionally, phosphorus and sulfur have high first ionization potentials (IP) of 10.5 eV and 10.4 eV respectively, resulting in relatively poor sensitivity compared to more typical elements whose IPs are in the range of ~6 – 8 eV.

Experimental

Instrumentation: Agilent 8800 #200.

Plasma conditions and ion lens tune: RF power =1550 W, Sampling depth = 8.0 mm and CRGS flow rate = 1.05 L/min were used with soft extraction tune, Extract 1 = 0 V and Extract 2 = -190 V.

Ultra pure methanol was spiked with silicon (Si), phosphorus (P) and sulfur (S) at 1, 5, 10 and 50 ppb and measured using the ICP-QQQ in several operational modes in order to evaluate the optimum conditions for the simultaneous analysis of all three analytes. Hydrogen and oxygen reaction gases were evaluated, with H_2 cell gas used in both Single Quad (SQ) and MS/MS modes. In addition, helium collision gas was investigated in both SQ and MS/MS mode to determine the effects of using MS/MS with a non-reactive cell gas.

The CRC conditions are outlined in Table 1, which includes the five analysis modes evaluated. Two Single Quad modes were tested, using both He and H_2 in the cell, to simulate the capability of a single quadrupole ICP-MS. In addition, three conditions using MS/MS mode were tested using H_2, He and O_2 as cell gases.

Table 1. 8800 ICP-QQQ acquisition conditions tested, including five operational modes

Parameter	Unit	He SQ	H_2 SQ	H_2 MS/MS	He MS/MS	O_2 MS/MS
Acquisition mode		SQ	SQ	MS/MS	MS/MS	MS/MS
Cell gas		He	H_2	H_2	He	O_2
Cell gas flow rate	mL/min	5.0	7.0	7.0	7.0	0.40
KED	V	5	0	0	5	-7

Results and discussion

The BECs and DLs results are summarized in Tables 2–4, for silicon, phosphorus and sulfur respectively, for all 5 analysis modes tested. SQ and optimum MS/MS results are in bold type for comparison. A few mass-pairs were measured in each mode as shown. For example, Table 2 shows silicon monitored in MS/MS mode with O_2 cell gas, using a mass-pair of Q1 = 28 and Q2 = 44. With Q1 set to m/z 28, only silicon 28 and any on-mass interferences are allowed to enter the ORS cell. The silicon 28 in the cell reacts with the oxygen cell gas to form SiO^+, and Q2 is set to measure at Q1 + 16 (m/z = 44), ensuring that only the M + ^{16}O reaction transition is measured.

Table 2. DLs and BECs for silicon. Silicon was not measurable at the spiked concentrations in helium mode

Mode	Mass or mass pair	BEC (ppb)	DL (ppb)
H_2 SQ	**Q2=28**	**25.46**	**0.12**
H_2 MS/MS	**Q1=28, Q2=28**	**2.17**	**0.03**
O_2 MS/MS	Q1=28, Q2=44	85.54	28.21
O_2 MS/MS	Q1=29, Q2=45	N/A	N/A
O_2 MS/MS	Q1=30, Q2=46	99.09	21.26

Table 3. DLs and BECs for phosphorus. Phosphorus was not measurable at the spiked concentrations in H_2 Single Quad mode

Mode	Mass or mass pair	BEC (ppb)	DL (ppb)
He SQ	**Q2=31**	**3.81**	**0.63**
He MS/MS	Q1=31, Q2=31	2.99	0.72
H_2 MS/MS	Q1=31, Q2=33	0.56	0.07
H_2 MS/MS	Q1=31, Q2=34	0.58	0.67
O_2 MS/MS	Q1=31, Q2=47	0.40	0.05
O_2 MS/MS	**Q1=31, Q2=63**	**0.41**	**0.02**

Table 4. DLs and BECs for sulfur using MS/MS mode with O_2 cell gas. Sulfur was not measurable at the spiked concentrations in helium or hydrogen mode

Mode (cell gas)	Mass or mass pair	BEC (ppb)	DL (ppb)
MS/MS (O_2)	Q1 = 34, Q2 = 34	51.17	4.37
MS/MS (O_2)	**Q1 = 32, Q2 = 48**	**3.13**	**0.10**
MS/MS (O_2)	Q1 = 34, Q2 = 50	3.11	0.20

Sample calibration plots are displayed in Figure 1. They are displayed in pairs showing the results obtained using SQ mode with a typical cell gas (upper calibration), compared to MS/MS mode using the optimum conditions (lower calibration).

Conclusions

It can be seen that in all cases the use of MS/MS mode significantly improves both the BEC and instrument detection limit when compared to Single Quad mode. The most notable improvement was for sulfur which cannot be measured at the spiked concentrations (1, 5, 10, 50 ppb) in SQ He mode due to the intense polyatomic background resulting from the methanol matrix. By contrast, on the 8800 ICP-QQQ using MS/MS mode with O_2 mass-shift, S can be measured with a DL of 0.1 ppb.

More information

Analysis of silicon, phosphorus and sulfur in 20% methanol using the Agilent 8800 Triple Quadrupole ICP-MS, Agilent application note, 5991-0320EN.

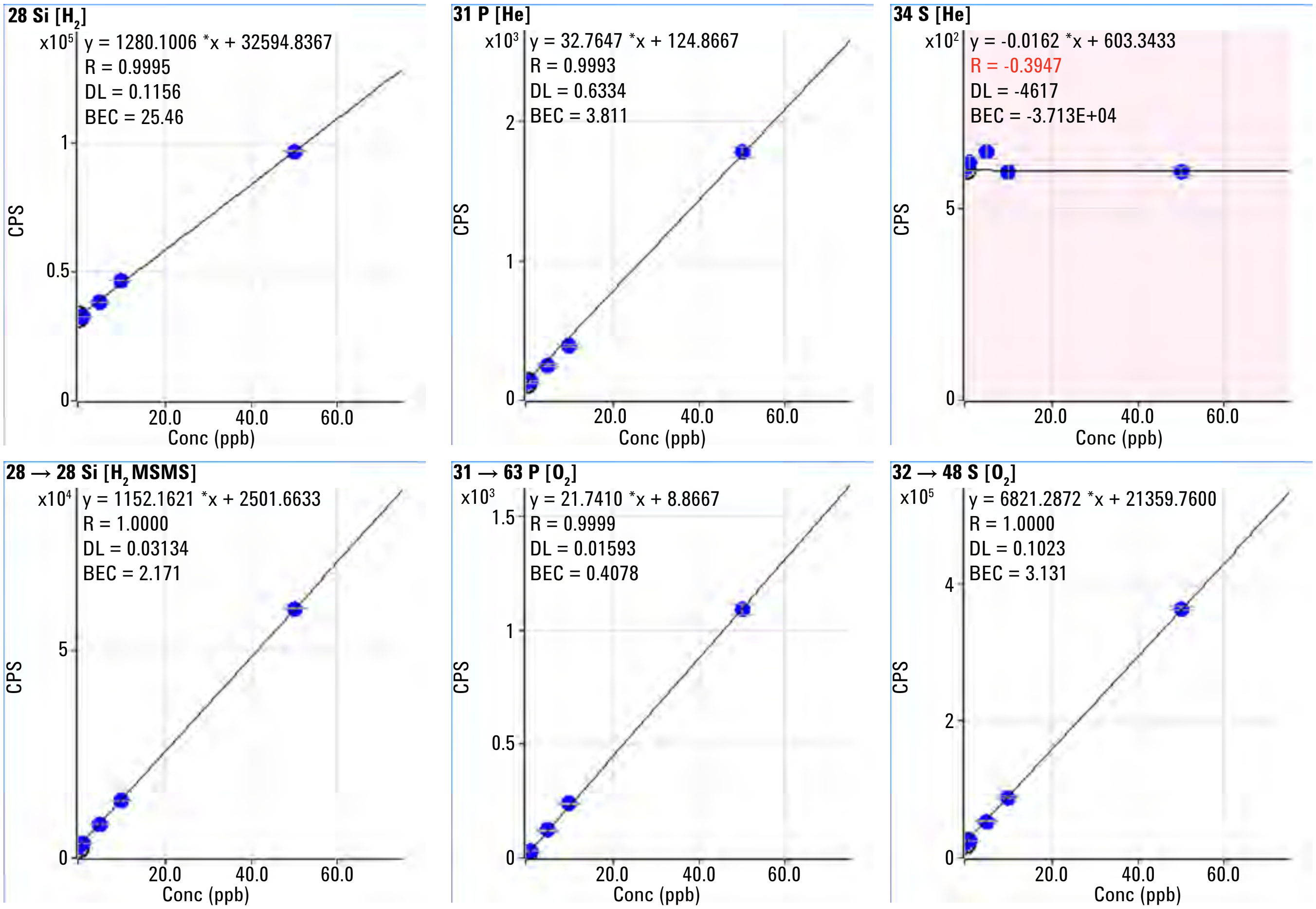

Figure 1. Calibration curves for Si, P and S showing SQ results (upper) compared with MS/MS results (lower). ^{32}S was not measurable at the spiked concentrations in methanol in SQ mode due to the intense $^{16}O_2^+$ polyatomic interference.

Ultratrace Measurement of Potassium and Other Elements in UPW Using ICP-QQQ in Cool Plasma/Reaction Mode

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Keywords

semiconductor, process chemicals, ultra pure water, UPW, potassium, cool plasma, ammonia on-mass

Introduction

The level of metal contaminants is strictly controlled in semicon device manufacturing processes, but the elements K, Ca and Fe are difficult to determine by ICP-MS due to argide interferences e.g. ArH^+ on $^{39}K^+$, Ar^+ on $^{40}Ca^+$ and ArO^+ on $^{56}Fe^+$. Cool plasma employs a relatively low temperature plasma to remove the argide interferences allowing the analyst to measure these elements at trace levels. The low temperature plasma also reduces the background signal from any Easily Ionized Elements (EIEs) such as Li and Na that may deposit of on the interface of the ICP-MS. Even after the introduction of high concentration of EIEs, cool plasma ensures a low background level of these elements is maintained.

The Agilent 8800 ICP-QQQ provides improved cool plasma performance in combination with reaction cell technology, to enable a BEC of 30 ppq for K to be achieved in ultrapure water (UPW), and BECs at the ppq level for all the other elements studied: Li, Na, Mg, Al, Ca, Cr, Mn, Fe, Ni and Cu.

Table 1. Cool plasma operating conditions

Parameter	Unit	Value
RF	W	600
Carrier gas	L/min	0.7
Makeup gas	L/min	0.8
Sampling depth	(mm)	18
NH_3 (10% in He) cell gas flow rate	mL/min	1

Experimental

Instrumentation: Agilent 8800 #200 (semiconductor configuration).

Plasma conditions: Cool plasma operating conditions (Table 1).

Reagents and sample preparation: The blanks and samples were acidified using high purity HNO_3 (TAMAPURE-AA-10, TAMA Chemicals Co. Ltd. Kanagawa, Japan). Standard solutions were prepared by serial dilution from a SPEX 331 mixed standard (SPEX CertiPrep, NJ, USA).

Cool plasma/NH_3 reaction cell mode

Investigation of the signal at *m/z* 39 under cool plasma conditions indicated the presence of $^{38}ArH^+$ which decreases with lowering plasma temperature, indicating a reduction in the ionization of the polyatomic ion. However, there was also a contribution from a water cluster ion, $(H_3O^+)(H_2O)$, which is likely to form under low temperature plasma conditions. The combination of these two interferences means that there is no plasma temperature at which both interferences can be minimized (Figure 1). As the water cluster ion is known to react with deuterated ammonia (ND_3) via a fast proton transfer reaction [1], it was assumed that reaction with NH_3 would proceed at a similar rate, so this cell gas mode was investigated in order to remove the water cluster ion in cool plasma conditions.

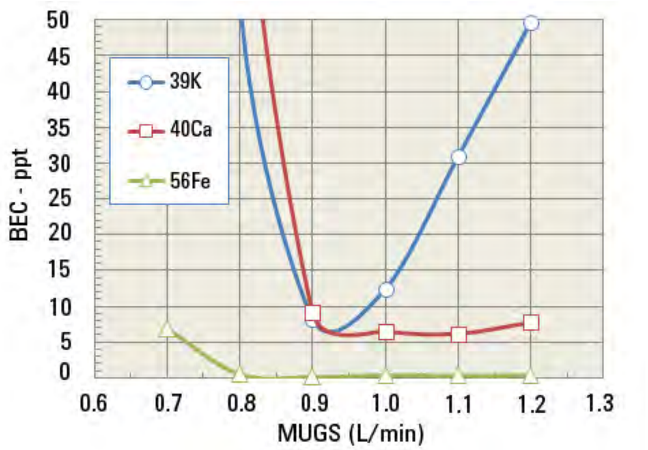

Figure 1. Investigation of the background signal under cool plasma conditions. BEC of K, Ca and Fe as a function of makeup gas (MUGS) flow rate.

Results and discussion

Ultra-low BEC for K using MS/MS mode

Ammonia reaction gas mode under cool plasma conditions was used to determine K in UPW. The BEC of K was measured at 30 ppq. A comparative study carried out using a 7500cs quadrupole ICP-MS in cool plasma/ NH_3 reaction mode achieved a BEC of 500 ppt for K [2]. It would be reasonable to attribute the improvement of BEC achieved with the 8800 to the MS/MS reaction capability of the ICP-QQQ. In conventional quadrupole ICP-MS, ions formed under cool plasma conditions enter the reaction cell and react with NH_3 or with impurity residues present in the cell to form product ions at *m/z* 39. MS/MS prevents any unwanted precursor ions from entering the cell, thus minimizing the production of undesired product ions.

Multielement analysis

The cool plasma/NH_3 reaction mode method was applied to the multielement analysis of UPW. As can be seen from the results in Table 2, a BEC < 150 ppq was achieved for all elements, including K, Ca and Fe.

Table 2. DL and BEC of elements in UPW

Mass/Element	Sensitivity, cps/ppt	DL, ppt	BEC, ppt
7 Li	6.2	0.000	0.000
23 Na	94.0	0.014	0.035
24 Mg	44.0	0.010	0.005
27 Al	42.7	0.010	0.002
39 K	96.8	0.000	0.030
40 Ca	42.5	0.035	0.091
52 Cr	36.5	0.029	0.037
55 Mn	64.5	0.020	0.011
56 Fe	42.2	0.488	0.134
60 Ni	13.4	0.270	0.101
65 Cu	15.5	0.014	0.029

Conclusions

The Agilent 8800 ICP-QQQ was used to show the background signal at *m/z* 39 under cool plasma conditions was due to a water cluster ion, $H_3O(H_2O)^+$, which was removed using NH_3 cell gas. The ICP-QQQ BEC for ^{39}K was more than a factor of 10 lower than that achieved using a conventional quadrupole ICP-MS. This demonstrates the benefit of MS/MS mode for reaction gas methods: MS/MS mode prevents all non-target ions from entering the cell, and thereby eliminates the possibility of unwanted reactions from occurring.

References

1. V. G. Anicich (2003.11), An Index of the Literature for Bimolecular Gas Phase Cation-Molecule Reaction Kinetics (p369), NASA

2. Junichi Takahashi et al., Use of collision reaction cell under cool plasma condition in ICP-MS, Asia Pacific Winter Plasma Conference 2008 (O-10)

More information

Ultra trace measurement of potassium and other elements in ultrapure water using the Agilent 8800 ICP-QQQ in cool plasma reaction cell mode, Agilent publication 5991-5372EN.

GC-ICP-QQQ Achieves Sub-ppb Detection Limits for Hydride Gas Contaminants

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Emmett Soffey, Steve Wilbur and Chris Scanlon, Agilent Technologies Inc., USA

Keywords

semiconductor, petrochemical, phosphine, arsine, hydrogen sulfide, carbonyl sulfide, germane, silane, oxygen mass-shift, hydrogen on-mass

Introduction

Hydride gases, such as phosphine and arsine, are important contaminants in process chemicals used in both the petrochemical and semiconductor industries. The presence of phosphine, arsine, hydrogen sulfide, and carbonyl sulfide in polymer grade ethylene or propylene can have a deleterious effect on catalysts used in the production of polypropylene plastics. In the semiconductor industry, phosphine is used as a precursor for the deposition of group III-V compound semiconductors, and as a dopant in the manufacturing of semiconductor devices, such as diodes and transistors. The presence of unwanted hydride gas impurities can have a profound effect on the performance of the final device.

To date, measurement of these contaminants at ppb levels has been sufficient, but increasing competition within the industry and evolving performance criteria are pushing specifications ever lower. In addition, high purity gas manufacturers often require analytical detection limits 5-10 times lower than reported specifications. In anticipation of increasing industry demand for lower level detection, a new high sensitivity GC-ICP-QQQ method was developed for this application.

Experimental

Instrumentation: An Agilent 7890 GC was coupled to an Agilent 8800 #200 using the Agilent GC-ICP-MS interface.

Acquisition conditions: MS/MS mass-shift mode using oxygen as the cell gas for the measurement of Ge, As, P and S. MS/MS mode with hydrogen cell gas was used for the on-mass measurement of the primary isotope of Si at *m/z* 28.

Table 1. Agilent 8800 ICP-QQQ operating conditions

	O_2 mode	H_2 mode
RF power (W)	1350	
Sample depth (mm)	8.4	
Argon carrier (makeup) gas flow (L/min)	0.85	
Extract 1 (V)	-150	
Extract 2 (V)	-190	
Kinetic Energy Discrimination (V)	-4	0
Cell gas/flow (mL/min)	0.35	5.0

Reagents and sample preparation: Gas standards of silane, phosphine, germane, arsine (all balanced with H_2), and hydrogen sulfide and carbonyl sulfide (balanced with Ar) were supplied by Custom Gas Solutions at a nominal value of 10 ppmv. These standards were dynamically diluted in helium using a pressure/fixed restrictor based diluter supplied by Merlin MicroScience.

Results and discussion

Low level phosphine analysis

The purpose of this experiment was to establish a detection limit for phosphine (PH_3) using GC-ICP-QQQ under ideal conditions. Q1 was set to *m/z* 31 (the precursor ion $^{31}P^+$) and Q2 was set to *m/z* 47 to measure the product ion $^{31}P^{16}O^+$. Since the eluting peaks are relatively narrow, with duration of no more than ~12 seconds, a maximum of 1 second was set for the total scan time. For the single element analysis of phosphine (measured as PO^+), an integration time of 1.0 second was used. A multi-point calibration curve was generated for PH_3 at concentrations of 8.2, 18.8 and 50.8 ppb. This covers the representative concentration range required for the measurement of this contaminant.

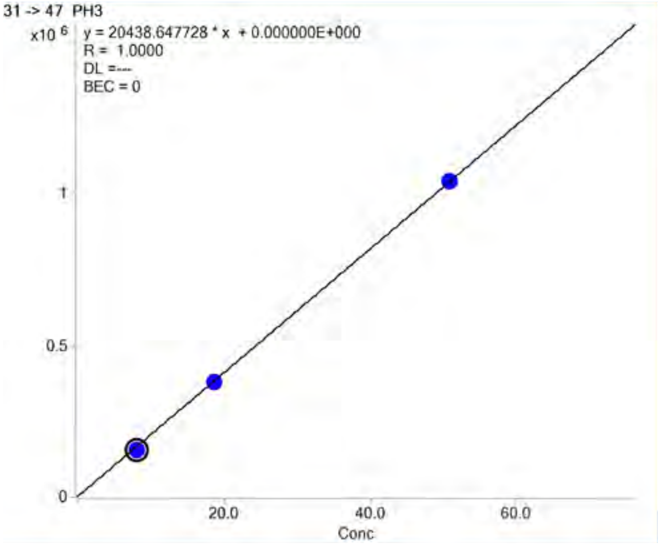

Figure 1. Phosphine calibration curve with an R value of 1.000 over the concentration range

A low level phosphine standard (~0.42 ppb) was also prepared, to allow the detection limit (DL) to be calculated. Two different methods for DL calculation were used:

i. Two times the signal to noise (S/N) of the phosphine peak in the low level standard based on "Peak to Peak" noise method

ii. The standard deviation of the concentrations measured in seven replicate analyses of the low level standard.

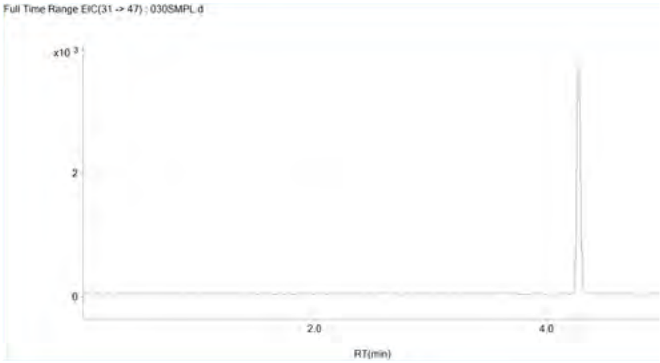

Figure 2. Chromatogram of 0.4 ppb PH_3 standard. S/N: 96.9

In the chromatogram shown in Figure 2, a S/N ratio of 96.9 was determined for the phosphine peak. Using the equation DL = 2 x ((concentration of standard) / (S/N)), a detection limit approximation of 8.67 ppt was calculated based on 2 x ((0.42 ppb) / (96.9)). Using the standard deviation method, where multiple replicates of the low level standard were analyzed, the detection limit was 19 ppt.

Analysis of additional hydride gases

The GC-ICP-QQQ method was applied to the multielement analysis of germane, arsine and phosphine within a single analysis. Ge and As were measured as their O_2 reaction product ions, GeO^+ and AsO^+, as was the case with P (PO^+). Hydrogen sulfide (H_2S) and carbonyl sulfide (COS) were also analyzed using O_2 mass-shift mode, based on the ICP-QQQ measurement of sulfur as the $^{32}S^{16}O^+$ reaction product ion at *m/z* 48. For the analysis of silane, Si was measured directly (on-mass) at its major isotope ^{28}Si, using H_2 cell gas. The primary polyatomic interferences on $^{28}Si^+$ are $^{12}C^{16}O^+$ and $^{14}N_2^+$, due to the presence of CO_2, N_2 and O_2 in the argon supply and from air entrainment into the plasma. H_2 was selected as the reaction gas as both the CO^+ and N_2^+ interferences react readily with H_2 cell gas. Si^+ remains unreactive and so can be measured, free from interferences, at its original mass.

Comparison of GC-ICP-QQQ and GC-ICP-MS DLs

For comparison purposes, H_2S, COS, PH_3, GeH_4, AsH_3, and SiH_4 were analyzed by both GC-ICP-QQQ with the 8800 ICP-QQQ, and GC-ICP-MS using the same GC method with an Agilent 7900 conventional quadrupole ICP-MS. A summary of the detection limits (DLs) for both techniques is given in Table 1. For analytes where the background noise is very low (Ge-74, As-75), single digit ppt level detection limits are easily achieved using either GC-ICP-MS or GC-ICP-QQQ. However, for analytes that are prone to higher backgrounds (P-31 and S-32), significantly lower detection limits can be achieved by using MS/MS with O_2 cell gas and measuring the oxygen addition reaction product ions PO^+ and SO^+ in mass-shift mode. In addition, MS/MS mode with H_2 cell gas provides effective removal of background interferences at mass 28, allowing on-mass measurement of Si at its primary isotope.

Table 1. Detection limit comparison between GC-ICP-QQQ and GC-ICP-MS

Hydride gas	8800 ICP-QQQ		7900 ICP-MS	
		DL, ppb		DL, ppb
H_2S	**32 -> 48 (O_2)**		**32 (No gas)**	
	MDL 7 reps	0.21	MDL 7 reps	0.62
	MDL 2 X S/N	0.11	MDL 2 X S/N	0.22
COS	**32->48 (O_2)**		**32 (No gas)**	
	MDL 7 reps	0.12	MDL 7 reps	0.51
	MDL 2 X S/N	0.11	MDL 2 X S/N	0.21
PH_3	**31->47 (O_2)**		**31 (No gas)**	
	MDL 7 reps	0.019	MDL 7 reps	0.139
	MDL 2 X S/N	0.009	MDL 2 X S/N	0.077
GeH_4	**74->90 (O_2)**		**74 (No gas)**	
	MDL 7 reps	NA	MDL 7 reps	0.013
	MDL 2 X S/N	0.0038	MDL 2 X S/N	0.0013
AsH_3	**75->91 (O_2)**		**75 (No gas)**	
	MDL 7 reps	NA	MDL 7 reps	0.016
	MDL 2 X S/N	0.0013	MDL 2 X S/N	0.006
SiH_4	**28->28 (H_2)**		**28 (H_2)**	
	MDL 7 reps	0.14	MDL 7 reps	1.09
	MDL 2 X S/N	0.196	MDL 2 X S/N	1.18

NA = not available

GC-ICP-QQQ sets benchmark detection limits

The significantly lower background and higher sensitivity of the Agilent 8800 ICP-QQQ resulted in a GC-ICP-QQQ method that shows a clear advantage for the determination of a range of contaminants in high purity gases at the low detection levels demanded by the industry. Compared to GC-ICP-MS with conventional quadrupole ICP-MS, GC-ICP-QQQ DLs for silane, phosphine, hydrogen sulfide, and carbonyl sulfide were lower by a factor of 5 to 10, with silane detection limits in the ~200 ppt range and phosphine detection limits in the ~15 ppt range.

More information

Sub-ppb detection limits for hydride gas contaminants using GC-ICP-QQQ, 5991-5849EN.

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Ultralow Level Determination of Phosphorus, Sulfur, Silicon, and Chlorine

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Keywords

sulfur, silicon, phosphorus, chlorine, ultralow level, UPW

Introduction

With the introduction of Agilent's second-generation ICP-QQQ instrument, the Agilent 8900 Triple Quadrupole ICP-MS, reaction cell operation with MS/MS mode has been further refined. This note describes the performance of the 8900 ICP-QQQ for the analysis of some of the most challenging elements for ICP-MS: phosphorus (P), sulfur (S), silicon (Si), and chlorine (Cl). As ICP-MS technology has developed, there has been a growing demand and expectation to measure these difficult elements, together with more conventional elements, in high purity chemicals and materials.

Experimental

Instrumentation: An Agilent 8900 Semiconductor configuration ICP-QQQ was used for all measurements. The sample introduction system comprised a PFA concentric nebulizer, a quartz spray chamber and torch, and platinum interface cones.

Table 1. Cell tuning conditions

Parameter	Unit	^{31}P	^{32}S	^{28}Si	^{35}Cl
Cell gas		O_2		H_2	
Flow rate	mL/min	0.41		5	
Mass pair		(31⟶47)	(32⟶48)	(28⟶28)	(35⟶37)
Octopole Bias	V	-3		-18	
KED	V	-8		0	
Axial Acceleration	V	1		0	

Tuning: Hot plasma conditions were used throughout this study. RF power = 1550 W, sampling depth = 8 mm, nebulizer gas flow rate = 0.70 L/min, and makeup gas flow = 0.52 L/min. Based on previous studies, oxygen (O_2) mass-shift mode was used for the analysis of P and S [1]; hydrogen (H_2) on-mass mode was used for Si; and Cl was determined using H_2 mass-shift mode [2]. Cell tuning conditions are summarized in Table 1.

Results and discussion

To prepare the ICP-QQQ for the analysis, a 1% HNO_3 solution was aspirated overnight to thoroughly clean the sample introduction system. Running the plasma for several hours would also help to remove any contaminants in the Ar gas flow line. P, S and Si were measured together, and Cl was analyzed in a separate batch since it benefited from an alkaline rinse between solutions. Figures 1 shows the calibration curves of the four elements in ultrapure water (UPW, supplied from Organo, Japan). The background equivalent concentrations (BEC) and detection limits (DL) are summarized in Table 2.

Table 2. BEC and DL of P, S, Si, and Cl in UPW

		^{31}P	^{32}S	^{28}Si	^{35}Cl
BEC	ppt	10.5	75.4	259	1830
DL (n=10 x 1s integration)	ppt	3.3	5.5	14.7	280

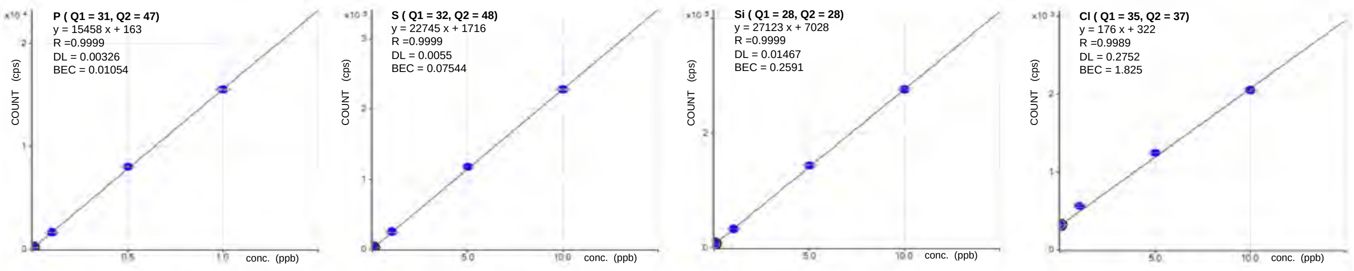

Figure 1. Calibration plots of P, S, Si, and Cl in UPW. All values in ug/L (ppb).

Conclusions

The Agilent 8900 ICP-QQQ operating in MS/MS mode with O_2 and H_2 cell gases successfully eliminated problematic spectral interferences on non-metallic impurities P, S, Si, and Cl in UPW. The results highlight the advanced performance of the second-generation ICP-QQQ for the analysis of challenging elements. The method delivered the lowest ever reported BECs for the four elements in UPW.

References

1. S. D. Fernández, N. Sugiyama, J. R. Encinar, and A. Sanz-Medel, Triple Quad ICP-MS (ICP-QQQ) as a New Tool for Absolute Quantitative Proteomics and Phosphoproteomics, Anal. Chem., 2012, 84, 5851- 5857

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More information

Ultra-low level determination of phosphorus, sulfur, silicon and chlorine using the Agilent 8900 ICP-QQQ, Agilent application note, 2016, 5991-6852EN.

Determination of Ultratrace Elements in SEMI Grade 5 High Purity Hydrogen Peroxide

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Keywords

SEMI, H_2O_2, hydrogen peroxide, semiconductor, high purity chemicals

Introduction

Hydrogen peroxide (H_2O_2) is one of the most important process chemicals used in semiconductor device manufacturing. As a strong oxidizer, it is used for cleaning silicon wafers, removing photoresists, and etching metallic copper on printed circuit boards.

Semiconductor Equipment and Materials International (SEMI) publishes standards regarding the specifications for semiconductor process chemicals including H_2O_2 (SEMI C30-1110). SEMI Grade 5 is the highest purity level, with maximum contamination levels of 10 ppt for most trace elements. The industry therefore requires analytical methods capable of measuring the trace elements at single- or sub-ppt level background equivalent concentrations (BECs). SEMI C30-1110 also includes specifications for the maximum concentrations of sulfate and phosphate allowed in high purity H_2O_2, with a limit of 30 ppb. This limit equates to elemental concentrations of sulfur and phosphorus of 10 ppb. These two contaminants are not currently measured by ICP-QMS. However, the recent development of triple quadrupole ICP-MS (ICP-QQQ) permits much lower limits of detection for S and P. It is now possible to monitor all SEMI elements using a single technique.

Experimental

Instrumentation: Agilent 8900 Semiconductor configuration ICP-QQQ.

Tuning: To achieve the lowest DLs, a multi-tune method was used. The tuning parameters are summarized in Table 1. For data acquisition, a 2 s integration time was used for all isotopes with three replicates (10 replicates for the blank to calculate the DLs).

Table 1. ICP-QQQ tuning conditions

	Cool	Cool-NH_3 (1)	Cool-NH_3 (2)	No gas	H_2	He	O_2 (1)	O_2 (2)
Scan mode	Single Q	MS/MS						
RF power (W)	600			1500				
Nebulizer gas flow (L/min)	0.70							
Makeup gas flow (L/min.)	0.90			0.48				
Sampling depth (mm)	18.0			8.0				
Ex1 (V)	-150.0		-100.0	4.2	4.7	4.2	4.5	3.5
Ex2 (V)	-18.0	-17.0	-12.0	-250.0				-120.0
Omega (V)	-70.0			-140.0				-70.0
Omega Bias (V)	2.0			10.0	8.0	-10.0	10.5	4.0
Q1 Entrance (V)	-15.0		-50.0					
Cell gas	–	NH_3		–	H_2	He	O_2	
Cell gas flow (ml/min)		2.0	2.0		7.0	5.0	0.3	0.3
Axial Acceleration (V)	0.0	1.5		0.0			1.0	
KED (V)	15.0	-5.0		5.0	0.0	3.0	-7.0	

Sample preparation

TAMAPURE-AA-10 hydrogen peroxide (35%, Tama Chemicals, Japan) was used as the sample matrix. To stabilize the spiked elements, ultrapure nitric acid (TAMAPURE-AA-10) was added to the H_2O_2 samples at one part of 70% HNO_3 to 1000.

Results and discussion

Table 2 shows quantitative results and detection limits for the SEMI specification elements in high purity 35% H_2O_2. Comparative quantitative results and DLs are also shown for the same elements in ultrapure water. Long-term stability was evaluated by measuring a H_2O_2 sample spiked at 10 ppt for most elements and 100 ppt for sulfur. Calibration curves were generated at the beginning of the sequence. The spiked samples were then run as unknown samples for a total analysis period of 3 h 40 min. The RSDs of the 13 results are shown in Table 2 (Stability RSD %).

Table 2. Quantification of trace elements and stability test results for SEMI specification elements in high purity 35% H_2O_2 and ultrapure water

					Hydrogen peroxide			Ultrapure water	
Element	Q1	Q2	Scan mode	Tune	Conc. (ppt)	DL (ppt)	Stability RSD (%)	Conc. (ppt)	DL (ppt)
Li		7	single quad	Cool	< DL	0.003	4.7	< DL	0.004
B	11	11	MS/MS	No gas	7.7	0.69	8.1	4.6	0.57
Na		23	single quad	Cool	0.39	0.031	3.3	0.5	0.069
Mg		24	single quad	Cool	0.017	0.017	4.1	< DL	0.012
Al		27	single quad	Cool	0.39	0.071	2.9	0.11	0.11
P	31	47	MS/MS	O_2 (1)	4.2	0.89	3.3	3.4	0.91
S	32	48	MS/MS	O_2 (1)	190	5.1	7.8	41	3.8
K	39	39	MS/MS	cool+NH_3 (2)	0.21	0.11	2.2	0.2	0.088
Ca	40	40	MS/MS	cool+NH_3 (2)	< DL	0.23	1.9	< DL	0.10
Ti	48	64	MS/MS	O_2 (2)	0.097	0.045	2.6	< DL	0.028
V	51	67	MS/MS	O_2 (2)	0.067	0.027	2.6	< DL	0.023
Cr	52	52	MS/MS	cool+NH_3 (1)	0.13	0.075	3.5	< DL	0.031
Mn	55	55	MS/MS	cool+NH_3 (1)	< DL	0.012	2.7	< DL	0.004
Fe	56	56	MS/MS	cool+NH_3 (1)	0.13	0.074	3.3	< DL	0.027
Ni	60	60	MS/MS	cool+NH_3 (1)	0.16	0.14	3.7	< DL	0.030
Cu	63	63	MS/MS	cool+NH_3 (1)	< DL	0.048	5.0	0.19	0.18
Zn	64	64	MS/MS	He	0.22	0.14	4.5	0.35	0.17
As	75	91	MS/MS	O_2 (2)	< DL	0.087	3.5	< DL	0.081
Cd	114	114	MS/MS	No gas	< DL	0.02	2.3	< DL	0.017
Sn	118	118	MS/MS	No gas	0.088	0.063	2.0	< DL	0.037
Sb	121	121	MS/MS	H_2	< DL	0.015	1.6	< DL	0.022
Ba	138	138	MS/MS	H_2	0.061	0.033	1.2	< DL	0.004
Pb	208	208	MS/MS	No gas	0.081	0.053	1.0	0.056	0.035

Conclusions

All the elements specified in SEMI C30-1110 were measured at sub-ppt to ppt levels in high purity 35% hydrogen peroxide using the Agilent 8900 ICP-QQQ. For almost all elements, sub ppt quantitative results were obtained, with the remaining elements having single-ppt detection limits (except Si, 25 ppt). Reproducibility between 1.0 – 8.1 % RSD was obtained at the 10 ppt level (100 ppt for S) for the spiked analytes in a high purity 35% hydrogen peroxide sample analysis sequence that lasted 3 hours 40 minutes. This performance demonstrates the suitability of the Agilent 8900 Semiconductor configuration ICP-QQQ instrument for the routine analysis of the highest-purity semiconductor reagents and process chemicals.

More information

Determination of ultra trace elements in high purity hydrogen peroxide with Agilent 8900 ICP-QQQ, Agilent application note, 2016, 5991-7701EN.

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Materials

Arsenic Measurement in Cobalt Matrix using MS/MS Mode with Oxygen Mass-Shift

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Keywords

arsenic, high purity metals, cobalt, zirconium, oxygen mass-shift

Introduction

Measuring the purity of materials such as high purity metals is of interest across advanced technology industries, to support the development of new materials and/or improve the performance of existing products. ICP-MS is widely used for determining elemental impurities in these materials due to its unique features: High sensitivity, low DLs, multi element analysis capability, wide dynamic range, fast analysis and minimal sample preparation requirements.

For many applications, the errors caused by spectral interferences in quadrupole ICP-MS have been adequately addressed by the introduction of CRC technology. However, the analysis of trace contaminants in high purity materials presents a particular challenge due to the high matrix levels and the need to determine impurities at the trace level. For example, the determination of As in Co is difficult for quadrupole ICP-MS due to the signal from CoO^+ that overlaps the only isotope of arsenic at *m/z* 75. Although only about 0.01% of the Co ions in the plasma are present as CoO^+ ions, the Co concentration in a 1000 ppm solution is 6 or 7 orders of magnitude higher than the trace levels of As that are of interest in this application. Consequently the CoO^+ interference is still very significant relative to the As^+ signal. This note describes the measurement of trace As in a 1000 ppm Co solution using an Agilent 8800 ICP-QQQ in MS/MS mass-shift mode, using oxygen as the reaction gas.

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/HMI-mid.

CRC conditions: O_2 gas at 0.3 mL/min,
Octopole bias = -5 V, KED = -7 V.

Acquisition conditions: Three oxygen (O_2) mass-shift operational modes were compared:

- Single Quad mode A with low mass cut off at *m/z* < 59
- Single Quad mode B with low mass cut off at *m/z* ≒ 59
- MS/MS mode with Q1 as a 1 amu mass filter, Q1 = 75 and Q2 = 91

Sample: SPEX CLCO2-2Y (SPEX CertiPrep Ltd., UK) was used as 1000 ppm Co solution.

Results and discussion

BEC of As in 1000 ppm Co solution using O_2 mass-shift method

From the equation and reaction enthalpy below, it can be seen that arsenic reacts readily with O_2 cell gas via an O-atom transfer reaction. This creates the reaction product ion AsO^+ at *m/z* 91, moving the analyte away from the CoO^+ interference on As^+ at *m/z* 75.

$$As^+ + O_2 \rightarrow AsO^+ + O \quad \Delta Hr = -1.21\ \text{eV}$$

The reaction enthalpy for CoO^+ with the O_2 cell gas is much less favorable, so the overlap from the CoO^+ polyatomic interference is successfully avoided.
To evaluate the effectiveness of MS/MS mode for this application, the 8800 ICP-QQQ was operated in three acquisition modes: MS/MS mode and two "Single Quad" modes, in which Q1 functions as a bandpass filter rather than a unit (1 amu) mass filter. In Single Quad mode A, Q1 was set to allow most of the plasma-formed ions to enter the cell; in Single Quad mode B, Q1 was set with a low mass cutoff around *m/z* 59 to allow only ions with a mass greater than 59 to enter the cell (most $^{59}Co^+$ ions are rejected); and finally in MS/MS mode Q1 was set to allow only ions at *m/z* 75 to enter the cell (all $^{59}Co^+$ rejected).

The BECs for As obtained using the three acquisition modes are shown in Figure 1. MS/MS mode achieved the lowest BEC for As of 330 ppt in 1000 ppm Co. The BEC obtained by the Single Quad modes were orders of magnitude higher, which suggests the occurrence of the following undesired reactions in the cell and indicates the incomplete rejection of Co^+ by Single Quad mode B:

$$^{59}Co^+ + O_2 \rightarrow {}^{59}CoO^+ + O;\ {}^{59}CoO^+ + O_2 \rightarrow {}^{59}CoO_2^+ + O$$

Note that this sequential reaction chemistry leads to a relatively intense signal for CoO_2^+, because the number

Figure 1. BEC of As in 1000 ppm Co solution with O_2 mass-shift method using three acquisition modes (note log intensity scale).

of precursor ions for the reaction (the Co^+ ions from the plasma) is so high (10000 times higher intensity than the CoO^+ signal in the plasma). Consequently, in Single Quad mode, the CoO^+ overlap cannot be successfully avoided by moving the As^+ to its AsO^+ product ion at *m/z* 91 using O_2 cell gas, because CoO_2^+ (also at *m/z* 91) is formed relatively easily when a large number of Co^+ ions are allowed to enter the cell.

AsO^+ in the presence of zirconium

To successfully avoid interferences using the mass-shift method, the mass of the analyte product ion must itself be free from interference. For example, in this application the AsO^+ product ion is measured at *m/z* 91 where it could be overlapped by an isotope of zirconium ($^{91}Zr^+$). The presence of Zr in a sample may therefore cause an error in the results for As measured as AsO^+ using O_2 reaction mode on ICP-QMS. The potential effect of co-existing Zr on AsO^+ measurement using ICP-QMS was investigated.

Figure 2 is a spectrum of 10 ppm Zr obtained using Single Quad mode A with O_2 mass-shift. Zr reacts with O_2 very efficiently ($\Delta Hr = -3.84$) and is converted to ZrO^+. However not all the Zr^+ ions are converted to ZrO^+ so some Zr^+ remains, interfering with the measurement of AsO^+ at *m/z* 91. In contrast, in MS/MS mode the $^{91}Zr^+$ ion is rejected by Q1, so the potential overlap on the AsO^+ product ion at *m/z* 91 is removed.

Conclusions

Trace levels of arsenic in a 1000 ppm cobalt matrix can be successfully measured (BEC of 330 ppt) using the 8800 ICP-QQQ operating in MS/MS mass-shift mode, with oxygen as the reaction gas. There are two main advantages of using MS/MS compared to ICP-QMS:

1. In MS/MS mode, Co^+ is prevented from entering the cell by Q1, which is set to *m/z* 75. In ICP-QMS, CoO_2^+ is formed in the cell via a chain reaction, and will interfere with AsO^+ at *m/z* 91.
2. In MS/MS mode, the potential $^{91}Zr^+$ overlap on the AsO^+ product ion at *m/z* 91 is eliminated, as $^{91}Zr^+$ ions (and all other ions apart from *m/z* 75) are rejected by Q1.

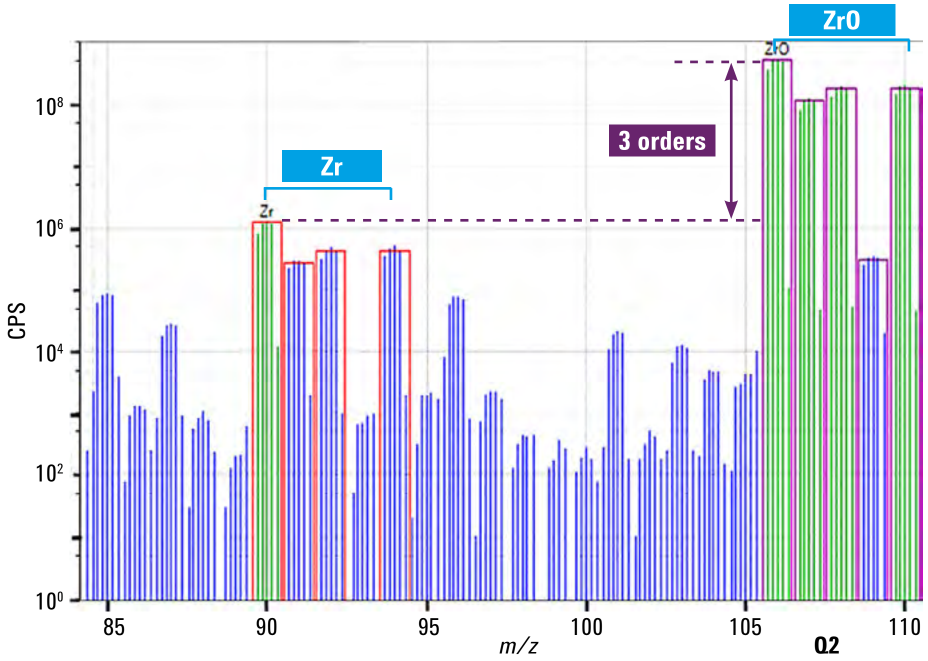

Figure 2. Spectrum of 10 ppm Zr obtained using Single Quad mode A with O_2 mass-shift-method

Determination of Sulfur, Phosphorus and Manganese in High Purity Iron

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Keywords

phosphorus, sulfur, manganese, iron, steel, JSS 001-6, JSS 003-6, abundance sensitivity, oxygen mass-shift

Introduction

ICP-MS is the analytical technique of choice for the analysis of trace elements in iron and steel. However, the sensitivity and interference removal performance of quadrupole ICP-MS (ICP-QMS) is not sufficient for the determination of difficult analytes such as phosphorus (P) and sulfur (S) at the low levels required. Furthermore, the determination of manganese (Mn) in an iron matrix is extremely challenging for ICP-QMS due to overlap (or tailing) from the very intense ^{54}Fe and ^{56}Fe peaks that occur either side of the single isotope of manganese at *m/z* 55.

The Agilent 8800 Triple Quadrupole ICP-MS (ICP-QQQ) provides more effective and reliable removal of polyatomic interferences, such as $^{14}N^{16}OH$ on ^{31}P and $^{16}O_2$ on ^{32}S, using controlled chemical reaction in the CRC. This note describes the performance of the 8800 ICP-QQQ operating in MS/MS mode, for the determination of the trace elements S, P and Mn in two high purity iron CRMs (JSS 001-6 and 003-6).

Experimental

Instrumentation: Agilent 8800 #100.

Plasma condition: Preset plasma/HMI-mid.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -175 V.

CRC and acquisition conditions:

- MS/MS O_2 mass-shift method to remove the $^{14}N^{16}OH^+$ and $^{16}O_2^+$ interferences on $^{31}P^+$ and $^{32}S^+$ respectively: O_2 gas at 0.3 mL/min, Octopole bias = -5 V and KED = -7 V.
- MS/MS He on-mass mode to measure $^{55}Mn^+$: He gas at 5.0 mL/min, Octopole bias = -18 V and KED = 4 V.

All other parameters were optimized by Autotune in the MassHunter software. Figure 1 shows the mechanism used on the 8800 ICP-QQQ to avoid the $^{14}N^{16}OH^+$ and $^{16}O_2^+$ interferences on $^{31}P^+$ and $^{32}S^+$ by mass-shift mode ($Q1 \neq Q2$) using O_2 reaction gas.

Sample preparation: Two Steel CRMs, JSS-001 and JSS-003 were purchased from The Japan Iron and Steel Federation (Tokyo, Japan). 0.1 g of each Steel CRM was digested in a mixture of 1 mL HCl and 2 mL HNO_3 and diluted to 100 mL with UPW. No further chemical matrix separation, e.g., solvent extraction, ion exchange, etc. was applied. The digested CRM samples containing 0.1% (1000 ppm) Fe were analyzed directly on the ICP-QQQ using the robust plasma conditions provided by Agilent's HMI aerosol dilution system.

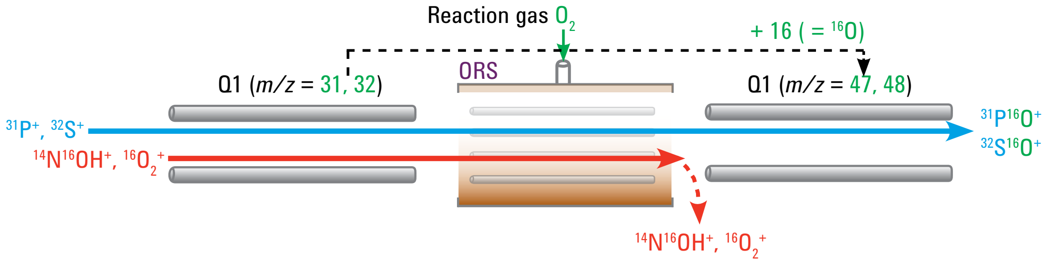

Figure 1. Mechanism of MS/MS mass-shift mode (Q2 = Q1+16) using O_2 reaction gas for the measurement of P as $^{31}P^{16}O^+$ and S as $^{32}S^{16}O^+$ at *m/z* 47 and 48 respectively.

Results and discussion

BEC and DL of P and S

The calibration plots shown in Figure 2 demonstrate that the 8800 ICP-QQQ with MS/MS mass-shift mode can successfully perform the trace level (single ppb) quantitation of P and S in 0.1% Fe solutions. The BEC and DL achieved for P were 0.14 ppb and 0.05 ppb respectively, and the BEC and DL for S were 6.45 ppb and 0.75 ppb respectively.

Trace Mn analysis in Fe matrix

The abundance sensitivity (AS, a measure of peak separation) of ICP-QQQ in MS/MS mode is the product of the Q1 AS x Q2 AS. This means the AS of the 8800 ICP-QQQ is theoretically about 2x that achievable on ICP-QMS, and the ICP-QQQ is therefore able to successfully separate the ^{55}Mn peak from the very intense overlaps from ^{54}Fe and ^{56}Fe in a high iron matrix. This is demonstrated in Figure 3 which shows the spectra of 10 ppb Mn in a 0.1% Fe matrix sample solution measured in Single Quad mode (left) and MS/MS mode on the ICP-QQQ (right). Helium was used as the cell gas in both cases to remove $^{54}FeH^+$ and $ArNH^+$ interferences by KED.

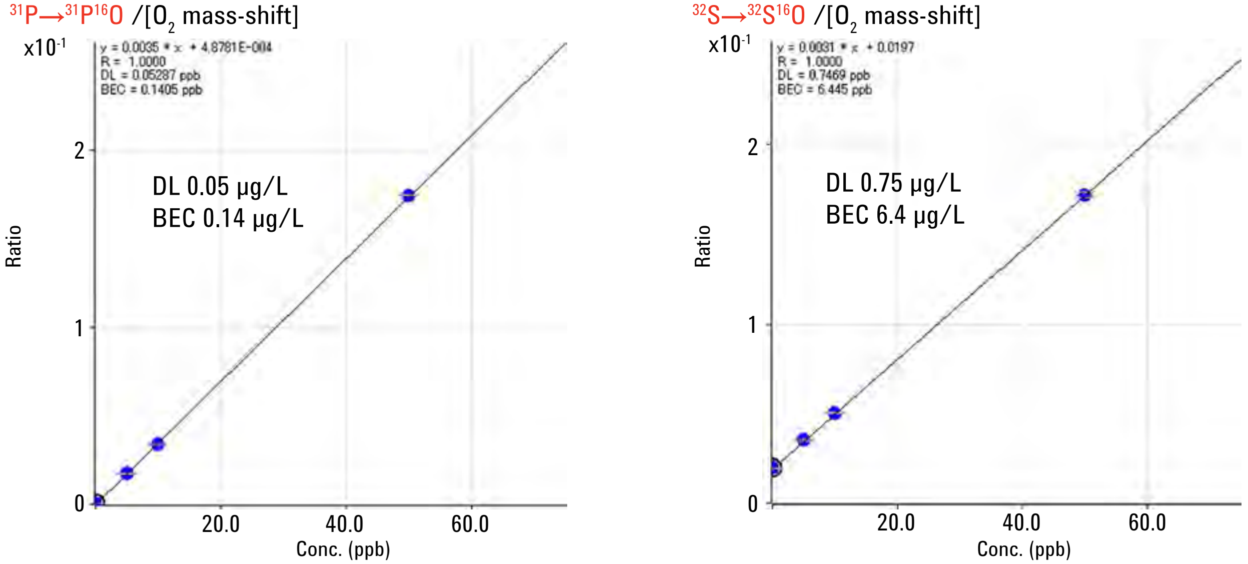

Figure 2. Calibration curve for P (left) and S (right) in 0.1% Fe matrix, obtained using O_2 mass-shift mode under robust plasma conditions.

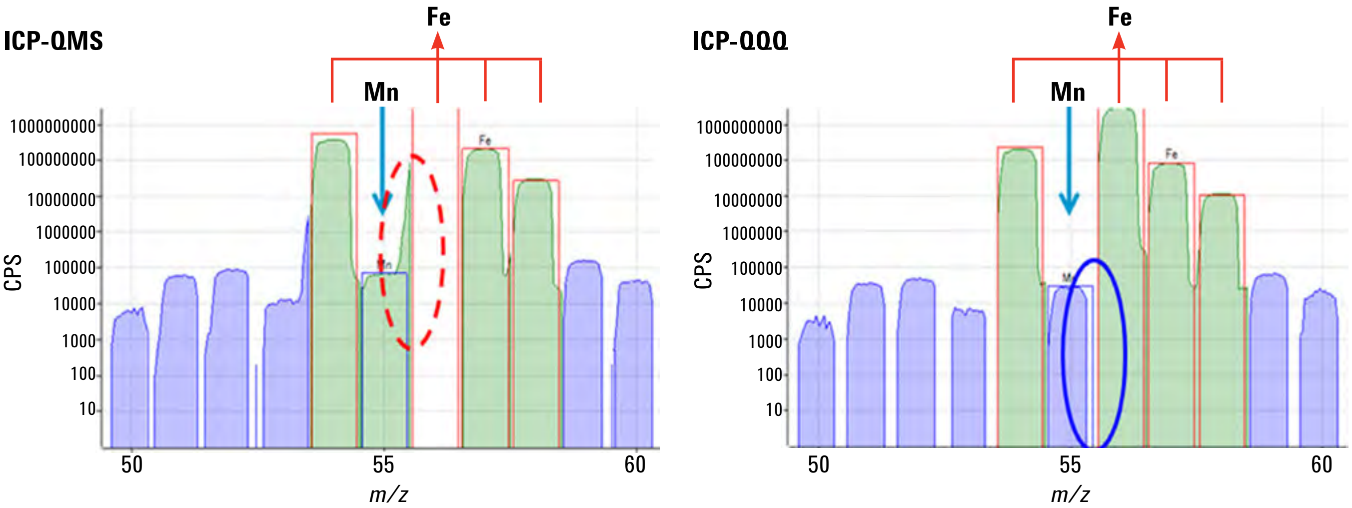

Figure 3. Spectra of 10 ppb Mn in a 0.1% Fe matrix sample solution obtained in Single Quad mode (left) and ICP-QQQ in MS/MS mode (right).

Determination of P, S and Mn in high purity iron CRMs

Trace elements including P, S and Mn were determined by ICP-QQQ in high purity iron CRMs: JSS 001-6 and 003-6, using O_2 mass-shift mode (for P and S) and He mode (for Mn). As summarized in Table 1, excellent agreement was obtained between the measured (found) and certified values for all three elements, indicating the effective interference removal offered by the 8800 ICP-QQQ in MS/MS mode. Excellent spike recovery at the 50 ppb level was also confirmed with JSS 003.

Table 1. Analytical results for P, S and Mn in two high purity iron CRMs

				JSS 001-6			**JSS 003-6**			
Element	**Q1**	**Q2**	**ORS**	**Certified value [mg/kg]**	**Uncertainty**	**Found [mg/kg]**	**Certified value [mg/kg]**	**Uncertainty**	**Found [mg/kg]**	**50 ppb spike recovery %**
P	31	47	O_2	**0.5***		0.458	**3.5**	0.7	3.170	103
S	32	48	O_2	**1.5**	0.3	1.512	**1.3**	0.5	1.287	92
Mn	55	55	He	**0.03***		0.036	**3.2**	0.2	3.432	101

*non-certified value

Direct Measurement of Trace Rare Earth Elements in High Purity REE Oxides

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Keywords

Rare Earth Elements, REE, rare earth oxide, REO, samarium oxide, gadolinium oxide, oxygen mass-shift, ammonia on-mass

Introduction

The rare earth elements (REEs) are widely used in advanced technologies including high-power permanent magnets, lasers, phosphors used in fluorescent lamps, radar screens and plasma displays. REEs are also used in petroleum refining, automobile catalytic converters and batteries, and in high-technology glasses. It is clear from these examples that REEs play a key role in many types of materials used in high-technology industries. However, the presence of other REEs as contaminants in a purified single-element REE material often impacts the functionality of the final product, so impurities in the REE oxide raw material must be carefully controlled.

ICP-MS is the most commonly used atomic spectrometry technique for the measurement of trace REEs due to its simple REE spectra — particularly when compared to emission techniques. The measurement of mid- and high-mass REEs in a low-mass REE matrix is, however, very challenging for ICP-MS because REEs have among the highest metal-oxide (M-O) bond strengths of any element, and the oxide ions of the low mass REE overlap the preferred isotopes of the mid-mass and high-mass REEs. Table 1 shows the interferences observed in the analysis of trace REEs in high-purity samarium (Sm) oxide and gadolinium (Gd) oxide.

Separation of the trace REE analytes from the REE matrix can be performed utilizing a chelating resin, but this technique is time-consuming and customization is needed according to the analyte and matrix element. The direct analysis of trace REEs in a variety of high-purity REE matrices is therefore desired. In this work, an Agilent 8800 Triple Quadrupole ICP-MS was used for the direct analysis of trace REE in two high-purity REE materials: Sm_2O_3 and Gd_2O_3. Operating the ICP-QQQ in MS/MS mode effectively removes the challenging interferences, enabling the determination of REE impurities at trace levels in these two materials.

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/General purpose.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -180 V.

Acquisition parameters: Three cell modes were used with MS/MS acquisition: No gas, O_2 mass-shift, and NH_3 on-mass mode. In MS/MS O_2 mass-shift mode, the REEs were determined as their oxide ions. REE ions react efficiently with the O_2 cell gas and are converted to the oxide ion REE-O^+. For example, in the measurement of $^{153}Eu^+$, Q1 is set to *m/z* 153 ($^{153}Eu^+$) and Q2 is set to *m/z* 169 ($^{153}Eu^{16}O^+$). Cell tuning parameters are summarized in Table 2.

Table 1. Preferred isotope for ICP-MS analysis of each REE, and the potential interferences caused by Sm_2O_3 and Gd_2O_3 matrices

Element	**La**	**Ce**	**Pr**	**Nd**	**Sm**	**Eu**	**Gd**	**Tb**	**Dy**	**Ho**	**Er**	**Tm**	**Yb**	**Lu**
Mass	**139**	**140**	**141**	**146**	**147**	**153**	**157**	**159**	**163**	**165**	**166**	**169**	**172**	**175**
Gd_2O_3							N/A	GdH^+					GdO^+	$GdOH^+$
Sm_2O_3					N/A	SmH^+			SmO^+	SmO^+	SmO^+	$SmOH^+$		

Table 2. CRC tuning parameters

Cell mode	Unit	No gas	O_2	*NH_3
Scan mode	MS/MS			
Cell gas		N/A	O_2	NH_3
Cell gas flow rate	mL/min	N/A	0.35	9.0
Octopole bias	V	-8	-5	-18
KED	V	5	-8	-8
Cell exit	V	-80	-90	-110
Deflect lens	V	20	10	-3
Plate	V	-80	-90	-110

*10% NH_3 balanced in Ar

Results and discussion

Two high purity REE oxide materials Gd_2O_3 (5N) and Sm_2O_3 (4N8) were gently dissolved in semiconductor grade HNO_3 and diluted to a concentration of 1 ppm (as the REE). The other (trace) REEs were measured in each matrix solution using the three cell modes. The results are given in Figure 1 and Figure 2. As expected, analysis of the 1 ppm Gd solution in no gas mode gave positive errors on some elements due to interferences from Gd polyatomic ions: GdH^+ interferes with $^{159}Tb^+$, GdO^+ interferes with $^{172}Yb^+$ and $GdOH^+$ interferes with $^{175}Lu^+$.

Preliminary studies showed that NH_3 cell gas reacts with many of the polyatomic ions that interfere with the REE. However, NH_3 also reacts quickly with some of the REE ions, leading to reduced sensitivity of < 1 cps/ppt [1], so this mode is only suitable for the measurement of the less reactive analytes: Pr, Eu, Dy, Ho, Er, Tm and Yb. For these elements, NH_3 on-mass mode gave excellent results, including for Yb in the Gd matrix, where the measured Yb background concentration was reduced by four orders of magnitude (Figure 1) indicating effective removal of the GdO^+ overlap. Background signals for Dy, Ho, Er and Tm in the Sm matrix were also dramatically improved (Figure 2).

For the REEs that react with NH_3 (La, Ce, Nd, Sm, Gd, Tb and Lu), O_2 mass-shift mode and measurement of the target analyte as its REE-O^+ ion is the preferred approach. Most REEs are effectively converted to the oxide ion via reaction with O_2 cell gas [1], and this mode was applied to the measurement of Lu in the Gd matrix, avoiding the $GdOH^+$ interference on the Lu^+ isotope and giving a good improvement in the background signal. Compared to no gas mode, O_2 mass-shift mode also gave a good improvement in the background signals for Dy, Ho, Er, Tm and Yb in the Sm matrix, but for all these analytes the backgrounds in NH_3 mode were lower still.

Reference

1. Direct measurement of trace rare earth elements (REEs) in high-purity REE oxide using the Agilent 8800 Triple Quadrupole ICP-MS with MS/MS mode, Agilent application note, 5991-0892EN.

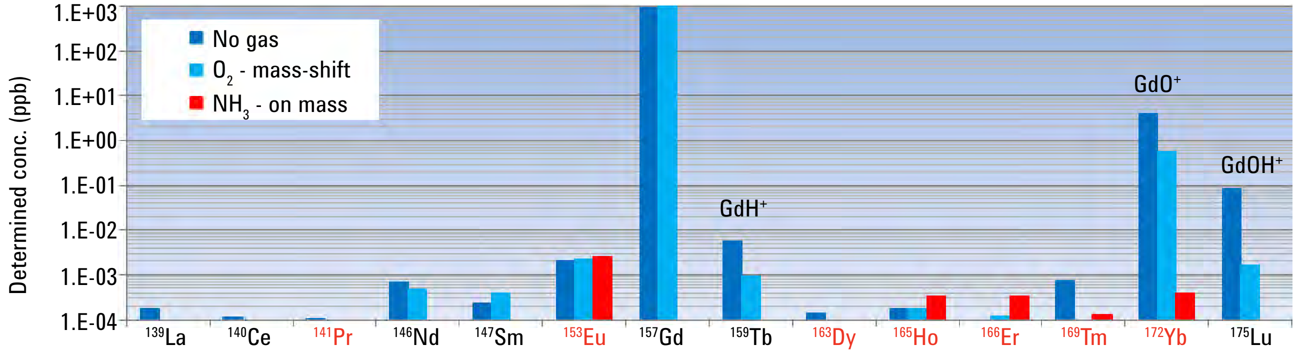

Figure 1. Measured concentration of REE impurities in 1 ppm Gd solution. Gd based interferences are observed on Tb, Yb and Lu. Only the elements in red were measured in NH_3 on-mass mode.

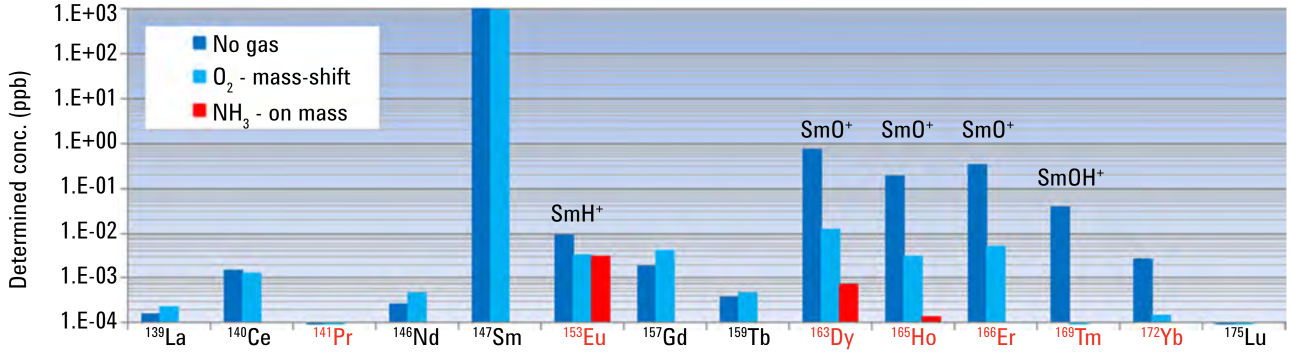

Figure 2. Measured concentration of REE impurities in 1 ppm Sm solution. Sm based interferences are observed on Eu, Dy, Ho, Er, Tm and Yb. Only the elements in red were measured in NH_3 on-mass mode.

The Benefits of Improved Abundance Sensitivity with MS/MS for Trace Elemental Analysis of High Purity Metals

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Keywords

quadrupole, resolution, hyperbolic, abundance sensitivity, copper, high purity zinc

Introduction

The use of a quadrupole mass filter for the separation of compounds in mass spectrometry is well established. Initially used for organic mass spectrometry and residual gas analysis, the quadrupole spectrometer was adopted for the earliest ICP-MS systems, and has remained the default choice throughout the history of ICP-MS. However, the performance characteristics of the quadrupole mass filter do impose several limitations on quadrupole ICP-MS (ICP-QMS).

The resolution (R) of a mass filter (meaning its ability to separate adjacent masses) is defined as M/ΔM, the mass of the target peak/the mass difference to nearest adjacent peak that can be distinguished (separated). However, for practical specifications, the resolution is often simply quoted as the width of the peak at a given peak height. The quadrupole mass filter used in an ICP-QMS instrument is typically operated with a nominal peak width of about 0.75 amu at 10% peak height, illustrated in Figure 1.

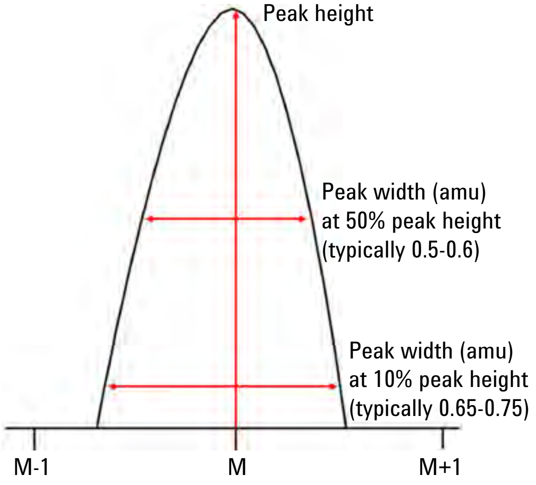


Figure 1. Illustration of resolution calculation for a mass spectrometer

For two peaks within the normal signal range of the instrument, this allows the complete, baseline separation of masses 1 amu apart, within the elemental mass range from Li (7 amu) to U (238 amu) and beyond. Higher resolution of 0.4 amu peak width is possible by adjusting the quadrupole voltages, but the signal is reduced (less ion transmission) due to rejection of a higher proportion of the ions that are nominally "on-mass". Typically the signal loss at higher resolution is around 10-50%, depending on the design and operating characteristics of the quadrupole.

Both the efficiency of transmission of ions at the set-mass (i.e., the sensitivity) and the rejection of ions at other masses (i.e., the resolution of adjacent peaks) are affected by the shape of the field within the quadrupole, and the frequency of the alternating RF fields.

A hyperbolic field (generated by rods with a hyperbolic profile) alternating at high frequency gives more effective filtering of the ion beam than a lower frequency field generated by round quadrupole rods. The practical benefit of hyperbolic rods and high frequency RF voltage is therefore better ion transmission at higher resolution. Some of the many real-world applications where the combination of high sensitivity and good peak separation is required for adjacent low/high concentration elements measured by ICP-MS are shown in Table 1.

Table 1. Elements that require improved separation of adjacent peaks for low level analysis

Low concentration	High signal	Example matrix
^{31}P	$^{16}O_2$, ^{32}S	Soil, plants, biological
^{55}Mn	^{56}Fe, $^{40}Ar^{16}O$	Blood, iron and steel, soil
^{63}Cu, ^{65}Cu	^{64}Zn, ^{66}Zn	Metal refining
^{11}B	^{12}C	Soils, solvents, petrochem
^{13}C	^{14}N	Laser imaging of biological

Due to the ion transmission characteristics of a quadrupole, the peak that is generated from the ion signals at each mass forms a non-symmetric Gaussian distribution with a negative skew; i.e., the peak has a longer tail on the leading edge (low mass side) than the trailing edge (high mass side). These "tails" may extend significantly beyond the limits of the nominal 0.75 amu peak width, but since they are at intensities far below 10% of the peak height, they cannot be measured using the simple resolution figure quoted above. The contribution that a peak at mass M makes to its neighbors at M-1 amu and M+1 amu can be quantified, however, and this figure is referred to as the abundance sensitivity (AS) of the quadrupole, illustrated in Figure 2.

For a good quadrupole mass spectrometer in ICP-QMS, the AS would typically be of the order of 10^{-7}, meaning that for an on-mass signal of 10^7 counts, there is a contribution of one count at the adjacent mass (M+/-1 amu).

In applications where the trace analyte must be separated from a very intense matrix peak at the adjacent M+1 mass, such as the examples shown in Table 1, the matrix peak may be at an intensity greater than 10^9 or 10^{10}, and the AS of a quadrupole mass spectrometer is insufficient for accurate trace measurement of an adjacent overlapped analyte at low/sub ppb levels.

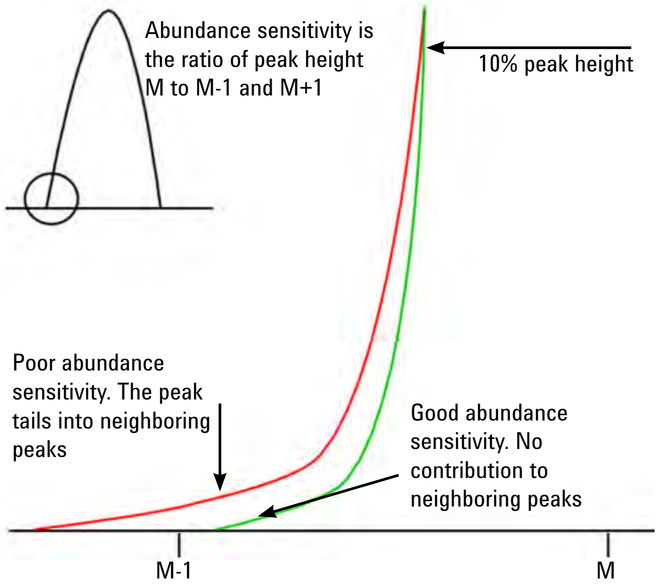


Figure 2. Illustration of abundance sensitivity calculation for a mass spectrometer

The problem of adjacent mass overlaps now has an elegant solution in the Agilent 8800 Triple Quadrupole ICP-MS (ICP-QQQ). The 8800 ICP-QQQ uses a tandem mass spectrometer configuration with two quadrupole mass filters (Q1 and Q2) separated by a collision/reaction cell. In MS/MS mode, both quadrupoles are operated as unit mass filters, so the overall AS of the instrument is the product of the Q1 AS x the Q2 AS. With two research-grade, high frequency, hyperbolic quadrupoles, each operating with AS of 10^{-7}, the combined AS of the 8800 ICP-QQQ is theoretically 10^{-14}, although this cannot be verified experimentally as the magnitude of the signal difference exceeds the dynamic range of the detector.

Experimental

Trace copper in high purity zinc

Major uses of Zn include galvanized coating to protect steel, die castings, and solder. Impurities in the metal cause Zn plating to lift, die casts to crack, or solder to 'de-wet', hence high purity zinc (>99.995 %) is a preferred commodity. Common impurities are Cu, Au and Sb, but may also include Cd, Al, Fe, Ag, Bi, As, In, Ni, P, and S.

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/Low matrix.

Ion lens tune: Auto tune was used for optimization.

CRC conditions: Helium cell gas at 4.8 mL/min with KED of 4 V.

Results and discussion

Analysis was performed on high purity Zn, dissolved to give a 0.1% (1000 mg/L) Zn solution in a final acid concentration of 2% HNO_3. The sensitivity of the 8800 ICP-QQQ was reduced to bring the signal for the major Zn isotopes (64, 66) within the detector's upper limit of dynamic range (~ 10^{10} cps). The intense Zn signals were measured automatically in analog detector mode, while the Cu isotopes were measured in pulse mode. It can clearly be seen in Figure 3 that the intense Zn peaks at *m/z* 64 and 66 made no contribution to the signal at the two adjacent trace Cu isotopes at *m/z* 63 and 65. The Cu isotope ratio matched the theoretical abundances (^{63}Cu/^{65}Cu natural ratio of 69.17/30.83), at 1 µg/L concentration. If there was a contribution from an adjacent Zn mass then the isotope ratio would be biased.

From the ^{63}Cu calibration (Figure 4), the BEC and DL measured for Cu in the 0.1% Zn matrix were 1.7 ppb and 0.01 ppb respectively, indicating a low and stable background signal. The sensitivity of Cu was 7700 cps/ppb in 1000 µg/L Zn, under the "de-tuned" conditions used to bring the Zn peaks within the detector range. This represents about a 2x reduction in the signal that would be obtained under normal tuning conditions for this type of matrix, if measurement of the matrix element peaks was not required.

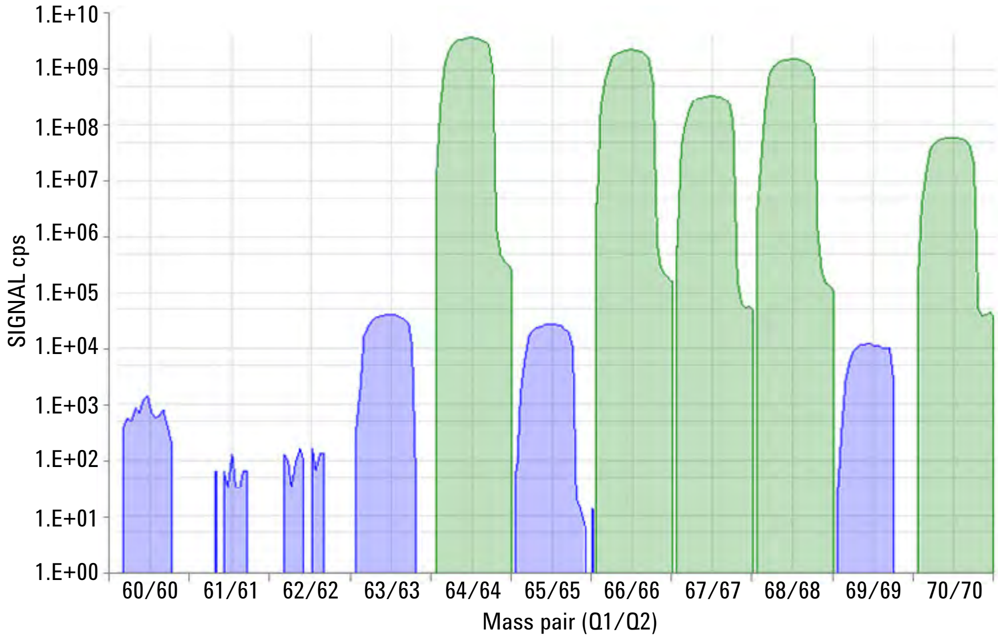
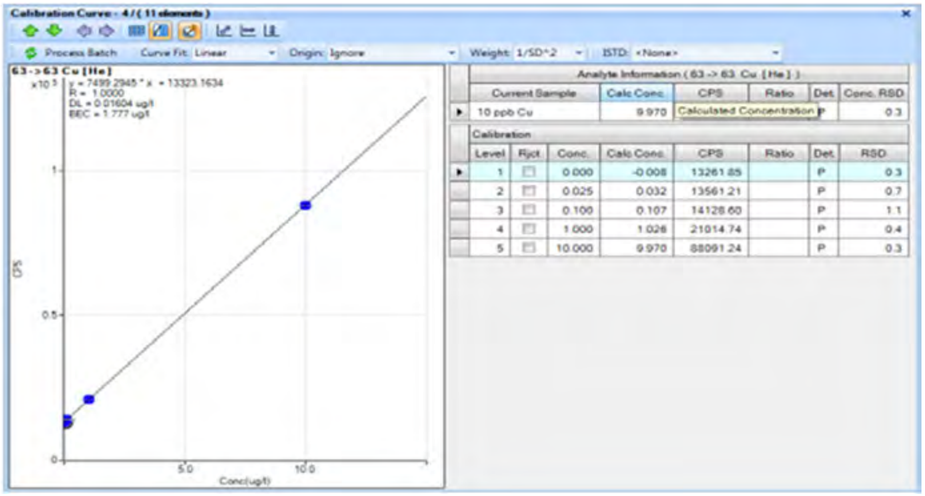


Figure 3. 1000 mg/L Zn spiked with 1 ug/L Cu. (1 ppb: 63/total = 0.667, 65/total = 0.333, no mass bias correction performed. If there was some contribution from Zn it would influence *m/z* 63 differently from *m/z* 65, because of the different abundance of the Zn isotopes).



Curve Fit: Linear
Origin: Ignore
Weight: 1/SD^2
ISTD: <None>

63 -> 63 Cu [He]
y = 7499.2945 * x + 13323.1634
R = 1.0000
DL = 0.01604 ug/l
BEC = 1.777 ug/l

Analyte Information (63 -> 63 Cu [He])

Current Sample	Calc Conc.	CPS	Ratio	Det.	Conc. RSD
10 ppb Cu	9.970			P	0.3

Calibration

Level	Rjct	Conc.	Calc Conc.	CPS	Ratio	Det.	RSD
1	☐	0.000	-0.008	13261.85		P	0.3
2	☐	0.025	0.032	13561.21		P	0.7
3	☐	0.100	0.107	14128.60		P	1.1
4	☐	1.000	1.026	21014.74		P	0.4
5	☐	10.000	9.970	88091.24		P	0.3

Figure 4. Standard addition calibration of ^{63}Cu in 1000 mg/L Zn

Ultra Trace Copper Analysis in a Semiconductor Grade Organometallic Titanium Complex

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Keywords

semiconductor, organometallic, copper, titanium, ammonia mass-shift

Introduction

Most quadrupole ICP-MS (ICP-QMS) instruments use CRC technology to resolve spectroscopic interferences. Helium collision mode is widely accepted due to its versatility and ease of use for multi-element analysis of complex and variable samples. While the performance achievable with He mode meets the requirements for most applications, there are some applications, for example impurity analysis of semiconductor materials, that require improved interference removal capability. For these applications, a reactive cell gas (reaction mode) may be used, but the use of highly reactive cell gases in quadrupole ICP-MS is prone to unexpected interferences and overlaps, especially when the matrix is complex, or other analytes are present at varying concentrations. The new Agilent 8800 Triple Quadrupole ICP-MS (ICP-QQQ) eliminates the variability associated with reactive cell gases in ICP-QMS, by using the first quadrupole (Q1) to control the ions that enter the CRC. This ensures that the reactions are predictable and the product ion spectrum is simple and consistent.

This report describes the measurement of trace Cu in a semiconductor grade organometallic Ti complex used in advanced semiconductor processing. It is a challenging application for quadrupole ICP-MS since both isotopes of copper, ^{63}Cu and ^{65}Cu, suffer interference from TiO and TiOH ions, and the use of reactive cell gases to avoid the overlap leads to a very complex product ion spectrum, particularly for organic samples. We demonstrate that the Agilent 8800 ICP-QQQ, operating in MS/MS mass-shift mode using ammonia as a reaction gas, was able to separate Cu$^+$ from the Ti-based interferences and measure Cu at low ppt levels in a matrix of 500 ppm Ti. Results were also acquired using MS/MS He collision mode, for comparison.

Experimental

Instrumentation: Agilent 8800 #200 with narrow injector (id = 1.5 mm) torch (G3280-80080) used for organic solvent analysis. A low flow PFA nebulizer (G3285-80002) was used in self-aspiration mode. An option gas flow of 20% O_2 balanced in Ar was added to the carrier gas via the standard option-gas line to prevent carbon build up on the interface cones.

Operating conditions: Table 1 summarizes plasma, ion lens and cell tuning conditions.

Acquisition conditions: MS/MS mode was used; cell gas was either NH_3 or He.

Sample and sample preparation: Semiconductor grade organometallic Ti complex (ADEKA Corp., Japan) was diluted with high purity IPA (Tokuyama Corp., Japan) to 500 ppm Ti solution. A spiked standard was prepared from the multi-element standard, xstc-331, purchased from SPEX CertiPrep Ltd. (UK).

Table 1. Experimental conditions

		Units	He collision cell mode	NH_3 reaction cell mode
Cell conditions	Cell gas		He	NH_3 (10% NH_3 in He)
	Cell gas flow rate	mL/min	8.0	6.5
	Octopole bias	V	-18	-18
	KED	V	4	-10
	Cell exit	V	-100	-70
	Deflect	V	-3	-12
	Plate	V	-70	-60
Plasma conditions	RF	W	1600	
	SD	mm	12.0	
	CRGS	L/min	0.70	
	MUGS		0.20	
	Opt gas flow rate		0.20	
Ion lens	Extract 1	V	-60	
	Extract 2	V	-10	

Results and discussion

He collision mode

The He cell gas flow rate was optimized for the lowest BEC of Cu in a 500 ppm Ti solution. As the BEC for ^{63}Cu was lower than the BEC for ^{65}Cu due to the higher abundance of the 63 isotope, and the more significant interference from TiO$^+$ at *m/z* 65, Cu was determined on-mass at *m/z* 63. In MS/MS mode, this is achieved by the acquisition conditions: Q1 = 63; Q2 = 63 (63, 63).

Two solutions were analyzed: 500 ppm Ti solution and 500 ppm Ti + 1 ppb Cu spike. Figure 1 (left) shows the signal at *m/z* 63 obtained from the analysis of the two solutions, plotted as a function of He flow rate. The BEC calculated from these signals is also given in the figure. It shows that the lowest Cu BEC in He mode was 46 ppt, achieved at a flow rate of 8.0 mL/min He.

NH_3 reaction cell mode

Cu$^+$ reacts efficiently with NH_3 to form NH_3 cluster ions with the general form $Cu(NH_3)_n^+$. TiO$^+$ does not follow the same reaction pathway as Cu$^+$, so the Cu product ion can be measured free from Ti overlap. Based on a preliminary study, one of the intense product ions, $Cu(NH_3)_2^+$, was selected to measure Cu separated from the original TiO$^+$ interference. A mass pair of Q1 = 63, Q2 = 97 was used with NH_3 as the reaction gas. Figure 1 (right) shows the result. A BEC of 11 ppt for Cu in 500 ppm Ti solution was achieved in NH_3 mode (10% NH_3/He mixed gas), at a flow rate of 6.5 mL/min NH_3.

Conclusions

Table 2 summarizes the analytical performance achieved by the 8800 ICP-QQQ operating in MS/MS mode with He collision and NH_3 reaction gas. As can be seen, NH_3 reaction mode is more effective than He collision mode for the removal of the TiO$^+$ interference on Cu. The BEC obtained for Cu in a Ti matrix by NH_3 reaction mode is four times lower than He mode, with seven times higher sensitivity.

Table 2. Summary of Cu measurement in Ti matrix

	Flow rate (mL/min)	BEC (ppt) of Cu in 500 ppm Ti	Sensitivity (cps/ppb)
He collision mode	8.0	45.5	810
NH_3 reaction mode	6.5	10.9	5900

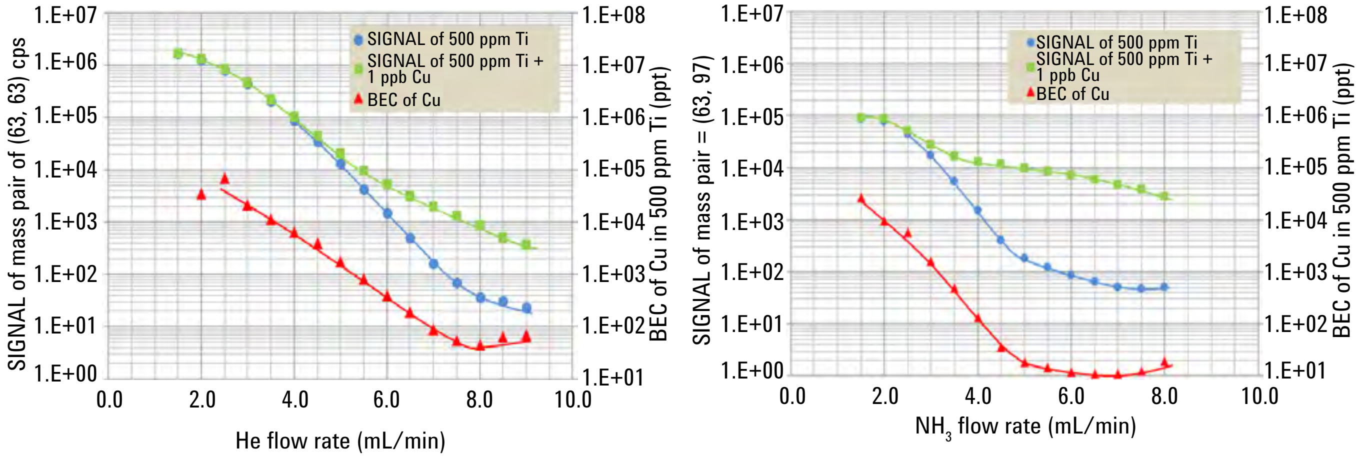

Figure 1. (Left) Cu signal (mass pair 63, 63) vs. He cell gas flow rate, for 500 ppm Ti matrix unspiked and with 1 ppb Cu spike, and calculated BEC.
(Right) Cu signal (mass pair 63, 97) vs NH_3 cell gas flow rate, for 500 ppm Ti matrix unspiked and with 1 ppb Cu spike, and calculated BEC.

Removal of MH^+ Interferences in Refined REE Material Analysis

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Keywords

Rare Earth Elements, REE, geochemistry, mining, material science, lanthanum, barium, cerium, method of standard additions, MSA, oxygen mass-shift

Introduction

The measurement of Rare Earth Elements (REEs) is of great importance in geochemistry, mining and material science. Manufacturers of high purity REE materials need to quantify metal impurities, including trace levels of the other REEs, in the refined, single element REE matrix. ICP-MS is the technique of choice for the measurement of REEs, but most of the REE isotopes suffer from interference by polyatomic species (predominantly hydride ions, MH^+ and oxide ions, MO^+) derived from other, lower-mass REE elements. While MH^+ interferences are lower in intensity than MO^+ interferences, they present a more challenging problem for REEs that have no isotope free from interference. For example $^{139}La^+$ is interfered by $^{138}BaH^+$ and $^{140}Ce^+$ by $^{139}LaH^+$. These interferences are too close in mass to be resolved by high-resolution (HR-)ICP-MS [1]. In this paper, we describe the removal of the MH^+ interferences using an Agilent 8800 ICP-QQQ in MS/MS mass-shift mode, with oxygen as the reaction gas.

Experimental

Instrumentation: Agilent 8800 #100. The standard glass nebulizer was replaced with a C-flow nebulizer (G3285-80000) for optimal washout between the high matrix samples.

Plasma conditions: Preset plasma/General purpose.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -180 V.

CRC conditions: O_2 gas at 0.3 mL/min, Octopole bias = -5 V, KED = -5 V.

Acquisition parameters: MS/MS mode with O_2 mass-shift method.

Figure 1 illustrates the mechanism of MS/MS O_2 mass-shift mode used for measuring Ce in a La matrix sample. The major isotope of Ce at *m/z* 140 suffers an interference from $^{139}LaH^+$. Q1 is set to *m/z* 140, allowing only the analyte ion $^{140}Ce^+$ and any other ions at *m/z* 140 to pass through to the cell. All other ions not at *m/z* 140 are rejected. In the cell, Ce reacts with oxygen to form CeO^+ at *m/z* 156. Q2 is set to *m/z* 156, allowing CeO^+ to pass to the detector. Since $^{139}LaH^+$ does not react with O_2 to form $^{139}LaOH^+$, it remains as LaH^+ at *m/z* 140 and is rejected by Q2. The same principle is used for the separation of $^{139}La^+$ from $^{138}BaH^+$ in a Ba matrix.

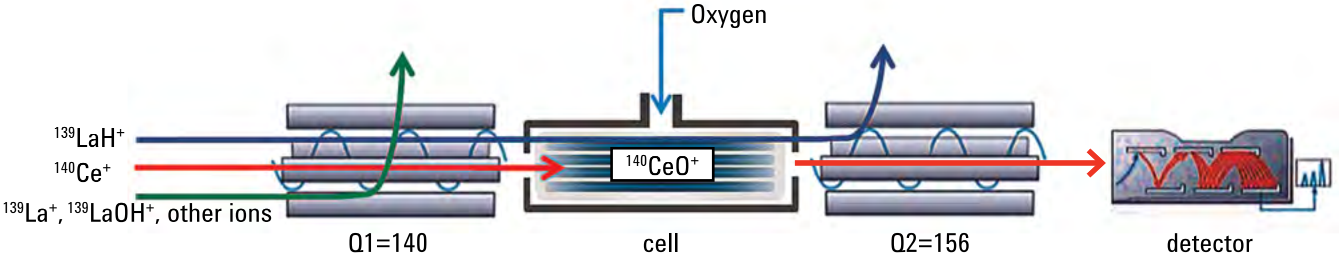

Figure 1. MS/MS mass-shift method with O_2 reaction gas; used for the measurement of Ce, as CeO at *m/z* 156, in a La matrix.

Results and discussion

Using the Method of Standard Addition (MSA), the BECs and DLs of La in a matrix of 50 ppm Ba, and Ce in a matrix of 50 ppm La were determined. Data was acquired using MS/MS mode with O_2 mass-shift, and also using Single Quad (SQ) mode with O_2 reaction gas to emulate conventional quadrupole ICP-MS (ICP-QMS) for comparison.

As shown in Figures 2A and 2B, SQ mode with O_2 reaction gas suffers from interferences that prevent the measurement of La in the Ba matrix and Ce in the La matrix, respectively. In contrast, the calibration plots shown in Figures 2C and 2D demonstrate that MS/MS mode with O_2 mass-shift can successfully remove the matrix overlaps to permit the trace quantitation of La in a Ba matrix and Ce in a La matrix. The BECs and DLs achieved were 8.5 ppt and 2.5 ppt respectively for La in a 50 ppm Ba solution, and 10.6 ppt and 0.8 ppt respectively for Ce in a 50 ppm La solution.

Investigation of unexpected product ion observed at *m/z* 156 in the 50 ppm La matrix

The background signals that contributed to the poor result obtained for Ce in the La matrix using SQ mode with O_2 reaction gas (Figure 2B) were investigated by carrying out a precursor ion scan for product ion mass 156. The precursor ion scan capability of the 8800 ICP-QQQ provides a uniquely powerful approach to identifying the source of potential polyatomic and reaction product interferences. Oxygen cell gas was introduced into the cell and a precursor ion spectrum was obtained by scanning Q1 from 2 to 260 amu (Figure 3) with Q2 fixed at mass 156. From the spectrum, we can identify which precursor ions react with O_2 to produce product ions at mass 156, overlapping $^{140}CeO^+$ in SQ mode.

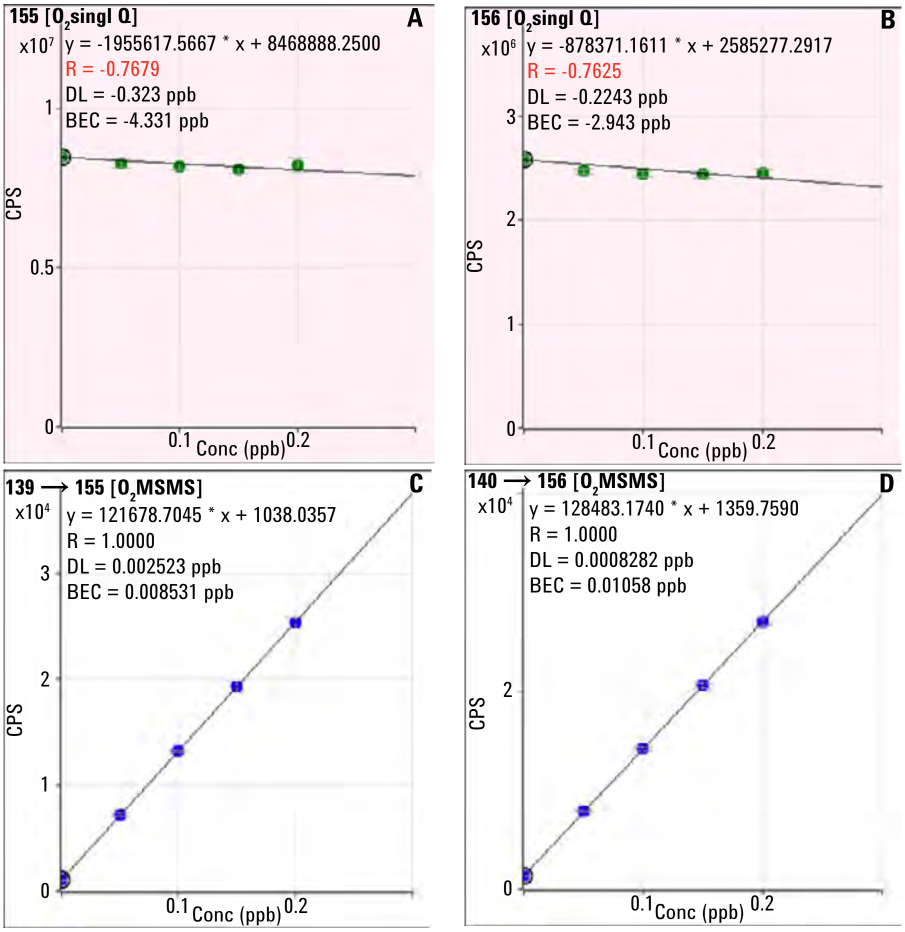

Figure 2. Top: Calibration plots up to 0.2 ppb for La in 50 ppm Ba matrix (A) and Ce in 50 ppm La matrix (B), acquired in SQ mode with oxygen reaction gas (emulating conventional quadrupole ICP-MS). Bottom: Calibration plots up to 0.2 ppb for La in 50 ppm Ba matrix (C) and Ce in 50 ppm La matrix (D) acquired in MS/MS mode with oxygen mass-shift.

Figure 3 shows the precursor ion scan spectrum for product ion mass 156 for the 50 ppm La matrix, with intense peaks at *m/z* 139 ($^{139}La^+$) and 156 ($^{139}La^{16}OH^+$). In SQ mode, as with conventional ICP-QMS, these ions all enter the cell, and with Q2 set to 156 amu, the $^{139}La^{16}OH^+$ polyatomic ions contribute to the signal measured at *m/z* 156 (^{140}Ce measured as analyte product ion $^{140}CeO^+$). These unwanted precursor ions cannot be rejected by a CRC operating as a bandpass filter in ICP-QMS, as they are too close in mass to the target analyte precursor ion. Only by using MS/MS mode on the 8800 ICP-QQQ, where Q1 operates as a unit mass filter, can non-target masses (like $^{139}La^{16}OH^+$ in this example) be prevented from entering the cell.

Reference

1. Sabine Becker and Hans Joachim Dietze, Journal of Analytical Atomic Spectrometry, 1997, vol.12, p881.

More information

Removal of hydride ion interferences (MH⁺) on Rare Earth Elements using the Agilent 8800 Triple Quadrupole ICP-MS, Agilent application note, 5991-1481EN.

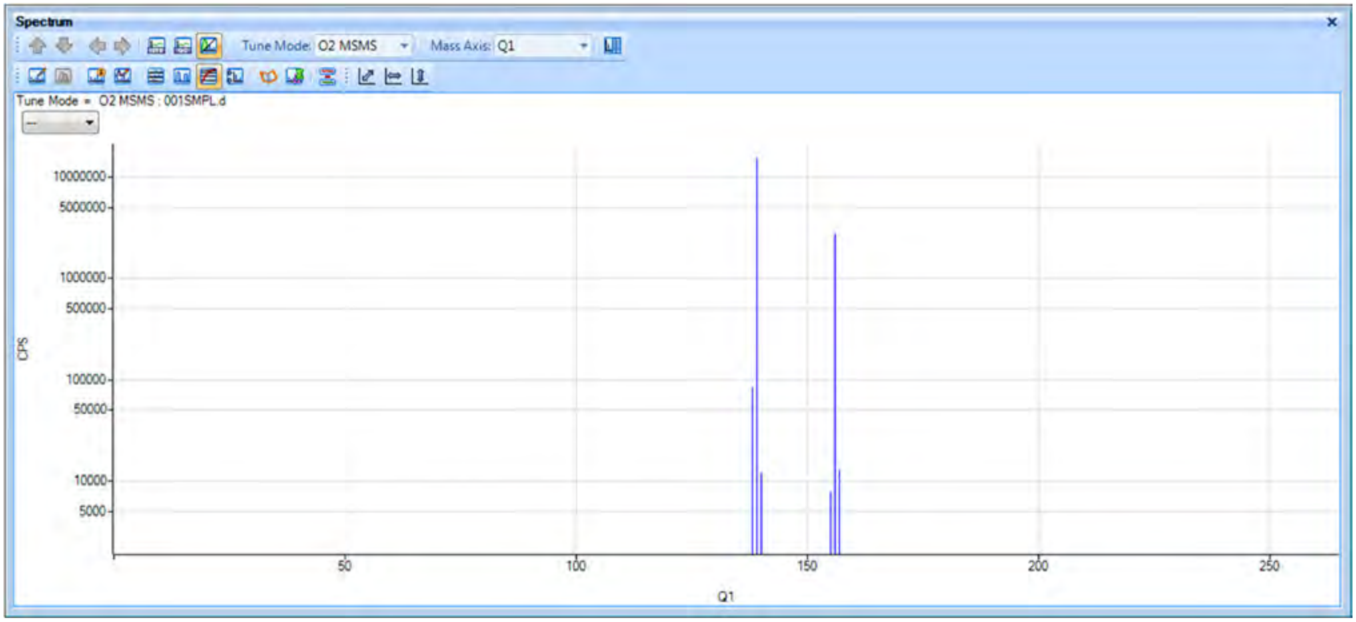
Tune Mode: O2 MSMS
Mass Axis: Q1
Tune Mode = O2 MSMS : 001SMPL.d

Figure 3. Precursor ion scan from 2-260 amu for product ion mass 156, in a 50 ppm La matrix. Six peaks are seen at *m/z* = 138, 139, 140, 155, 156 and 157, with the intense peaks at *m/z* 139 and *m/z* 156 being due to $^{139}La^+$ and $^{139}La^{16}O^1H^+$ respectively.

Direct Analysis of Trace REEs in High Purity Nd_2O_3

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Keywords

Rare earth elements (REE), high purity metals, neodymium, neodymium (III) oxide, oxygen mass-shift, ammonia on-mass, ammonia mass-shift, geochemistry, mining, materials science

Introduction

Advanced technology products containing Rare Earth Elements (REEs) are increasing at a rapid rate. However, the presence of other REEs as contaminants in a purified single-element REE material may affect the functionality of the final product, so impurities in the REE oxide raw material must be carefully controlled.

The measurement of mid- and high-mass REEs in a low-mass REE matrix is challenging for ICP-MS because REEs have high metal-oxide (M-O) bond strengths, and the oxide ions of the low mass REEs overlap the preferred isotopes of the mid-mass and high-mass REEs. For example, in the analysis of trace REEs in high purity Nd_2O_3, $^{145}Nd^{16}OH_2^+$ and $^{146}Nd^{16}OH^+$ overlap the preferred isotope of dysprosium ($^{163}Dy^+$), $^{143}Nd^{16}O^+$ overlaps the only isotope of terbium ($^{159}Tb^+$) and $^{148}Nd^{16}OH^+$ overlaps the sole isotope of holmium ($^{165}Ho^+$). While separation of the trace REEs from the REE matrix can be performed using a chelating resin, this technique is time-consuming and needs to be customized to the particular analyte and matrix under investigation. Clearly there is a requirement for a method capable of the direct analysis of trace REEs in a variety of high purity REE matrices.

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/HMI-L.

Acquisition parameters:
Five operational modes were evaluated:

- No gas
- Helium mode, 5 mL/min
- O_2 mass-shift, 0.3 mL/min
- NH_3 on-mass, 8 mL/min (NH_3 as 10% NH_3 in He)
- NH_3 mass-shift, 3 mL/min, (NH_3 as 10% NH_3 in He).

Sample and sample prep: High purity Nd_2O_3 (99.999%, purchased from the Baotou Research Institute of Rare Earths, China) was dissolved gently in semiconductor grade HNO_3, and diluted to 500 ppm as Nd_2O_3.

Results and discussion

Thirteen trace REEs were measured in the Nd_2O_3 sample using the five different cell modes, and the results are summarized in Table 1. As expected, the BEC of low- and mid-mass REEs, such as La, Ce, Pr, Sm, Eu and Gd (Pr and Sm were present as impurities) were comparable in all modes, as these elements are free from interferences due to Nd. In contrast, the BECs for high-mass REEs in He mode were lower in He mode than in no gas mode, suggesting that high mass REEs suffered interferences from Nd-derived polyatomic ions.

Table 1. BECs of 13 REEs in 500 ppm Nd_2O_3. All units ug/kg (ppb)

Element	Isotope	No gas	He	O_2 mass shift	NH_3 on mass	NH_3 mass shift
La	139	0.143	0.127	0.143	-	-
Ce	140	0.018	0.012	0.011	-	-
Pr	141	1.376	1.202	1.056	-	-
Sm	152	1.061	0.950	0.999	-	-
Eu	153	0.032	0.026	0.028	-	-
Gd	155	0.035	0.046	0.033	-	-
Tb	159	442.6	74.6	1.258	-	0.022
Dy	163	250.3	196	1.161	0.040	-
Ho	165	20.43	16.2	0.101	0.004	-
Er	170	0.065	0.020	0.013	-	-
Tm	169	0.084	0.031	0.003	-	-
Yb	174	0.251	0.120	0.058	-	-
Lu	175	0.014	0.006	0.004	-	-

O_2 mass-shift mode

All 13 REEs react with O_2 efficiently to form REE-oxide ions, as shown below.

$$REE^+ + O_2 \rightarrow REE\text{-}O^+ + O$$

The MS/MS capability of the 8800 ICP-QQQ enables the removal of spectral interferences on each element using "mass-shift". For example in O_2 mass-shift mode, all 13 REEs can be detected as REE-O^+ ions at 16 amu higher than the original elemental mass (M+16). From Table 1, it can be seen that O_2 reaction mode with mass-shift further reduced the BEC for Tb, Dy, Ho, Er, Tm, Yb, and Lu, compared to He mode.

While the improvement in O_2 mass-shift mode is significant for Tb, Dy and Ho that suffer intense interference from NdO^+, the BECs of the other high-mass REEs such as Er, Tm, Yb and Lu were also improved in this mode, indicating that these elements also suffer interferences from Nd-based polyatomic ions: $^{150}NdOH_3^+$ interferes with $^{169}Tm^+$, $^{142}NdN_2^+$ (or $^{142}NdCO^+$) and $^{144}NdCN^+$ with $^{170}Er^+$, $^{142}NdO_2^+$ with $^{174}Yb^+$, $^{143}NdO_2^+$ and $^{144}NdONH^+$ (or $^{144}NdC_2H^+$) with $^{175}Lu^+$. The contribution of the above mentioned interferences on Er, Tm, Yb and Lu are not overly significant. However, O_2 mass-shift mode was shown to be an effective approach for the removal of all polyatomic ion interferences, typically leading to a 5-10x lower BEC compared to no gas mode.

NH_3 on-mass mode for Dy and Ho

A previous study showed that NH_3 cell gas reacts with many of the polyatomic ions that interfere with the REEs. However, NH_3 also reacts quickly with some of the REE ions, leading to reduced sensitivity of < 1 cps/ppt for La, Ce, Nd, Sm, Gd, Tb and Lu. NH_3 on-mass mode is valuable for the determination of a limited number of REEs; Pr, Eu, Dy, Ho, Er, Tm and Yb [1]. The results in Table 1 show that NH_3 on-mass mode gave excellent results for Dy and Ho in the Nd_2O_3 matrix, with an improvement in BECs of 20x compared to O_2 mass-shift mode.

NH_3 mass-shift mode for Tb

For the REEs that react efficiently with NH_3 (La, Ce, Nd, Sm, Gd, Tb and Lu), NH_3 mass-shift mode can be used. In this study, NH_3 mass-shift mode was investigated for the determination of Tb, and the reaction product ion $TbNH^+$ (*m/z* 174) was found to give the lowest BEC. A BEC of 22 ppt for Tb in a 500 ppm Nd_2O_3 solution was achieved, which is 50x lower than the result achieved in O_2 mass-shift mode, indicating the effective removal of the NdO^+ overlap.

Conclusions

The Agilent 8800 ICP-QQQ with MS/MS capability was used to successfully measure 13 REE impurities in a high-purity Nd_2O_3 sample solution. Tandem MS with MS/MS mode is essential for accurate reaction mode analysis in a complex matrix. On conventional quadrupole ICP-MS, there is no additional quadrupole (Q1) to select which ions can enter the cell. As a result, all ions enter the cell so, when a reactive cell gas is used, a complex and variable population of reaction product ions is created, depending on the sample matrix and other analytes. With ICP-QQQ, the first quadrupole selects only the target mass to pass into the cell, so the reaction chemistry is controlled and consistent. With the combination of HMI and MS/MS reaction cell mode, the 8800 ICP-QQQ provided effective removal of the polyatomic interferences from the Nd matrix.

Reference

1. Naoki Sugiyama and Glenn Woods, Direct measurement of trace rare earth elements (REEs) in high-purity REE oxide using the Agilent 8800 Triple Quadrupole ICP-MS with MS/MS mode, Agilent publication, 2012, 5991-0892EN.

More information

Application note: Routine determination of trace rare earth elements in high purity Nd_2O_3 using the Agilent 8800 ICP-QQQ, 5991-5400EN.

Determination of Trace Level Impurities of 49 Elements in High Purity Copper

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Keywords

high purity metal, high purity copper, material science, mass-shift, m-lens, alkali elements

Introduction

Metals such as Cu, Al, Ta, W, and Hf are widely used in semiconductor devices. High purity metals are required to ensure reliable performance and a high production-yield. ICP-MS is often used for the quality-control of these metals. The application is not easy though due to the requirement for ultralow level impurity measurements in relatively high-matrix metal sample digests. The ultra-trace measurement of alkali elements in the presence of the high matrix is especially challenging. Cool plasma is accepted in the semiconductor industry as a reliable technique to remove argon-based interferences such as Ar^+ and ArO^+. The method enables the low-level analysis of Ca and Fe by ICP-MS. It can also be applied to the analysis of the alkali elements, providing lower background equivalent concentrations (BECs) than hot plasma conditions. However, the cooler, lower energy plasma has a poorer matrix tolerance, making it unsuitable for the analysis of high-matrix metal sample digests.

Experimental

Instrumentation: Agilent 8900 Semiconductor configuration ICP-QQQ fitted with an optional m-lens.

Tuning and method: Tuning parameters are summarized in Table 1.

- Internal standards (ISTD) Be, Sc and In were added to all solutions before analysis.
- Hot plasma conditions were optimized to give a 1% CeO^+/Ce^+ ratio.
- A single cell gas mode, O_2 = 0.2 (mL/min) + H_2 = 7.0 (mL/min), was used for all 49 analytes + 3 ISTD elements.
- Mass-shift mode was used for the analysis of P, S, As, Zr, Nb, Mo, Hf, Ta, W, Th, and U. On-mass mode was used for all other elements.

Sample preparation

All samples and standards were prepared in 5% nitric acid (HNO_3) using TAMAPURE AA-100 semiconductor grade HNO_3 (TAMA Chemicals Co. Ltd, Kanagawa, Japan).

A 0.1% Cu sample was prepared as follows. A piece of 9N high purity copper was cleaned in diluted HNO_3 then rinsed with ultrapure water (UPW). It was weighed (about 0.05 g) and dissolved in 5 mL of 50% HNO_3 (UPW : HNO_3 = 50 : 50). The solution was then brought up to 50 mL with UPW.

Table 1. ICP-QQQ tuning conditions

Parameter	Unit	Value
RF power	W	1550
Carrier gas flow rate	L/min	0.70
Makeup gas flow rate	L/min	0.46
Sampling depth	mm	8.0
Extract 1	V	0.0
Extract 2	V	-70.0
Omega	V	8.0
Omega bias	V	-60.0
Cell gas and flow rate	mL/min	O_2 = 0.2 and H_2 = 7.0
Octopole bias	V	-10.0
KED	V	-10.0
Axial Acceleration	V	2.0

Results and discussion

BECs in 5% HNO_3

Background equivalent concentrations (BECs) for each element in 5% HNO_3 were obtained from the calibration plots. The results are summarized in Figure 1. The plot shows that parts per trillion (ppt) level BECs were achieved for the alkali elements, Li, Na, and K, using hot plasma conditions. In addition, impressive BECs were achieved for the most challenging elements: S (84 ppt) and Si (231 ppt).

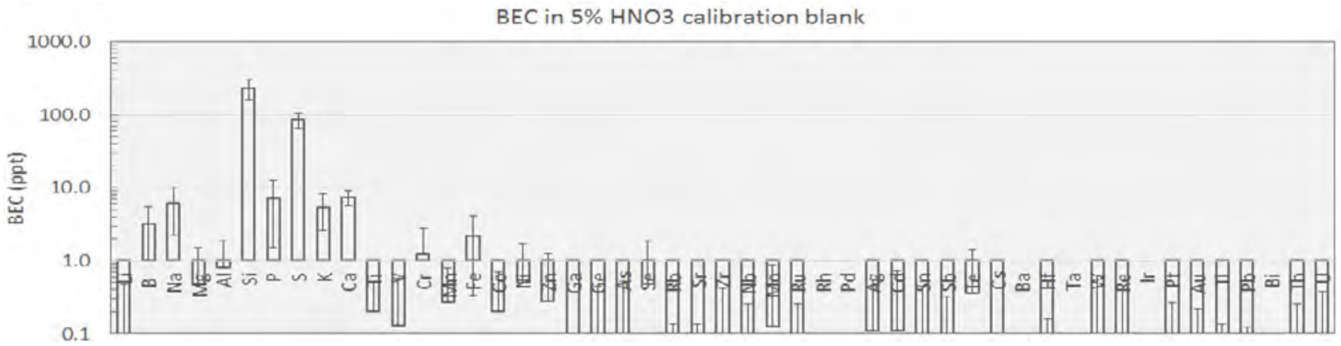

Figure 1. BECs of 49 elements in 5% HNO_3 blank. Error bar = 3σ DL.

Measured concentrations in 0.1% high purity copper
The method was used to determine the concentration of 49 elements in the 0.1 % high purity copper solution. The results are summarized in Figure 2. The observed matrix suppression for low mass elements like Li and B was 30%, and 10% or less for mid and high mass elements. Except for Si, S and Te, all elements were present at < 10 ppt concentration level.
The O_2+H_2 reaction cell gas removed significant spectral interferences caused by $ArCu^+$ on Ru^+, Rh^+ and Pd^+, allowing the determination of these elements at ultralow levels.

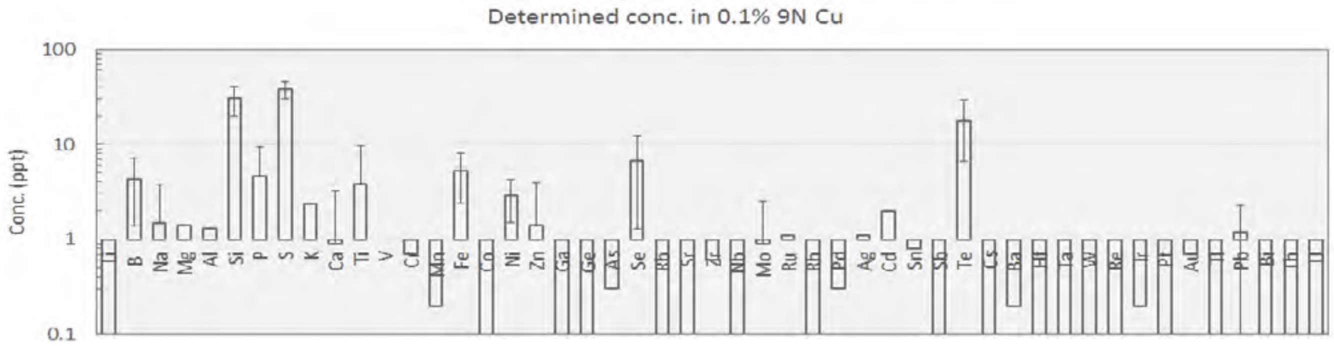

Figure 2. Measured concentrations of 49 elements in 0.1% high purity copper

Conclusions

Using a single cell gas with MS/MS on-mass and mass-shift modes of the ICP-QQQ and hot plasma conditions, ppt level BECs were achieved for the alkali elements. Low-level BECs were also obtained for challenging elements, sulfur and silicon. Overall, 49 elements were determined at ultralow levels in 0.1% high purity Cu sample using a simple, single tune method.

Direct Determination of Challenging Trace Rare Earth Elements in High Purity Lanthanide REE Oxides

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Keywords

Rare Earth Elements, REE, rare earth oxides, REO, oxygen mass-shift, ammonia on-mass, ammonia mass-shift

Introduction

ICP-MS is widely used for trace impurity analysis of high purity rare earth element (REE) oxide materials. But the analysis of trace REEs in high purity REE oxide materials remains challenging. Matrix-based polyatomic ions such as $REEO^+$, $REEOH^+$, and $REEH^+$ cause severe spectral interferences on some REE elements. Trace REE analytes can be separated from the REE matrix using a chelating resin, but this technique is time-consuming, and customization is needed per the analyte and matrix element.

In this study, trace REEs in lanthanide oxide materials were determined using an Agilent 8900 ICP-QQQ with O_2 and NH_3 reaction cell gases. Since the analysis of La_2O_3, Tm_2O_3 and Lu_2O_3 is relatively interference free, these matrices weren't included in the study.

Experimental

Instrumentation: An Agilent 8900 Advanced Applications configuration ICP-QQQ was used without any modification. For the analysis of 500 ppm REE matrix samples, 'general-purpose plasma' conditions were selected in the MassHunter software. The preset plasma function automatically sets all plasma-related parameters, simplifying instrument set-up.

Five cell modes were investigated: no gas, helium (He), oxygen (O_2), and ammonia (20% NH_3 in He). Tuning conditions are summarized in Table 1. In NH_3 mass shift mode, a pre-study was done using 'product ion scan' to identify the most abundant NH_3 cluster ion. The masses of the cluster ions used for the analysis are given in Tables 2 and 3, together with the analytical results.

Table 1. Cell gas mode-related tuning parameters

Cell gas mode	No gas	He	O_2 Mass-shift	NH_3 On-mass	NH_3 Mass-shift
Scan Mode	Single Quad		MS/MS		
Octopole bias (V)	-8	-18	-3	-5	-5
Octopole RF (V)	140	180	180	180	180
KED (V)	+5	+4	-7	-7	-7
Axial Acceleration (V)	0	1	1.5	0.5	0.5
He (mL/min)		5		1	1
O_2 (mL/min)			0.45		
NH_3 (mL/min)				4.0 ~ 6.0	1.0 ~ 8.0

Results and discussion

Ten REE oxide materials of the highest-grade purity (5N) including Ce_2O_3, Pr_6O_{11}, Nd_2O_3, Gd_2O_3, Sm_2O_3, Eu_2O_3, Tb_4O_7, Dy_2O_3, Er_2O_3, and Yb_2O_3 were dissolved in semiconductor grade HNO_3 and diluted to 500 ppm (as REE oxide). H_2O_2 was added during the dissolution of Ce_2O_3 and Tb_4O_7. REEs were measured in each matrix solution using the five cell modes specified in Table 1. The results are given in Tables 2 and 3.

As expected, in no gas mode, the BECs for the REEs were relatively high due to spectral interferences. He collision cell mode was able to alleviate some of the interferences, but not all. Previous studies have shown that both O_2 and NH_3 are effective for the removal of polyatomic ions that interfere with the REEs [1, 2]. A drawback of NH_3 mode has been low sensitivity. However, Axial Acceleration of cluster ions in the cell of the 8900 ICP-QQQ increases sensitivity. The results reported in Tables 2 and 3 show that the BECs for all REEs were dramatically improved using a reactive cell gas. The improvement factor data relates to the difference in BEC obtained in reaction mode compared to no gas mode.

Table 2. BECs of REE impurities in 500 ppm Ce, Pr, Nd, and Gd oxide solutions

Sample			Ce_2O_3			PrO	Nd_2O_3			Gd_2O_3		
Analyte			Pr	Gd	Tb	Tb	Tb	Dy	Ho	Tb	Yb	Lu
Isotope			141	160	159	159	159	163	165	159	172	175
Interference			$^{140}CeH^+$	$^{142}Ce^{18}O^+$	$^{142}Ce^{16}OH^+$	$^{141}Pr^{18}O^+$	$^{142}NdOH^+$, $^{143}NdO^+$	$^{145}Nd^{18}O^+$	$^{148}NdOH^+$	$^{158}GdH^+$	$^{156}GdO^+$	$^{159}GdOH^+$
BEC (ppb)	No gas		6.17	3.36	29.2	10.3	721	163	13.4	2.23	3420	75.0
	He		3.79	11.9	0.725	2.50	234	36.6	3.06	2.16	1200	66.4
	O_2		**0.064**	**0.030**	9.76	**0.001**	1.95	0.804	0.070	**0.106**	284	**0.444**
	NH_3	BEC			**0.284**	0.055	**0.039**	**0.255**	**0.021**		**0.030**	7.16
		mass pair			(159/174)	(159/244)	(159/174)	(163/163)	(165/165)		(172/172)	(175/260)
Improvement factor			x100	x100	x100	x10,000	x20,000	x1000	x1000	x20	x100,000	x200

Table 3. BECs of REE impurities in 500 ppm Sm, Eu, Tb, Dy, Er, and Yb oxide solutions

Sample			Sm_2O_3				Eu_2O_3	Tb_4O_7	Dy_2O_3	Er_2O_3	Yb_2O_3
Analyte			Dy	Ho	Er	Tm	Tm	Lu	Ho	Tm	Lu
Isotope			162	165	167	169	169	175	165	169	175
Interference			$^{147}SmO^+$	$^{148}SmOH^+$, $^{149}SmO^+$	$^{150}SmOH^+$	$^{152}SmOH^+$	$^{141}EuO^+$	$^{159}TbO^+$	$^{164}DyH^+$	$^{168}ErH^+$	$^{174}YbH^+$
BEC (ppb)	No gas		0.408	185	44.9	39.0	64.8	3270	2.13	1.26	0.97
	He		0.169	61.9	18.1	13.6	38.20	1670	1.28	1.57	1.38
	O_2		0.083	0.158	0.916	0.240	2.73	26.1	**0.057**	**0.025**	**0.195**
	NH_3	BEC	**0.035**	**0.055**	**0.092**	**0.127**	**0.002**	**0.244**	0.074		
		mass pair	(162/162)	(165/165)	(167/167)	(169/169)	(169/169)	(175/260)	(165/165)		
Improvement factor			x10	x3000	x500	x200	x30,000	x10,000	x50	x50	x5

Conclusions

The Agilent 8900 ICP-QQQ method was used to measure REE impurities in high purity REE oxide materials. REE matrix-based hydride, oxide, and hydroxide polyatomic ion interferences were removed by operating the ICP-QQQ in MS/MS mode with O_2 and NH_3 reaction cell gases. The BECs were improved by one to four orders of magnitude using reactive cell gases compared to no gas mode. The method is suitable for the direct analysis of trace REEs in the presence of high concentration matrix-REEs.

References

1. Direct measurement of trace rare earth elements (REEs) in high-purity REE oxide using the Agilent 8800 Triple Quadrupole ICP-MS with MS/MS mode, Agilent application note, 2012, 5991-0892EN

2. Routine determination of trace rare earth elements in high purity Nd_2O_3 using the Agilent 8800 ICP-QQQ, Agilent application note, 2015, 5991-5400EN

Analysis of 10 nm Gold Nanoparticles using the High Sensitivity of the Agilent 8900 ICP-QQQ

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Michiko Yamanaka, Takayuki Itagaki, and Steve Wilbur, Agilent Technologies

Keywords

nanoparticles, single nanoparticle analysis, TRA, dwell time, gold nanoparticles

Introduction

The measurement of nanoparticles (NPs) is of public and scientific interest. More information is needed to understand the fate of NPs in the environment and the potential toxic effects once absorbed into the body. Gold (Au) NPs have a broad range of uses in medical, industrial, and technology applications. Au is a relatively easy element to measure by ICP-MS, as it is not affected by common spectral interferences. However, the detection of very small particles (<20 nm) remains challenging for ICP-MS, due to the low signal generated from such particles. The Agilent 8900 ICP-QQQ has a low background (<0.2 cps) and sensitivity up to Gcps/ppm, making it suited to small particle detection.

Experimental

Instrumentation: Agilent 8900 Advanced Applications configuration ICP-QQQ with 1-mm i.d. injector torch and standard sample introduction system.

Method: All aspects of method setup and data analysis were carried out using the fully integrated Single Nanoparticle Application Module option for ICP-MS MassHunter. The "Batch at a Glance" data table shown in Figure 1 summarizes the sample results for an entire batch. Detailed graphical results are displayed for each selected sample, allowing results to be viewed and compared, or method settings to be optimized if necessary. Reference [1] gives details of the particle size calculation used in the module.

Tuning conditions: For highest sensitivity, ^{197}Au was measured in single quad mode with no cell gas.

	Sample						197 Au						
		Rjct	Data File	Acq. Date-Time	Type	Sample Name	Nebulization Efficiency	# of Particles	Conc. (particles/l)	BED (nm)	Median Size (nm)	Mean Size (nm)	Ionic
1		☐	001SMPL.d	4/6/2016 1:13:35 PM	Sample	blank	0.066	15	6.4E+5	2.05	6	7	
2		☐	002_RM.d	4/6/2016 1:16:49 PM	RM	8013 50ppt	0.066	498	2.1E+7	4.25	56	56	
3		☐	003SMPL.d	4/6/2016 1:19:06 PM	Sample	8013 50ppt	0.066	449	1.9E+7	4.08	56	57	
4		☐	005SMPL.d	4/6/2016 1:24:37 PM	Sample	8011 0.25ppt	0.066	721	3.1E+7	2.93	9	9	
5		☐	006SMPL.d	4/6/2016 1:27:16 PM	Sample	8011 0.25ppt	0.066	611	2.6E+7	2.94	9	9	
6		☐	007SMPL.d	4/6/2016 1:29:44 PM	Sample	8011 0.25ppt	0.066	689	2.9E+7	3.04	9	9	
7		☐	011SMPL.d	4/6/2016 2:16:13 PM	Sample	8012 5ppt	0.066	493	2.1E+7	2.29	27	27	
8		☐	012SMPL.d	4/6/2016 2:19:52 PM	Sample	8012 5ppt	0.066	507	2.2E+7	2.26	27	27	

Peak Response Calculation
☑ Peak Integration Mode
Particle Size Distribution
☐ Analyze within Specified Particle Detection Range
Particle Detection Threshold: 736866 cps
Instrument Setting
Sample Inlet Flow: 0.355 ml/min

Figure 1. Data analysis view of the Single Nanoparticle Application software module

Plasma parameters: RF power =1550 W, sampling depth = 7.0 mm, and carrier gas flow rate = 0.78 L/min.

Data acquisition: TRA analysis with a dwell time of 0.1 ms. Data acquisition time was 60 s.

Reference materials and sample preparation:
Three Au NP reference materials (RMs) were used in the study: NIST 8011 with a nominal diameter of 10 nm (8.9 ± 0.1 nm determined by Transmission Electron Microscopy (TEM)); NIST 8012 with a nominal diameter of 30 nm (27.6 ± 2.1 nm determined by TEM); and NIST 8013 with a nominal diameter of 60 nm (56.0 ± 0.5 nm determined by TEM). All final solutions containing Au nanoparticles or ionic Au standards were prepared in 0.01% L-cysteine for stabilization.

Results and discussion

Analysis of Au NP samples

Solutions containing gold NPs with particle sizes of 10 nm, 30 nm, and 60 nm were prepared at concentrations of 0.25 ng/L, 5 ng/L and 50 ng/L, respectively. The solutions were measured using fast TRA acquisition. Figure 2 shows the measured raw signal event frequency and the calculated size distribution for a solution containing 10 nm particles. From the results, the practical detection limit of the particle diameter was estimated to be around 30,000 cps (equivalent to ~6.5 nm) and the background equivalent diameter (BED) was 3 nm.

The 30 nm and 60 nm particles were also measured, and the results are summarized in Table 1. The results for the median, mode, and mean particle sizes for all three standards agreed well with the reference sizes obtained by TEM.

Conclusions

The low background and high sensitivity of the Agilent 8900 ICP-QQQ make it suitable for single particle analysis of solutions containing the smallest-sized nanoparticles. The size and composition of gold NP solutions were characterized from 10 nm up to 60 nm, with good accuracy. The practical detection limit of the particle diameter was estimated to be 6.5 nm and the BED was 3 nm.

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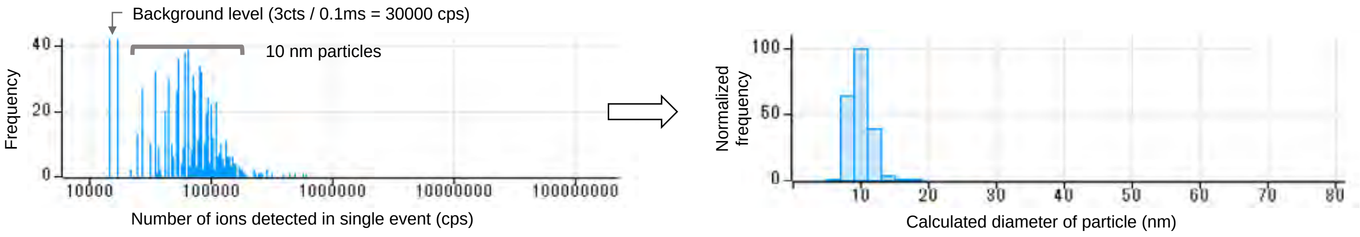

Figure 2. Raw signal event frequency (left) and calculated size distribution of 10 nm particles (right)

Table 1. Measured particle size for Au NPs in three NIST RMs

Nominal size (nm)	Particle size (nm) by TEM		Measured partcle size (n = 10)					
			Median		Mode		Mean	
			size (nm)	RSD (%)	size (nm)	RSD (%)	size (nm)	RSD (%)
10	8.9	± 0.1	9.0	3.3	10	0.0	9.2	3.3
30	27.6	± 2.1	26.9	0.3	28	0.0	27.0	0.3
60	56.0	± 0.5	56.1	0.3	56	1.8	57.2	0.4

High Sensitivity Analysis of SiO_2 Nanoparticles using the Agilent 8900 ICP-QQQ

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Keywords

nanoparticles, single nanoparticle analysis, TRA, dwell time, silicon dioxide NPs

Introduction

ICP-MS is a well-established technique for measuring the elemental content of materials. With the recent development of Single Particle ICP-MS (spICP-MS) acquisition mode, ICP-MS can also be used to characterize the nanoparticle (NP) content of a sample.

Silicon dioxide (SiO_2) NPs are used for many applications including paints, coatings, adhesives, food additives, polishing micro-electronic devices etc. Given their wide spread use, there is a clear requirement for SiO_2 NPs to be monitored. Si measurement by ICP-MS is not easy since the major isotope of Si, ^{28}Si (92.23% abundance), is interfered by the background polyatomic ions CO^+ and N_2^+. The interferences can be addressed using reaction chemistry in the collision/reaction cell of an ICP-MS. However, for controlled and consistent reaction processes, a tandem mass spectrometer instrument such as the Agilent 8900 Triple Quadrupole ICP-MS (ICP-QQQ) is required.

Experimental

Instrumentation: Agilent 8900 Advanced Applications configuration ICP-QQQ fitted with a 1 mm i.d. injector torch and standard sample introduction system.

Method: All aspects of the method setup and data analysis were carried out using the fully integrated Single Nanoparticle Application Module option of the ICP-MS MassHunter software. The "Batch at a Glance" data table summarizes the sample results for an entire batch. The detailed graphical results are displayed for each selected sample, allowing results to be viewed and compared, or method settings to be optimized if necessary. References [1 and 2] provide details of the particle size calculation used in the module.

Tuning conditions: H_2 on-mass mode was used to remove potential interferences by CO^+ and N_2^+ on $^{28}Si^+$. H_2 cell gas flow = 3 mL/min.

Plasma parameters: RF power =1550 W, sampling depth of 7.0 mm and carrier gas flow rate of 0.76 L/min.

Data acquisition: TRA analysis with dwell time of 0.1 ms.

Reference materials and sample preparation: SiO_2 NP reference materials (RMs) with nominal diameters of 50 nm, 60 nm, 100 nm, and 200 nm were bought from nanoComposix (San Diego, USA). They were diluted to a particle concentration of between 40 and 1000 ng/L with de-ionized (DI) water, and sonicated for 5 min to ensure sample homogeneity. A Si ionic standard of 5 µg/L was prepared with DI water and used to measure the elemental response factor.

Results and discussion

Analysis of SiO_2 NPs in UPW

The frequency distribution plots of the signals obtained from 50 nm SiO_2 NPs are shown in Figure 1. The particle signals were clearly distinguished from the background (dissolved, ionic component). From the results, we can estimate that the practical detection limit for the particle diameter was below 50 nm and the background equivalent diameter (BED) was 22 nm.

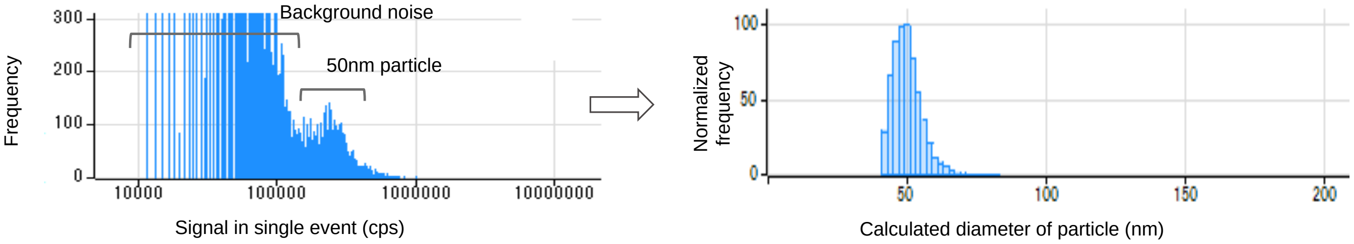

Figure 1. Raw signal event frequency (left) and calculated size distribution of 50 nm particles (right)

The results for the size analysis of different SiO_2 NP solutions are summarized in Table 1. The results for median, mode, and mean particle sizes agreed well with the reference sizes obtained by TEM.

Table 1. Measured particle size for SiO_2 NPs in four RMs

Nominal size (nm)	Particle size (nm) by TEM	Prepared particle concentration (ng/L)	Measured partcle size (n = 10)		
			Median size (nm)	Mode size (nm)	Mean size (nm)
50	46.3 ± 3.1	40	49	50	50
60	57.8 ± 3.5	40	61	62	62
100	97.0 ± 4.8	100	99	100	102
200	198.5 ± 10	1000	200	204	200

Analysis of SiO_2 NPs in a high-level carbon matrix

Real samples such as biological samples, food matrices, pharmaceutical ingredients, and organic solvents contain carbon matrices that give rise to a $^{12}C^{16}O^+$ polyatomic ion interference on $^{28}Si^+$. Figure 2 shows the particle size distribution for a mixed solution of the 100 and 200 nm SiO_2 measured in a sample containing 1% ethanol. Despite the high concentration of carbon, the size distribution for each group of particle sizes was consistent with the results obtained by TEM. The 8900 ICP-QQQ in MS/MS mode with hydrogen cell gas was able to eliminate the $^{12}C^{16}O^+$ interference effectively.

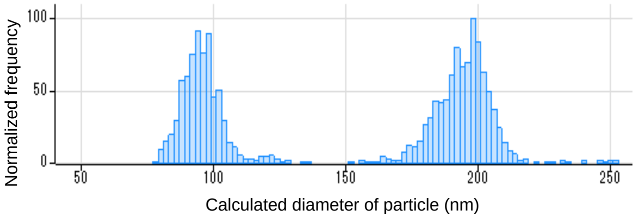

Figure 2. Size distribution result of 100 and 200 nm SiO_2 NPs in 1% ethanol

Conclusions

SiO_2 NPs can be determined and characterized successfully using the Agilent 8900 ICP-QQQ operating in MS/MS mode with H_2 cell gas. Even in the presence of a high level of carbon matrix. The Single Nanoparticle Application Module for ICP-MS MassHunter was used to calculate the particle sizes. The spICP-QQQ method provides fast analysis times, excellent detection limits for particle size and concentration, and accurate results for SiO_2 particles less than 100 nm.

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More information

High sensitivity analysis of SiO_2 nanoparticles using the Agilent 8900 ICP-QQQ in MS/MS mode, Agilent application note, 2016, 5991-6596EN.

Foods

Accurate and Sensitive Analysis of Arsenic and Selenium in Foods using ICP-QQQ to Remove Doubly-Charged REE Interferences

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Keywords

arsenic, selenium, rare earth elements, environmental, agricultural, human health, NIST 1547 Peach Leaves, NIST 1515 Apple Leaves, oxygen mass-shift

Introduction

Concern about the impact on public health from potentially toxic elements and compounds present in everyday foodstuffs has led to new legislative guidance [1, 2]. The inorganic forms of arsenic (As) are known to be toxic and carcinogenic to humans, and food and drinks are a potential source of exposure [3]. Selenium (Se) is an essential micro-nutrient that can be deficient in the diet as Se-poor soils yield Se-poor food crops. Accurate quantification of Se in food is necessary to assess nutrient status.

As and Se can be difficult to quantify accurately at trace levels by conventional quadrupole ICP-MS (ICP-QMS), as all the analytically useful isotopes can suffer from multiple spectral interferences, as shown in Table 1. Potential interferences on As and Se include the doubly-charged ions of the Rare Earth Elements (REE^{++}) and matrix and plasma-born polyatomic ions. The quadrupole mass spectrometer separates ions based on mass to charge ratio (m/z), so the REE^{++} ions appear at half their true mass, overlapping the singly-charged analyte ions of As and Se. Typically the REE content in food samples is low, but crops grown in REE-enriched soils may take up higher concentrations of these elements [4, 5] leading to false positive results for As and Se. In this study, we evaluated the capability of the Agilent 8800 ICP-QQQ in MS/MS reaction mode to remove interferences, including REE^{++}, on As and Se.

Table 1. Spectroscopic interferences on As and Se isotopes

As and Se isotope			Interference		
Element	Mass	Abundance %	Doubly charged	Matrix	Dimer
As	75	100	$^{150}Sm^{++}$, $^{150}Nd^{++}$	$^{40}Ar^{37}Cl^+$, $^{40}Ca^{37}Cl^+$	
Se	77	7.63	$^{154}Sm^{++}$, $^{154}Gd^{++}$	$^{40}Ar^{37}Cl^+$, $^{40}Ca^{37}Cl^+$	
	78	23.77	$^{156}Gd^{++}$, $^{156}Dy^{++}$	$^{41}K^{37}Cl^+$	$^{38}Ar^{40}Ar^+$, $^{39}K^{39}K^+$
	80	49.61	$^{160}Gd^{++}$, $^{160}Dy^{++}$,	$^{32}S_2{}^{16}O^+$, $^{32}S^{16}O_3{}^+$, $^{40}Ca^{40}Ar^+$, $^{45}Sc^{35}Cl^+$	$^{40}Ar^{40}Ar^+$, $^{40}Ca^{40}Ca^+$
	82	8.73	$^{164}Dy^{++}$, $^{164}Er^{++}$	$^{45}Sc^{37}Cl^+$	

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/General purpose.

Acquisition parameters: MS/MS mass-shift mode using O_2/H_2 at a gas flow of 0.6 mL/min and 1.0 mL/min respectively. As was measured as the reaction product ion AsO^+ at m/z 91, and Se was measured as SeO^+ at m/z 96.

Reagents: Two National Institute of Standards and Technology (NIST) standard reference materials (SRMs), NIST 1547 Peach Leaves and NIST 1515 Apple Leaves, were studied. These SRMs contain low µg/kg levels of As and Se in the presence of mg/kg levels of REEs.

Sample prep: All samples were acid digested using a closed vessel microwave digestion system. The SRMs were prepared in triplicate. First, 0.25 g sample was digested in 2.5 mL of 9:1 HNO_3:HCl acid mix, and the digest was then diluted to a final weight of 25 g with ultra-pure water. 5% butanol was added to the internal standard mixture to equalize the organic plasma load between samples and standards. NIST 1547 and 1515 contain low µg/kg concentrations of As and Se (Table 2) and high concentrations of REEs. Reference (non-certified) values for Nd, Sm and Gd are 7, 1, and 1 mg/kg in NIST 1547, and 17, 3, and 3 mg/kg in NIST 1515, respectively.

Results and discussion

Both SRM digests were analyzed using the 8800 ICP-QQQ with O_2/H_2 as the reaction gas (Table 2). A previous study showed that the presence of H_2 in the cell further improved Se detection capability [6]. The measured values for As and Se in NIST 1547 and 1515 were well within the certified range for both SRMs, demonstrating the successful elimination of the REE^{++} interferences in O_2/H_2 MS/MS mode on the 8800. These results were obtained without the need for correction equations (i.e. uncorrected).

Results obtained using ICP-QMS are included for comparison purposes. "Corrected" refers to the use of correction equations. ICP-QMS operating in helium mode is suitable for the analysis of As and Se in general routine sample types that might contain a small amount of REEs, and H_2 mode has been shown to be effective at reducing doubly charged species. Compared to these conventional methods, ICP-QQQ had 10-fold lower detection limits, which makes it particularly suited to low level determination of As and Se in complex sample matrices.

Table 2. Analysis of As and Se in NIST 1547 and 1515 in He mode and H_2 mode using ICP-QMS (both uncorrected and corrected data is given) and by ICP-QQQ in MS/MS mode. All concentrations are in mg/kg, and are averages of 3 replicate sample digests expressed as mean ± standard deviation.

		ICP-QMS He mode		ICP-QMS H_2 mode		ICP-QQQ O_2/H_2 mass-shift
SRM	Certified	Uncorrected	Corrected	Uncorrected	Corrected	Uncorrected
As (mg/kg)						
NIST 1547	0.060±0.018	0.170±0.016	0.068±0.003*	0.113±0.004	0.079±0.004*	0.065±0.002*
NIST 1515	0.038±0.007	0.250±0.016	0.026±0.021*	0.126±0.005	0.047±0.004*	0.032±0.002*
Se (mg/kg)						
NIST 1547	0.120±0.009	0.394±0.04	0.113±0.02*	0.119±0.009*	0.119±0.009*	0.127±0.006*
NIST 1515	0.050±0.009	0.808±0.04	0.013±0.04*	0.050±0.003*	0.050±0.003*	0.047±0.006*

*95% confidence interval overlaps with the certified range

ICP-QMS can also use O_2 mass-shift mode but, with ICP-QMS, all matrix and analyte ions enter the cell, so the analyte reaction product ions measured ($^{75}As^{16}O^+$ at *m/z* 91, and $^{78}Se^{16}O^+$ at *m/z* 94), could suffer overlap from existing analyte or matrix ions at the product ion mass (e.g. $^{91/94}Zr^+$ and $^{94}Mo^+$). To confirm that the ICP-QQQ MS/MS method can be applied to samples that contain high concentrations of Zr and Mo, an aliquot of NIST 1547 was spiked with 1 mg/L (1000 ppm) Zr and Mo, and the results are shown in Table 3. The measured values for As (as AsO^+) and Se (as SeO^+) in the spiked sample are the same as for the unspiked samples, demonstrating that MS/MS mode is effective at rejecting existing overlapping ions present at the mass of the cell-formed analyte product ions. This capability is unique to the tandem mass spectrometer configuration of the 8800 ICP-QQQ, where the ions that enter the cell are controlled by an additional mass filter, Q1, positioned in front of the collision/reaction cell.

Table 3. ICP-QQQ measured results for As and Se in NIST 1547 unspiked and spiked with 1 mg/L Zr and Mo. No correction equations were applied.

		ICP-QQQ with O_2/H_2 mass-shift	
SRM NIST 1547	Certified	Unspiked (n=3)	Spiked with 1 mg/L Zr & Mo (n=1)
As (mg/kg)	0.060±0.018	0.065±0.002	0.063
Se (mg/kg)	0.120±0.009	0.127±0.006	0.13

Conclusions

The Agilent 8800 ICP-QQQ with MS/MS capability has been shown to be the optimum method to successfully measure trace levels of As and Se in the presence of high concentration of REEs in NIST 1547 Peach Leaves and NIST 1515 Apple Leaves. All REE doubly-charged and matrix-based polyatomic interferences that affect As and Se measurement at *m/z* 75 and *m/z* 78 are avoided using O_2/H_2 cell gas and MS/MS mass-shift mode. Arsenic is shifted to its product ion AsO^+ which is measured at *m/z* 91, and Se is shifted to SeO^+, measured at *m/z* 94. Importantly, MS/MS mode also eliminates potential ion overlaps at *m/z* 91 and *m/z* 94 from $^{91/94}Zr^+$ and $^{94}Mo^+$, as these ions are rejected by Q1. The extent and concentration of REEs in food products is not well studied. However, monitoring for the presence of Nd^{++}, Sm^{++}, and Gd^{++} at *m/z* 150 and 156 during an analysis would identify samples where doubly charged REE formation might be problematic.

More information

For a full account of this application see publication: Advantages of reaction cell ICP-MS on doubly charged interferences for arsenic and selenium analysis in foods, Brian P. Jackson, Amir Liba and Jenny Nelson, J. Anal. At. Spectrom., 2015, Advance Article. DOI: 10.1039/C4JA00310A.

Acknowledgements

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High Throughput Determination of Inorganic Arsenic in Rice using Hydride Generation-ICP-QQQ

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Helga Gunnlaugsdóttir Matis, Environment and Genetics Department, Reykjavik, Iceland

Keywords

arsenic, arsenite, arsenate, IMEP-7 rice, NIST 1568a Rice Flour, oxygen mass-shift

Introduction

The concentration of potentially toxic chemicals such as arsenic in rice is closely monitored to ensure food safety. However, the toxicity of arsenic depends on the chemical form or "species" of the element that is present rather than total concentration. Inorganic arsenic (iAs) species, arsenite (As(III)) and arsenate (As(V)), are known to be carcinogenic and highly toxic, whereas the common organoarsenic species monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) are less toxic [1].

Rice is an important food source for a large percentage of the world's population, but it does contain relatively high concentrations of iAs due to the uptake of As from the soil and water in which the rice plants are grown. Available As from soils can be both naturally occurring and due to anthropogenic sources such as As-based pesticides that were widely used until the 1970s. Clearly there is an urgent food-safety requirement for a simple and quick analytical method to screen large numbers of rice and other food samples for iAs. In this study, a fast and sensitive method using hydride generation (HG) with ICP-QQQ is described for the separation and detection of iAs in commercial rice samples.

Experimental

Instrumentation: A Hydride Generation (HG) accessory for Agilent's ICP-MS Integrated Sample Introduction System (ISIS) was used with an Agilent 8800 #100 ICP-QQQ. When treated with $NaBH_4$ under acidic conditions, iAs is very efficiently converted into volatile arsine (AsH_3), whereas organically bound As compounds are not converted, or form only less volatile arsine species such as dimethylarsine $(CH_3)_2AsH$, which has a boiling point of 35°C. Adding high concentrations of HCl further reduces the production of the less volatile arsines, and iAs is almost entirely converted to arsine, enabling the measurement of iAs without species separation using chromatography.

Plasma conditions and ion lens tune: RF power =1550 W, Sampling depth = 8.0 mm and CRGS flow rate = 0.93 L/min were used with soft extraction tune, Extract 1 = 0.5 V and Extract 2 = -170 V.

Acquisition parameters: MS/MS mass-shift mode using O_2 cell gas at a flow rate of 2.0 mL/min. As was measured as the reaction product ion AsO^+ at *m/z* 91.

Samples: Samples included 31 different rice products purchased from local stores. Sub-samples (30g) of the commercially sourced rice samples were ground to a fine homogeneous powder using a coffee grinder. Two rice reference materials IMEP-107 rice (Institute for Reference Materials and Measurements Geel, Belgium) and rice SRM NIST 1568a Rice Flour were used as quality control for iAs concentration measurements.

Sample prep: 0.15g of each rice sample was digested in 1 mL concentrated HNO_3 and 2 mL H_2O_2 (30 % w/w) using open vessel digestion in a CEM Mars microwave system. All samples were diluted to a final volume of 30 mL using deionized water.

Table 1. Operating parameters for hydride generation

Sample flow rate (mL/min)	0.5
HCl flow rate (mL/min)	2.5
$NaBH_4$ flow rate (mL/min)	0.5
Reaction coil volume (mL)	0.23
Ar flow rate (for HG) (L/min)	0.3
Ar flow rate (for nebulization of IS) (L/min)	0.85–0.95

Results and discussion

The speciation results for iAs in IMEP-7 rice and NIST 1568a Rice Flour obtained using HG-ICP-QQQ were in good agreement with the values obtained using HPLC-ICP-QQQ and with the reported values (Table 2).

Table 2. iAs results obtained using HG-ICP-QQQ and HPLC-ICP-QQQ.

Inorganic As			
	HG-ICP-QQQ (µg/kg)	HPLC-ICP-QQQ (µg/kg)	Reported value (µg/kg)
IMEP-7 rice	100 ± 11 (n=15)	110 ± 12 (n=15)	107 ± 14 [2]
NIST 1568a	94 ± 8 (n=3)	105 ± 4 (n=3)	94 ± 12

A summary of the values for iAs, DMA and total As determined in the commercial rice samples is given in Table 3. The dominant arsenic species found in rice are iAs and dimethylarsinic acid (DMA), with only trace amounts of methylarsonic acid (MA). The method uses HCl (5 M) and $NaBH_4$ for the selective generation of arsines where iAs and DMA are converted almost exclusively to AsH_3, with only minor (2-4%) conversion of DMA to dimethylarsine. MA forms methylarsine at approximately 40% efficiency with the method; however, since MA is generally absent from rice – or only present in trace amounts – this should not affect the quantification of iAs.

Table 3. Speciation results of iAs in 31 rice products determined by HG-ICP-QQQ and HPLC-ICP-QQQ. Results are also given for DMA and MMA, and the total As concentration determined by ICP-QQQ. All data ± SD, with n=3 for speciation and n=2 or 3 for total As.

Rice product	HG iAs (µg/kg)	HPLC iAs (µg/kg)	HPLC DMA (µg/kg)	HPLC MMA (µg/kg)	Total As (µg/kg)
Arborio Risotto	113 ± 13	120 ± 18	63 ± 7	<LOQ	236 ± 15
Organic ArbRis	109 ± 12	119 ± 13	60 ± 8	<LOD	150 ± 7
Basmati, 1	41 ± 4	53 ± 7	8 ± 1	<LOD	100 ± 12
Basmati, 2	76 ± 6	88 ± 6	28 ± 4	<LOD	91 ± 8
Basmati (white)	72 ± 11	69 ± 9	24 ± 1	<LOD	240 ± 5
Organic Basmati (white)	95 ± 3	104 ± 3	21 ± 2	<LOD	117 ± 13
Brown Rice	127 ± 6	137 ± 5	35 ± 2	<LOD	205 ± 2
Japanese Rice	101 ± 5	99 ± 5	123 ± 1	<LOQ	252 ± 10
Long Grain (white)	89 ± 2	85 ± 1	16 ± 1	<LOD	121 ± 11
Long Grain Rice, 1	103 ± 2	94 ± 1	218 ± 9	<LOQ	392 ± 23
Long Grain Rice, 2	40 ± 2	52 ± 10	39 ± 3	<LOQ	111 ± 8
Long Grain white	47 ± 2	61 ± 4	19 ± 4	<LOD	102 ± 9
Organic Long Grain (brown)	111 ± 7	131 ± 14	54 ± 7	<LOQ	207 ± 15
Organic (white)	65 ± 4	65 ± 2	11 ± 1	<LOD	92 ± 4
Paella, 1	60 ± 5	65 ± 2	38 ± 1	1.2 ± 0.1	136 ± 1
Paella, 2	66 ± 4	70 ± 3	17 ± 1	<LOD	121 ± 6
Spanish Paella	67 ± 2	67 ± 3	13 ± 1	<LOD	109 ± 7
Pudding Rice	124 ± 9	125 ± 11	44 ± 5	<LOD	202 ± 4
Rice Flour	40 ± 1	46 ± 5	19 ± 2	<LOD	102 ± 6
Carnaroli Risotto Rice	81 ± 2	82 ± 4	84 ± 2	<LOD	210 ± 15
Risotto Rice	97 ± 11	114 ± 10	72 ± 9	<LOQ	221 ± 17
FLG Thai (white)	88 ± 3	102 ± 3	52 ± 5	<LOD	197 ± 9
Thai Jasmine	61 ± 4	64 ± 3	49 ± 5	<LOD	143 ± 3
Thai Jasmine (white)	62 ± 4	62 ± 3	49 ± 2	<LOD	171 ± 5
Vietnamese Rice Paper	21 ± 2	28 ± 1	<LOQ	<LOD	58 ± 10
White Rice	71 ± 5	76 ± 5	14 ± 4	<LOQ	124 ± 1
Whole Grain	133 ± 2	127 ± 2	151 ± 12	7.2 ± 0.3	370 ± 19

LOQ HG-ICP-QQQ: 5 µg/kg, HPLC-ICP-QQQ: 1.1 µg/kg

Conclusions

Inorganic arsenic (iAs) was quantified at low ppb levels in extracts of 31 rice samples using an Agilent Hydride Generator/ISIS coupled to an Agilent 8800 ICP-QQQ. Results obtained using HG-ICP-QQQ were in good agreement with HPLC-ICP-QQQ values across a wide linear range, with comparable limits of detection.

Following a simple sample preparation using microwave extraction, quick separation of iAs and DMA by HG-ICP-QQQ was performed online. A previous study has shown that HG-ICP-QQQ requires only 4 minutes total run time per sample (5 replicate measurements) compared to speciation with HPLC which commonly takes between 5 and 10 minutes for each sample replicate [3]. Data handling for the HG method is also straightforward as no peak-integration is necessary.

The new HG-ICP-MS method offers fast analysis time, high throughput, and simple, reliable operation. This makes it ideally suited to screening large numbers of food samples to meet the increasing demand for the routine determination of iAs in food, especially rice-based products.

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More information

For a full account of this application see publication: Ásta H. Pétursdóttir *et al.*, Hydride generation ICP-MS as a simple method for determination of inorganic arsenic in rice for routine biomonitoring, Anal. Methods, 2014,6, 5392-5396.

Determination of Pesticides using Phosphorus and Sulfur Detection by GC-ICP-QQQ

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Keywords

pesticides, GC-ICP-MS, GC-ICP-MS/MS, GC-ICP-QQQ, sulfur, phosphorus

Introduction

The determination of pesticide residues in food products is important. Most pesticide residue laboratories use some variation of the QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) extraction methods. Typically, the extracted material is analyzed using GC/MS/MS the thermally stable, less polar pesticides, or LC-MS/MS for the less volatile and/or more polar ones. A more recently developed alternative technique involves coupling GC to triple quadrupole ICP-MS (GC-ICP-QQQ). Pesticides can be quantified using GC-ICP-QQQ by measuring the heteroatoms P and S (also Cl and Br) contained in most pesticides. GC-ICP-QQQ offers good selectivity, specificity, and sensitivity that can be greater than the established methods.

Experimental

Instrumentation: An Agilent 7890 GC was coupled to an Agilent 8800 #100 ICP-QQQ using an Agilent GC-ICP-MS interface (G3158D).

GC: Two Agilent columns were used in series. The first column was a 5 m length cut from a 20 m x 0.18 mm x 0.18 µm film thickness DB-35ms Ultra Inert (UI) capillary column (p/n 121-3822UI). This column was installed between the inlet and one end of the purged union. It was back flushed shortly before the run had ended to prevent high boiling point contaminants from entering the second column. The second column was a 15 m x 0.25 mm i.d. 0.25 µm film thickness DB-5MS UI capillary column (p/n 19091S-431UI). The column was installed between the other end of the purged union and the ICP-QQQ transfer line connection inside the GC oven. Sample injections of 1 µL volume were made under splitless conditions with the inlet held at 280 °C. GC operating parameters are detailed in a previous study [1].

ICP-QQQ: O_2 mass-shift method was applied to detect P and S. The O_2 flow rate was 0.2 mL/min. P and S were detected as PO^+ and SO^+, respectively.

Samples and preparation: Three standard pesticide mixes were obtained from Ultra Scientific (Kingstown, RI, USA) and Agilent Technologies (p/n 5190–0468). The standard solutions were diluted with high purity grade acetonitrile to form intermediate solutions. These solutions were then used to prepare calibration standard solutions following serial dilutions in acetonitrile.

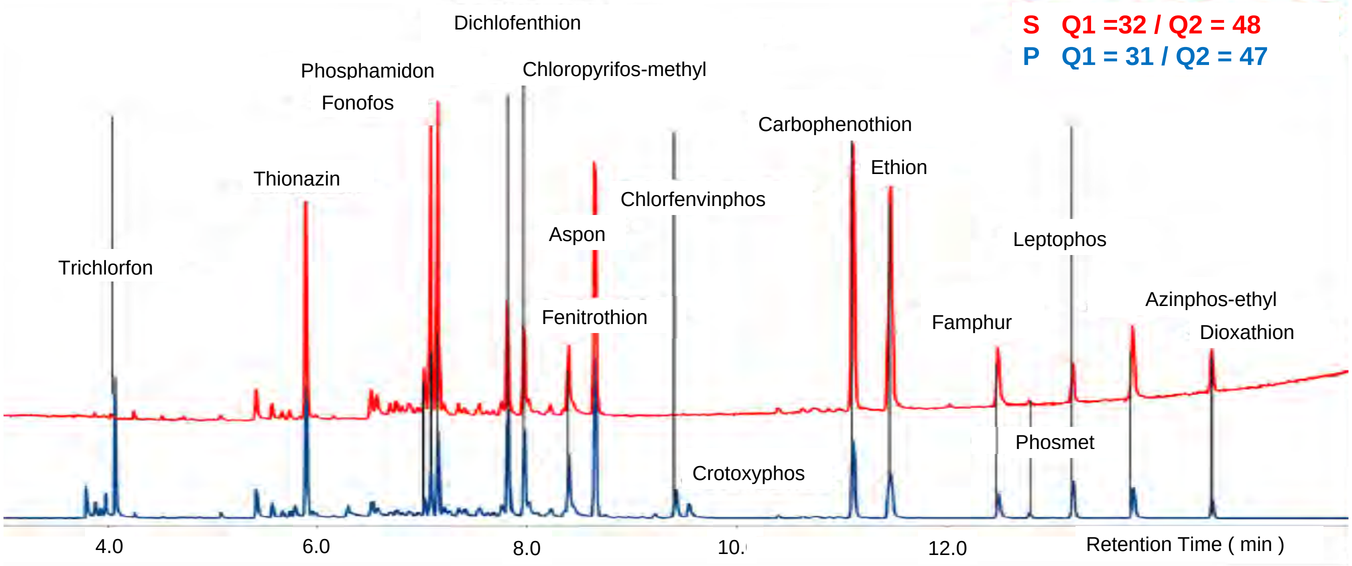

Figure 1. Chromatograms showing the heteroatom traces for P and S in the mixed pesticide standard, with identified pesticide compounds. *Reprinted with permission from J. Agric. Food Chem., 2015, 63, 4478–4483. Copyright 2015 American Chemical Society.*

Results and discussion

Figure 1 shows overlaid chromatograms for P and S in a mixed pesticide standard. The pesticides that contain more than one hetero-element can be identified easily.

Table 1 summarizes the retention time and compound detection limits (DLs) of the pesticides. DLs for pesticides using current GC/MS/MS instrumentation typically vary from about 0.1 to 10 µg/L depending on the pesticide and instrument used. The data in Table 1 suggests that GC-ICP-QQQ offers similar or slightly lower DLs than GC/MS/MS for the determination of organophosphorus pesticides. For S-containing pesticides, detection limits are similar to, or slightly higher than DLs achieved by GC/MS/MS. All of the pesticides listed in Table 1, which were detected via their P content, were quantified well below the 10 µg/L limit of quantitation (LOQ) required by most food safety laboratories.

Table 1. Detection limits as the compound for pesticides

Pesticide	RT (min)	Compound DL (µg/L)	
		P	S
Trichlorfon	4.103	0.178	
Thionazin	5.926	0.221	11.93
Terbufos	7.071	0.718	9.708
Fonofos	7.185	0.455	7.917
Phosphamidon	7.299	0.923	
Dichlofenthion	7.858	0.362	15.8
Chloropyrifos-methyl	7.973	0.613	24.18
Fenitrothion	8.44	0.907	19.52
Aspon	8.705	0.200	9.912
Chlorfenvinphos	9.486	2.020	
Crotoxyphos	9.541	3.338	
Carbophenothion	11.158	0.583	9.585
Ethion	11.527	0.707	11.51
Famphur	12.547	2.206	20.61
Phosmet	12.851	3.829	
Leptophos	13.263	1.125	18.35
Azinphos-ethyl	13.827	1.812	21.33
Dioxathion	14.587	1.392	7.84

Conclusions

The GC-ICP-QQQ method is suitable for the selective and sensitive detection of organophosphorus and organosulfur pesticides by measurement of their heteroatoms. Due to the significantly lower background of the Agilent 8800 ICP-QQQ, GC-ICP-QQQ provides good sensitivity performance for the determination of organophosphorus pesticides compared to GC/MS/MS.

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Environmental

The Accurate Measurement of Selenium in Reference Materials using Online Isotope Dilution

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Keywords

selenium, environmental, agricultural, human health, online isotope dilution analysis, OIDA, oxygen mass-shift

Introduction

Selenium (Se) is an important element in environmental and agricultural studies and in human health, as it is an essential trace nutrient but is toxic in excess. The role of certain chemical forms of Se is the subject of significant research into cancer prevention. ICP-MS is the analytical method of choice for both total and speciated Se measurements, but Se is a difficult element to quantify accurately at trace levels by ICP-MS for several reasons:

- The signal for Se is low, since it is poorly ionized in the plasma due to its high Ionization Potential (IP) of 9.75 eV.
- Because Se is poorly ionized, it suffers signal suppression in high matrix samples — an issue that is further compounded by the lack of a suitable internal standard element with a similar mass and IP.
- All the analytically useful Se isotopes suffer from multiple spectral interferences, as summarized in Table 1.
- The resolution required to separate all of the spectral interferences is beyond the capabilities of sector-type high resolution (HR-)ICP-MS.

The Agilent 8800 ICP-QQQ in MS/MS mode has a unique ability to remove the complex spectral interferences from all the Se isotopes shown in Table 1, allowing the use of Isotope Dilution (ID) analysis, which requires at least two interference-free isotopes. ID is the most accurate quantification technique as it is based on direct measurement of isotopic abundances in each sample, rather than a relative measurement of analyte response compared to a standard. As a result, it offers better traceability and improved correction of non-spectroscopic interferences encountered in high matrix sample analysis. This note describes the application of the Agilent 8800 ICP-QQQ using ID for the accurate quantification of Se in a range of certified reference materials (CRMs).

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/General purpose.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -180 V.

CRC conditions: O_2 gas at 0.4 mL/min plus H_2 gas at 2.0 mL/min, Octopole bias = -18 V and KED = -6 V.

Acquisition parameters: MS/MS O_2 mass-shift method. The reaction of Se^+ with O_2 to form SeO^+ is endothermic ($\Delta Hr = 0.71$ eV) , but the reaction is efficiently promoted using high collision energy using a low octopole bias voltage setting [1]. Preliminary studies have shown that low BEC for Se isotopes can be achieved via the addition of a small amount of H_2 in MS/MS O_2 mass-shift method.

Table 1. Spectral interferences on Se isotopes

Se isotope		Interference						
Mass	**Abundance %**	**Isobaric**	**Argide**	**Oxides**	**Hydride**	**Chloride**	**Doubly charged**	**Dimer**
77	7.63		$^{39}K^{38}Ar^+$	$^{61}Ni^{16}O^+$, $^{59}Co^{18}O^+$	$^{76}GeH^+$, $^{76}SeH^+$	$^{40}Ar^{37}Cl^+$, $^{40}Ca^{37}Cl^+$	$^{154}Sm^{++}$, $^{154}Gd^{++}$	
78	23.77	$^{78}Kr^+$	$^{40}Ca^{38}Ar^+$	$^{62}Ni^{16}O^+$	$^{77}SeH^+$	$^{41}K^{37}Cl^+$	$^{156}Gd^{++}$, $^{156}Dy^{++}$	$^{38}Ar^{40}Ar^+$, $^{39}K^{39}K^+$
80	49.61	$^{80}Kr^+$	$^{40}Ca^{40}Ar^+$	$^{64}Ni^{16}O^+$, $^{64}Zn^{16}O^+$, $^{32}S_2{}^{16}O^+$, $^{32}S^{16}O_3{}^+$	$^{79}BrH^+$	$^{45}Sc^{35}Cl^+$	$^{160}Gd^{++}$, $^{160}Dy^{++}$,	$^{40}Ar^{40}Ar^+$, ^{40}Ca-$^{40}Ca^+$
82	8.73	$^{82}Kr^+$	$^{42}Ca^{40}Ar^+$	$^{66}Zn^{16}O^+$	$^{81}BrH^+$	$^{45}Sc^{37}Cl^+$	$^{164}Dy^{++}$, $^{164}Er^{++}$	

Method: Online isotope dilution analysis (OIDA) [2] was used. OIDA is a useful development of traditional isotope dilution, as it removes the time consuming step of spiking enriched-isotope standards into each individual sample. A ^{82}Se enriched standard purchased from Oak Ridge National Laboratory (USA) was prepared at the appropriate concentration and added via the standard online ISTD mixing kit to the samples. Product ions derived from the ^{16}O-atom addition transition were measured for the three most analytically useful isotopes of Se. On the 8800 ICP-QQQ, this is simply achieved by defining the acquisition method with Q1/Q2 settings: Q1=78/Q2=94, Q1=80/Q2=96 and Q1=82/Q2=98 for the Se isotopes at *m/z* 78, 80 and 82 respectively.

It should be noted that the use of MS/MS (where Q1 acts as a 1 amu mass filter) is essential for this measurement, as it ensures that only one Se isotope enters the cell for any given mass pair measurement, and only the ^{16}O atom addition is measured because the mass difference between Q1 and Q2 is 16 amu. This ensures that there is no overlap due to the precursor ions from different Se^+ isotopes giving SeO^+ product ions at the same mass, such as the $^{80}Se^{18}O^+$ product ion overlap on $^{82}Se^{16}O^+$, both of which appear at *m/z* 98. ICP-QQQ in MS/MS mode thereby removes one of the critical limitations of reaction chemistry with ICP-QMS, where all the sample ions enter the cell together so no specific reaction transition can be defined. Each Se isotope mass pair was measured with an integration time of 1 s and three replicates.

Sample preparation: The CRMs were microwave digested using a Milestone ETHOS closed vessel microwave digestion system (Milestone, Sorisole, Italy) and following the manufacturer's recommended procedures. The final dilution factor of the samples varied from 250 to 500x.

Results and discussion

Study of cell gases for spectroscopic interference removal

Figure 1 shows the result of a preliminary study of the effects of the choice of cell gas on interference removal. The findings of the study showed that O_2/H_2 mass-shift (Figure 1) enables the measurement of ^{78}Se, ^{80}Se and ^{82}Se relatively free from interferences in the range of synthetic matrices tested.

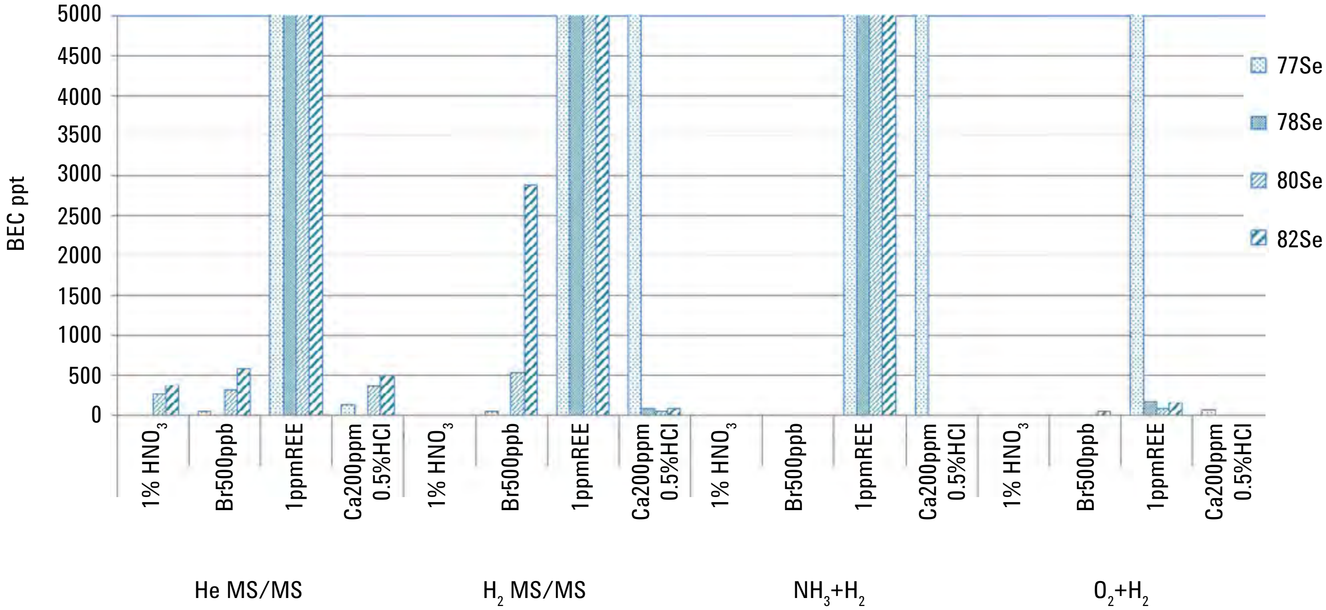

Figure 1. Preliminary study of the effectiveness of different cell gases for interference removal. Four synthetic matrices likely to give rise to interferences on the Se isotopes were measured using each of the 4 different cell gas modes.

Measurement of Se in CRMs

The concentration of Se was determined in 12 different CRMs using the OIDA method. The CRMs were obtained from NIST (Gaithersburg MD, USA), GSJ Geochemical Reference Samples (Tokyo, Japan), Japan Society for Analytical Chemistry (Tokyo, Japan), and National Institute of Metrology (Beijing, China). The matrices included environmental waters (NIST 1643e and JASC 0302-3 River Water), rock (JB-3 basalt), sedimentary rock (JSI-1 and NIST 1646a Estuarine Sediment), soil (JSAC0411 Volcanic Ash Soil), biological samples (NIST 1566a Oyster Tissue, NCSZC 81002 Human Hair, NIST 2976 Mussel Tissue), and plant materials (NIST 1575a Pine Needles, NIST 1515 Apple Leaves, NIST1573a Tomato Leaves).

Figure 2 shows the Se results for each CRM expressed as % recovery relative to the certified value. The measured results for Se were in good agreement with the CRM values (90%-112%), using two Se isotope pairs: 78/82 and 80/82. This demonstrates the effectiveness of the Agilent 8800 ICP-QQQ in MS/MS mode for the removal of multiple interferences on ^{78}Se, ^{80}Se and ^{82}Se.

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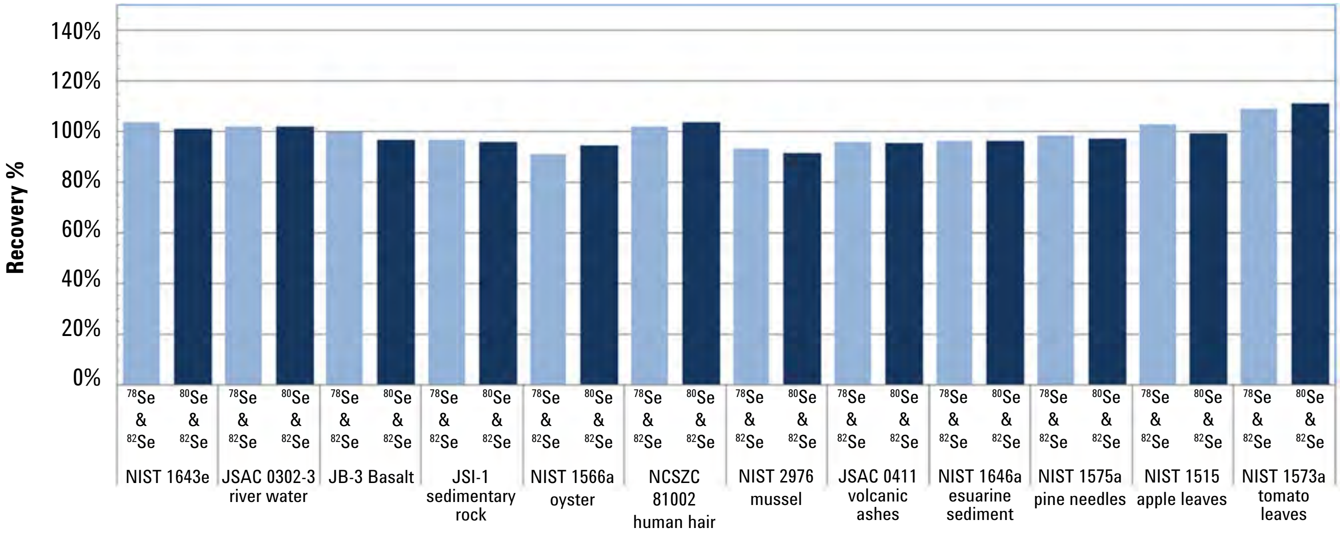

Figure 2. Result of Se quantification using OIDA in various CRMs

Accurate Sulfur Quantification in Organic Solvents using Isotope Dilution Mass Spectrometry

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Based upon the published work “Accurate determination of S in organic matrices using isotope dilution ICP-MS/MS” JAAS 2012 DOI: 10.1039/c2ja30265a by:

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Keywords

sulfur, ID-MS, biodiesel, environmental, ethanol, NIST SRM 2773, oxygen mass-shift

Introduction

Accurate measurement of sulfur in aqueous and organic media is relatively difficult for ICP-MS due to intense spectral interferences from polyatomic ions formed mainly from oxygen and nitrogen. Sulfur is an important element in environmental terms as it forms SO_x when combusted, contributing to acid rain and photochemical smog. It is also a catalyst poison for some industrial processes and its accurate measurement can be critical.

Experimental

A quadrupole ICP-MS (ICP-QMS) with a collision/reaction cell set up for O_2 mass-shift reaction chemistry can be used to avoid the $^{16}O_2^+$ overlap on $^{32}S^+$ by converting the S^+ to SO^+ reaction product ions that are then measured at a new mass (*m/z* 48) that is free from the O_2^+ overlap. However, in practice, this approach has been of relatively limited use, as ICP-QMS has no way to reject existing ions at the mass of the new analyte product ions, so not all of the interferences are eliminated, particularly when complex or variable matrices are investigated. There has also been some limited success reported by using Xe as a reaction gas to attenuate the O_2-based interference particularly on the ^{34}S isotope. Neither of these approaches reduces the backgrounds significantly enough to allow reliable trace level measurement of S, and they do not necessarily preserve the S isotopic abundances. In this investigation, ethanol was used as an example organic solvent and the Agilent 8800 ICP-QQQ was used to determine S by ID-MS in a biodiesel reference material to assess the measurement accuracy of MS/MS mode with O_2 mass-shift for S determination.

Instrumentation: Agilent 8800 #100 with Micromist nebulizer (free aspiration). For organic solvent analysis, a narrow injector torch with id 1.0 mm (G3280-80005) and Pt cones were used. 20% O_2 balanced in Ar was introduced via an option gas flow line to prevent carbon build up.

Plasma conditions: Plasma conditions were optimized manually. (RF power = 1450 W, CRGS flow rate = 0.98 L/min, Option gas flow rate = 0.75 L/min and spray chamber temp. = -5˚C).

CRC conditions: O_2 gas at 0.4 mL/min, Octopole bias = -9 V, KED = -8 V.

Sample: Biodiesel certified reference material NIST SRM 2773.

Results and discussion

When using mass-shift mode for sulfur (or any element) it is important to eliminate any potential interferences at the target mass of the reaction product ion, as well as on the primary element mass (the precursor ion). If the target mass suffers from interferences then the measurement would still be compromised. For sulfur, the corresponding isotopes are shifted as follows using M + 16 amu mass-shift:

$^{32}S \rightarrow SO$ at 48 amu

$^{33}S \rightarrow SO$ at 49 amu

$^{34}S \rightarrow SO$ at 50 amu

Unfortunately, the SO^+ product ion masses (*m/z* 48, 49 and 50) can suffer from multiple interferences including Ca^+, Cr^+, V^+, Ti^+, ArC^+ and CCl^+ in natural samples. Furthermore the ^{33}S and ^{34}S isotopes can suffer from overlaps due to other combinations of SO^+ product ions, as well as pre-existing ions at the target mass. For example, the $^{34}S^{16}O^+$ product ion formed at *m/z* 50 is overlapped by $^{32}S^{18}O^+$ and $^{33}S^{17}O^+$, as well as $^{50}Cr^+$, $^{50}V^+$, $^{50}Ti^+$, $^{38}Ar^{12}C^+$, and $^{13}C^{37}Cl^+$. When operating the 8800 ICP-QQQ in MS/MS mass-shift mode, these overlaps are eliminated and the sulfur isotope pattern is preserved. Figure 1 provides a graphical representation of the ICP-QQQ setup and the method of interference elimination.

This method would not be useful if the reaction were not quantitative, so to check for linearity, a blank ethanol sample was spiked with sulfur – see Figure 2. Despite the wide variation in absolute sensitivity for the different S isotopes, the BEC was the same for all three isotopes, indicating that the background is due to sulfur in the ethanol.

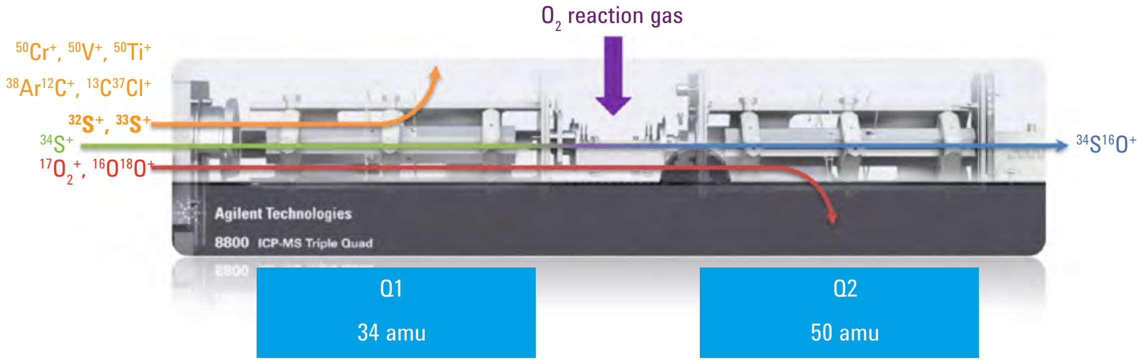

Figure 1. Mechanism of MS/MS mass-shift for sulfur isotope analysis. The mass difference between Q1 and Q2 is fixed at 16 amu, so only the + ^{16}O-atom transition is observed – the other oxygen isotope transitions are eliminated so the original sulfur isotopic pattern is preserved.

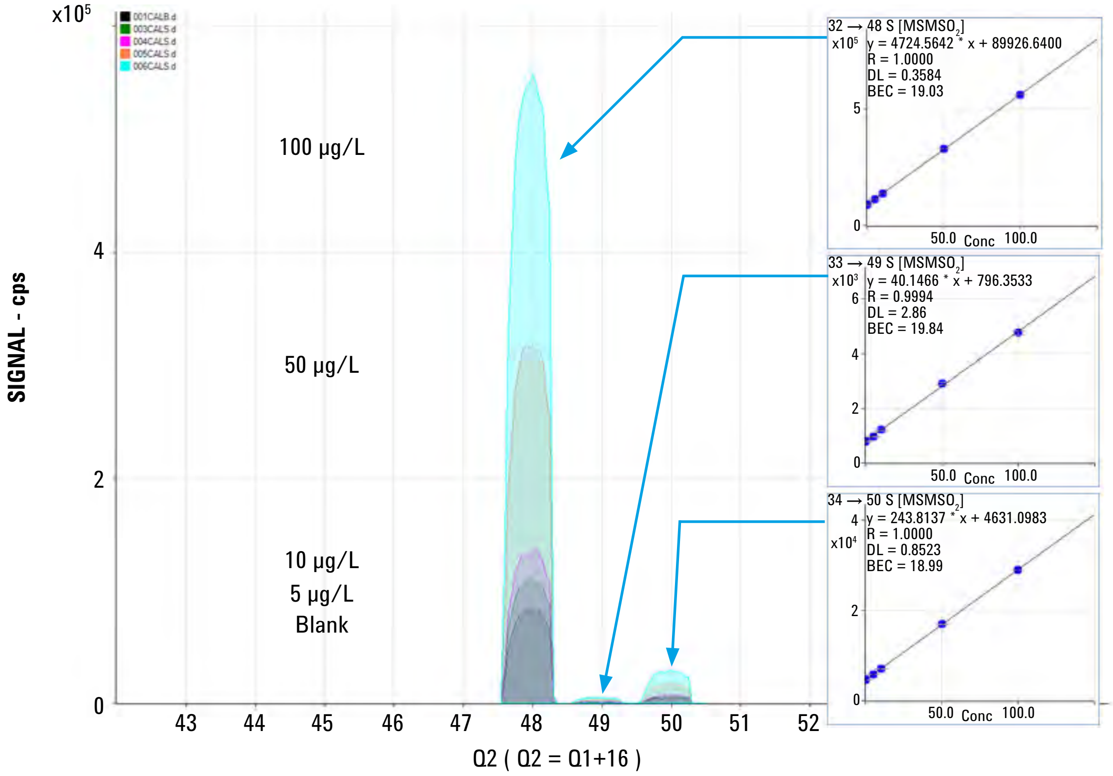

Figure 2. Ethanol with 0, 5, 10, 50 and 100 µg/L sulfur spikes and corresponding calibration curves.

An isotope dilution (ID) method was used to evaluate the accuracy of the 8800 ICP-QQQ MS/MS method, using a biodiesel certified reference material (NIST SRM 2773) and an enriched ^{34}S spike. The biodiesel sample was simply diluted into the ethanol solvent and the appropriate spike added. Reproducibility was tested by analyzing three separate samples of the CRM. The results are presented in Table 1. Repeat measurements were within the expected recovery limits for the material.

Table 1. Isotope dilution analysis of S in diluted biodiesel reference material NIST 2773

Sample	Certified value (µg/g)	Determined conc. (µg/g)
SRM 2773 - 1	7.39 ± 0.39	7.234
SRM 2773 - 2		7.227
SRM 2773 - 3		7.231
Average		7.231
Standard Deviation		0.003
95% confidence interval		7.231 ±0.015

Conclusions

Until the introduction of ICP-QQQ with MS/MS capability, it was impossible to obtain reliable results for reaction chemistry methods combined with an ID approach, using a quadrupole-based ICP-MS. The novel QQQ configuration of the 8800 ICP-QQQ enables operation in MS/MS mode, which ensures precise control over the reaction chemistry in the cell. This allows the unique isotopic information of the analyte to be retained, while removing the interferences that could affect both precursor and product ions of the target analyte.

Removal of REE^{++} Interference on Arsenic and Selenium

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Keywords

Rare Earth Elements, REE, arsenic, selenium, environmental, food, CRMs, oxygen mass-shift

Introduction

Trace analysis of arsenic (As) and selenium (Se) in environmental and food samples is of a great interest, since both elements can be toxic even at quite low levels. It is difficult to quantify As and Se accurately at trace levels in some matrices by quadrupole ICP-MS as all the analytically useful isotopes can suffer from multiple spectral interferences, as summarized in Table 1. This application investigates ICP-QQQ in MS/MS reaction mode to remove interferences on As and Se, with an emphasis on the removal of the doubly-charged ions arising from Rare Earth Elements (REE^{++}). While the concentration of REEs in environmental and food samples is usually low, some plants will accumulate REEs from the soil, and a high concentration will lead to false positive results for As and Se.

Table 1. Selected spectral interferences on As and Se isotopes

As and Se isotope		Interference			
Element	**m**	**Abundance %**	**Doubly charged**	**Chloride**	**Dimer**
As	75	100	$^{150}Sm^{++}$, $^{150}Nd^{++}$	$^{40}Ar^{37}Cl^+$, $^{40}Ca^{37}Cl^+$	
Se	77	7.63	$^{154}Sm^{++}$, $^{154}Gd^{++}$	$^{40}Ar^{37}Cl^+$, $^{40}Ca^{37}Cl^+$	
	78	23.77	$^{156}Gd^{++}$, $^{156}Dy^{++}$	$^{41}K^{37}Cl^+$	$^{38}Ar^{40}Ar^+$, $^{39}K^{39}K^+$
	80	49.61	$^{160}Gd^{++}$, $^{160}Gd^{++}$	$^{45}Sc^{35}Cl^+$	$^{40}Ar^{40}Ar^+$, $^{40}Ca^{40}Ca^+$
	82	8.73	$^{164}Dy^{++}$, $^{164}Er^{++}$	$^{45}Sc^{37}Cl^+$	

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/Low matrix.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -180 V.

CRC conditions: O_2 gas flow rate of 0.2 mL/min, Octopole bias = -8 V and KED = -6 V.

Acquisition parameters: MS/MS O_2 mass-shift method to measure As^+ (as AsO^+) and Se^+ (as SeO^+), as illustrated in Figure 1. Unlike conventional quadrupole ICP-MS, the 8800 ICP-QQQ mass-shift method can be applied to complex matrix samples that may contain Zr and/or Mo. The MS/MS configuration prevents undesired ions such as $^{91}Zr^+$ and $^{94}Mo^+$ from overlapping the MO^+ product ions, as they are rejected by Q1.

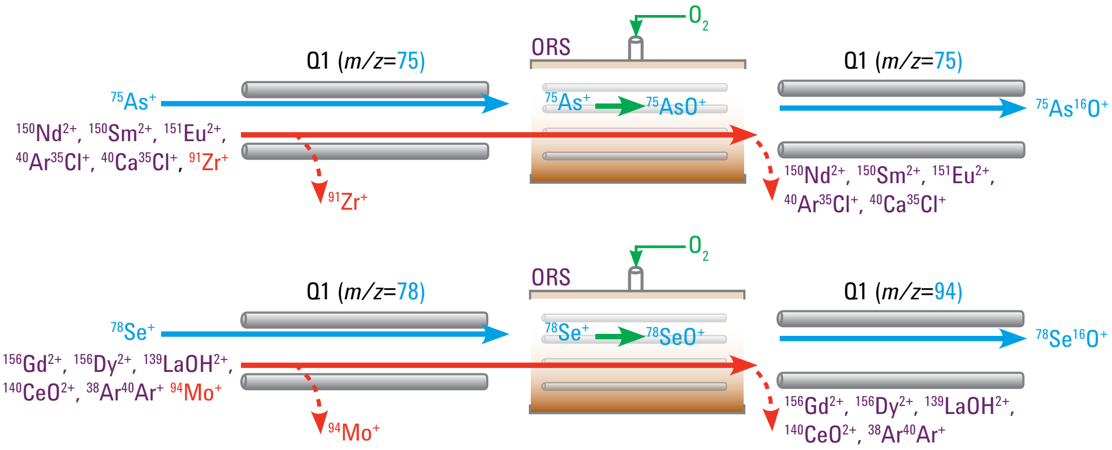

Figure 1. ICP-QQQ MS/MS O_2 mass-shift method for measuring ^{75}As (top) and ^{78}Se (bottom)

Samples and sample preparation: SPEX XSTC-1 (a mixture of 10 ppm each of Ce, Dy, Er, Eu, Gd, Ho, La, Lu, Nd, Pr, Sm, Sc, Tb, Tm, Yb and Y) purchased from SPEX CertiPrep Ltd. (UK) was used. Four certified reference materials (CRMs): NIST 1515 Apple Leaves, NIST 1573a Tomato Leaves, NIST 1575a Pine Needles and NMIJ 7531a Brown Rice, were used for the method validation. It should be noted that NIST 1515 contains 3 mg/kg Sm and Gd, and 0.2 mg/kg Eu. NIST 1573a contains 0.19 mg/kg Sm, 0.17 mg/kg Gd, 5% Ca and 2.7% K, a combination of matrix elements that might be expected to cause severe interferences on As and Se. All CRMs were microwave-digested in HNO_3 and H_2O_2, diluted and analyzed.

Results and discussion

Effectiveness of O_2 mass-shift method for removing REE^{++} interferences

To investigate the effectiveness of interference removal modes on the 8800 ICP-QQQ, As and Se were measured in a mixed REE solution containing 1 ppm each of Ce, Dy, Er, Eu, Gd, Ho, La, Lu, Nd, Pr, Sm, Sc, Tb, Tm, Yb and Y.

Three different 8800 ICP-QQQ cell modes were used:

- Single Quad (SQ); no gas
- Single Quad (SQ); reaction mode using hydrogen (H_2) cell gas
- MS/MS; reaction mode using O_2 cell gas with + 16 amu mass-shift

"Single Quad" represents the performance of conventional ICP-QMS while MS/MS mode is unique to ICP-QQQ.

Figure 2 shows the BECs of As and Se in each of the measurement modes. The results in Figure 2 illustrate the excellent interference removal performance of the O_2 mass-shift method for the detection of As and Se in a matrix containing REEs.

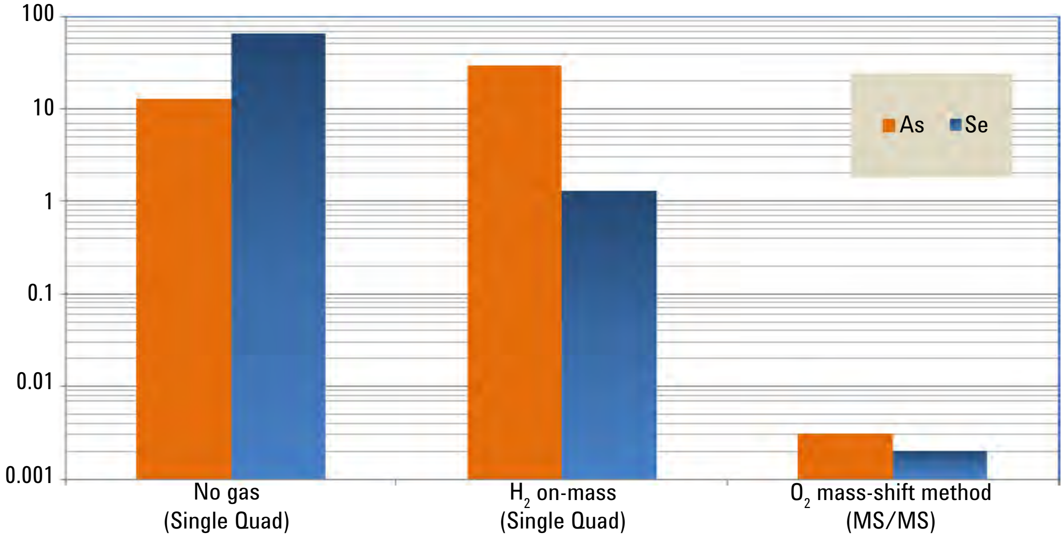

Figure 2. BEC of As and Se in 1ppm REE mixed solution with three measurement modes: no gas, H_2 on-mass and O_2 mass-shift mode.

Figure 3 shows the product ion scan spectra obtained using O_2 mass-shift mode for a solution containing 1 ppm REEs without (left) and with (right) a 1 ppb As spike. As illustrated in the schematic, Q1 was fixed at *m/z* = 75 and Q2 was scanned across the selected mass range, to monitor all existing and cell-formed ions derived from precursor ions at *m/z* 75. Figure 3 (left) shows the product ions from *m/z* 75 in the blank REE matrix; the signal at Q2 *m/z* = 75 (mass of As) is due to REE^{++}. The absence of a signal at *m/z* = 91 (the mass of AsO^+) in the blank REE matrix, indicates that the REEs do not react with O_2 in the cell to give rise to product ions (such as $REEO_2^{++}$) that overlap AsO^+ at *m/z* 91. Consequently, As can be successfully measured as AsO^+ at *m/z* = 91 as shown in Figure 3 (right).

Method validation with CRMs

The ICP-QQQ method was applied to the measurement of As and Se in four CRMs. Table 2 summarizes the results. The measured concentrations of As and Se in the CRMs were all in good agreement with the certified values.

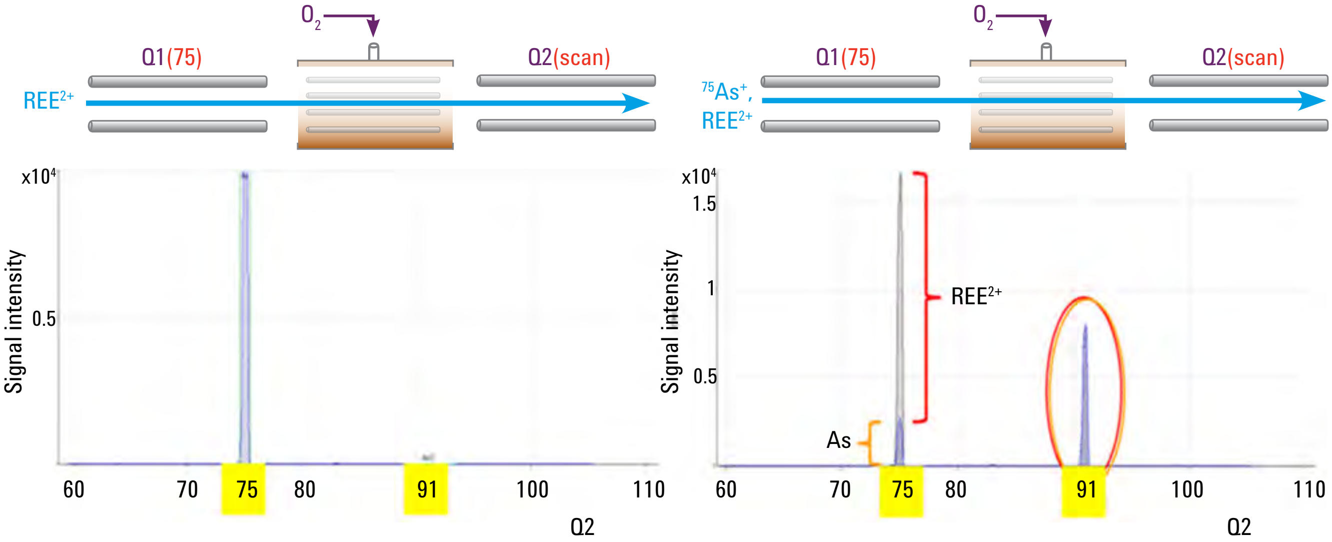

Figure 3. Product ion scan spectrum of O_2 mass-shift method. (Left) 1 ppm mixed-REE solution and (right) 1 ppm mixed-REE plus 1 ppb As spike.

Table 2. Results of the determination of As and Se in four CRMs using MS/MS O_2 mass-shift mode on the 8800 ICP-QQQ

	As (as AsO^+ at *m/z* 91)			**Se (as SeO^+ at *m/z* 94)**		
	Certified	**Found average**	**Recovery**	**Certified**	**Found average**	**Recovery**
	mg/kg	**mg/kg**	**%**	**mg/kg**	**mg/kg**	**%**
NIST1515 Apple Leaves	0.038±0.007	0.037	97	0.050±0.009	0.050	100
NIST1575a Pine Needles	0.039±0.002	0.038	97	0.099±0.004	0.099	100
NIST1573a Tomato Leaves	0.112±0.004	0.113	101	0.054±0.003	0.058	107
NMIJ 7531a Brown Rice	0.280±0.009	0.258	92	NA	0.032	NA

Removal of Molybdenum Oxide Interference on Cadmium

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Agilent Technologies, Japan

Keywords

cadmium, molybdenum oxide, environmental, food, CRMs, hydrogen on-mass

Introduction

Cadmium (Cd) is a well-known toxic element along with As, Hg and Pb. The maximum contamination level of these elements in food, pharmaceuticals, drinking water, wastewater and other matrices is strictly controlled under national and international legislation. Out of the eight natural isotopes of Cd, only ^{111}Cd is free from direct overlap by an atomic isobar (an isotope of a different element at the same mass as the Cd isotope), and even ^{111}Cd is potentially subject to spectroscopic interference by ^{95}MoO$^+$. Fortunately, the concentration of Mo is low in most samples, and quadrupole ICP-MS (ICP-QMS) operating in helium collision mode can remove the interference, allowing the accurate measurement of Cd. However, there are some cases where the Mo concentration is high and a better interference removal technique is required in order to accurately determine Cd. This paper describes the application of MS/MS H_2 reaction mode on the Agilent 8800 ICP-QQQ for the determination of trace Cd in the presence of a high concentration of Mo.

Experimental

Instrumentation: Agilent 8800 #100. Indium (In) was introduced as the internal standard using the on-line ISTD kit.

Plasma conditions and ion lens tune: RF power = 1550 W; sampling depth = 8.0 mm; carrier gas = 1.01 L/min; makeup gas/dilution gas (MUGS/DiGS) = 0.0 L/min; Soft extraction tune: Extract 1 = 0 V, Extract 2 = -165 V, Omega bias = -100 V, Omega = 11.4 V.

CRC conditions: H_2 flow rate 9.0 mL/min, Octopole bias = -22 V, KED = +5 V.

Acquisition parameters: MS/MS H_2 on-mass method i.e. ^{111}Cd was measured at *m/z* 111 using quadrupole settings of (Q1 = 111, Q2 = 111).

Results and discussion

Optimization of H_2 flow rate

Figure 1 (left) shows the signal at *m/z* 111 for a 10 ppm Mo solution and a 10 ppm Mo + 1 ppm Cd solution, plotted as a function of H_2 flow rate. Figure 1 (right) shows the calculated BEC of Cd in the presence of 10 ppm Mo. The optimum cell gas flow rate of 9.0 mL/min was used for subsequent experiments.

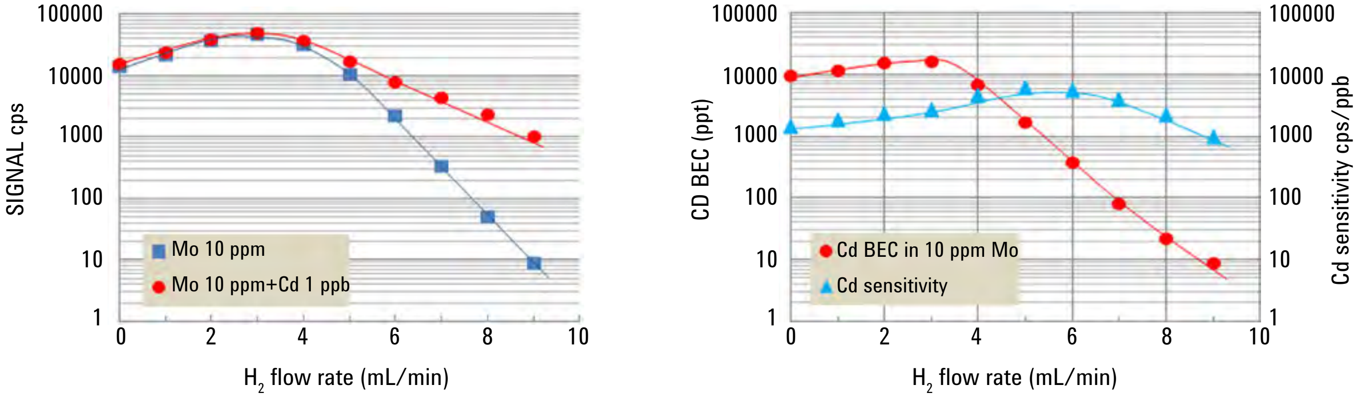

Figure 1. (Left): Signal for *m/z* 111 with 10 ppm Mo and 10 ppm Mo + 1 ppb Cd, plotted as a function of H_2 flow rate. (Right): Estimated Cd BEC in the presence of 10 ppm Mo as a function of H_2 flow rate.

In order to test the effectiveness of MS/MS mode with H_2 cell gas in comparison to no gas mode, a spike recovery test of 1 ppb Cd in a series of Mo matrix solutions ranging from 0.1 to 100 ppm was conducted. Figure 2 summarizes the results. In no gas mode, the error in quantification of the 1 ppb Cd spike dramatically increases with the concentration of Mo; in contrast, H_2 reaction mode delivers a consistent and accurate result for Cd even in the presence of 100 ppm Mo.

Method validation: Analysis of Cd in CRMs

The concentration of Cd was determined in four different CRMs: NIST 1515 Apple Leaves, NIST 1573a Tomato Leaves, NIST 1575a Pine Needles and NMIJ 7531a Brown Rice Flour (National Metrology Institute of Japan). Each sample was microwave digested following the manufacturer's recommended procedures, then diluted and analyzed by ICP-QQQ; the final dilution factor was around 100–200. For each CRM, the digested sample was analyzed using the developed method. A second sample of each CRM was prepared and analyzed after the addition of a 10 ppm Mo spike. As summarized in Table 1, good recoveries were obtained for all four references materials both for the unspiked samples and the duplicates with the high added Mo concentration, demonstrating the validity of the method for real sample analysis.

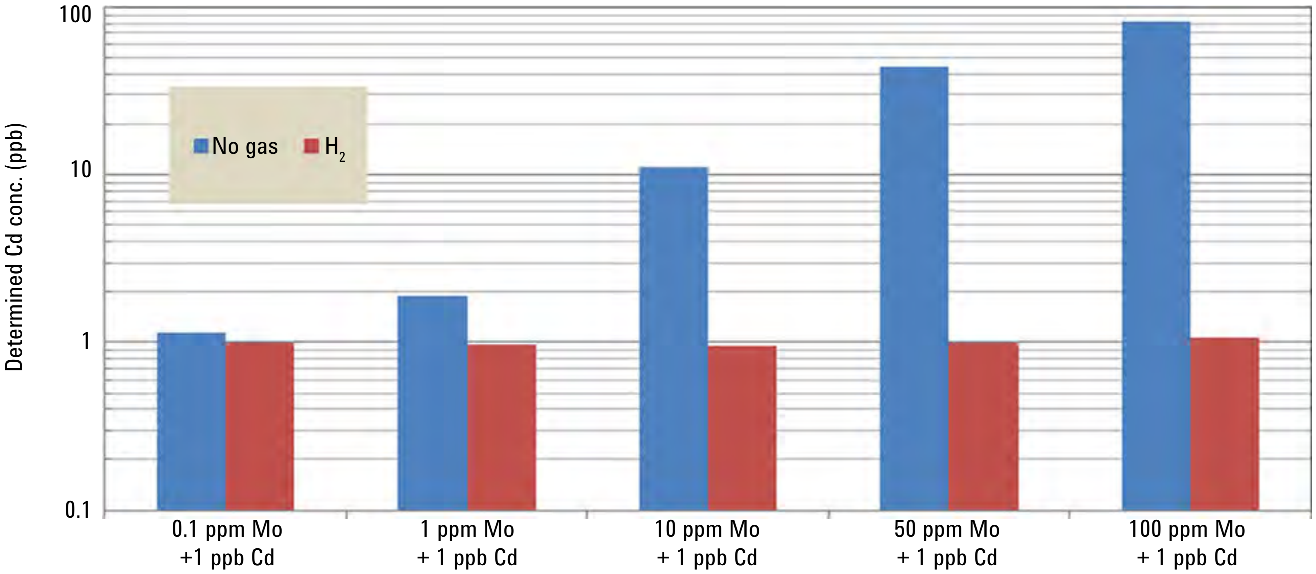

Figure 2. 1 ppb Cd spike recovery in a series of Mo matrix solutions using no gas mode and MS/MS H_2 mode

Table 1. Measurement of Cd in four CRMs using the 8800 ICP-QQQ in MS/MS mode with H_2 reaction gas

		Without Mo addition		With 10 ppm Mo addition	
CRMs	Certified	Determined	Recovery	Determined	Recovery
	mg/kg	mg/kg	%	mg/kg	%
NIST 1515 Apple Leaves	0.014	0.013	93	0.016	115
NIST1573a Tomato Leaves	1.52	1.496	98	1.475	97
NIST1575a Pine Needles	0.223	0.220	99	0.224	100
NMIJ 7531a Brown Rice Flour	0.308	0.298	97	0.293	95

Feasibility Study of Fluorine Detection by ICP-QQQ

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Keywords

fluorine-containing polyatomic ions, barium, oxygen on-mass, ammonia mass-shift

Introduction

Fluorine (^{19}F) cannot be directly detected by conventional quadrupole ICP-MS (ICP-QMS) because of severe water-derived interferences at *m/z* 19 from $^{1}H_3{}^{16}O^+$ and $^{1}H^{18}O^+$, and extremely low sensitivity due to the fact that it is very difficult to convert fluorine atoms to the positive ions that are measured in ICP-MS. The interference problem can be resolved by high resolution ICP-MS, but the sensitivity issue remains a challenge because almost no F atoms are ionized in an argon plasma due to F having an ionization potential (17.423 eV) that is higher than that of Ar (15.760 eV).

However, fluorine-containing polyatomic ions (XF^+) can be formed in the plasma and they may be used to determine fluorine. Candidate ions are those with a high bond-dissociation energy for the X^+-F bond and low ionization potential of X or XF. Since oxygen is present in the plasma (from the water matrix or from air entrainment), the formation of XO^+ or XO often competes against that of XF^+. Therefore, a low bond-dissociation energy for X^+-O and X-O bonds (low affinity of X^+ and X for O) is also desirable for the efficient formation of XF^+. Barium was selected as "X" for this feasibility study, based on its thermochemical properties (Table 1).

Experimental

Instrumentation: Agilent 8800 #200 with a Micromist nebulizer.

Plasma conditions and ion lens tune: RF power = 1500 W; Sampling depth = 8 mm; CRGS flow rate = 1.00 L/min; sample uptake rate 0.33 mL/min; 100 ppm Ba uptake rate = 0.03 mL/min; MUGS flow rate = 0.32 L/min; Extract 1 = -150 V, Extract 2 = -4 V.

CRC conditions: O_2 gas at 1 mL/min (100%), Octopole bias = -60 V, Energy discrimination = -10 V in O_2 mode; 10% NH_3/90% He flow rate 8.5 mL/min (85%), Octopole bias = -20 V, Energy discrimination = -10 V in NH_3 mode.

Acquisition parameters: MS/MS O_2 on-mass and MS/MS NH_3 mass-shift. Integration time per mass for BaF and $BaF(NH_3)_3$ = 1 sec; integration time per mass for $BaF(NH_3)_4$ = 10 sec.

In order to produce BaF^+ in the plasma, Ba solution was mixed online with fluorine standards per a fixed mixing ratio of 1:10. The mixing occurred just before the nebulizer. BaF^+ was efficiently formed under general plasma conditions with the BaO^+/Ba^+ ratio at about 11%. Under hotter plasma conditions, the formation of BaF^+ decreases because it tends to break apart. Under cooler plasma conditions, the formation of BaF^+ also decreases because of the formation of BaO^+ or, possibly, BaO. The signal intensity of BaF^+ was proportional to the concentration of Ba, which was fixed at about 10 ppm (after mixing).

Table 1. Gas phase thermochemical properties of elements having an affinity for fluorine*

Element X	$D_0(X^+$-F)	IP (X)	D_0(X-F)	IP (XF)	$D_0(X^+$-O)	D_0(X-O)
C	7.77	11.27	5.60	9.11	8.35	11.15
Al	3.16	5.99	6.99	9.73	1.81	5.31
Si	7.01	8.15	5.69	7.54	4.99	11.49
Ba	6.39	5.21	5.98	4.70	5.60	5.80
La	6.83	5.61	6.86	5.56	8.73	8.50
Eu	6.05	5.67	5.59	5.90	4.00	5.90

**Unit: eV. D_0(A-F) is the bond-dissociation energy for A-F bond (affinity of A for F) and IP(B) is the ionization potential of B.*

Interference removal using MS/MS mode

$^{138}Ba^{19}F^+$ (*m/z*=157) suffers an interference from $^{138}Ba^{18}O^1H^+$. O_2 and NH_3 were tested as reaction gases to reduce the interference. It was found that O_2 reacts with $BaOH^+$ more efficiently than it reacts with BaF^+ in high energy reaction mode (octopole bias < -50 V). Therefore, using MS/MS mode, a mass pair (Q1 → Q2) = (157 → 157) was selected to detect BaF^+ in O_2 mode. With Q1 set to 157 amu, $^{138}Ba^+$ was prevented from entering the cell and forming new interferences through unwanted reactions.

NH_3 was found to react with BaF^+ at a high NH_3 flow rate to form $BaF(NH_3)_n^+$, where n = 2, 3, 4. The most abundant complex ion was $BaF(NH_3)_3^+$ at *m/z* = 208, but $BaF(NH_3)_4^+$ at *m/z* = 225 was preferable in terms of signal to background ratio or BEC. Mass pairs (Q1 → Q2) = (157 → 208) and (157 → 225) were selected in NH_3 mode.

Results and discussion

Figures 1 and 2 show calibration curves up to 2 mg/L (ppm) for fluorine in deionized water. The lowest detection limit (27 ppb) was obtained in O_2 mode. The lowest BEC (87 ppb) was obtained by measuring $BaF(NH_3)_4^+$ in NH_3 mode. Table 2 shows the BEC and DL results for F obtained from this study in comparison with the literature values.

Conclusions

Based on this preliminary study, it is clear that the controlled reaction chemistry that is possible with MS/MS mode on the 8800 ICP-QQQ can provide a novel approach to the measurement of F by ICP-MS. In addition to demonstrating detection limits that are comparable with published data measured using conventional quadrupole ICP-MS or high-resolution ICP-MS, the 8800 ICP-QQQ also allows unprecedented flexibility to monitor specific reaction transitions, making it invaluable for method development.

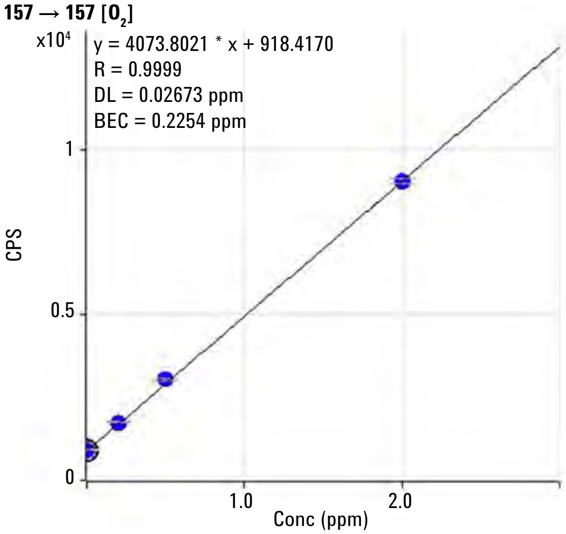

Figure 1. Calibration curve for F measured as BaF^+ in O_2 mode

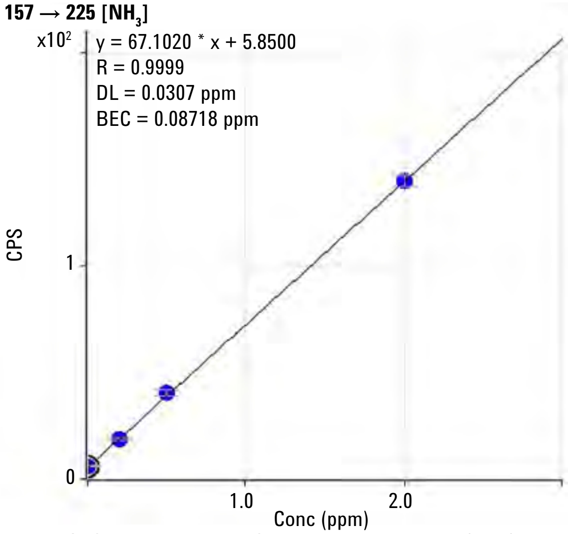

Figure 2. Calibration curve for F measured as $BaF(NH_3)_4^+$ in NH_3 mode

Table 2. Analytical performance for fluorine detection by ICP-MS

Analyte ion	Sensitivity [cps/ppm]	BEC [ppm]	DL [ppm]	Technique, reference
F^-	60,000	NA	0.11	Negative ion mode ICP-MS, Appl. Spectrosc, 42, 425 (1988)
F^+	3,000	NA	0.023	He-ICP-MS, Japan analyst 52(4), 275-278, 2003
Al^+ (AlF^{2+} complex)	NA	0.0033	0.0001	IC-ICP-MS (indirect determination), Analyst. 1999 Jan;124(1):27-31
F^+	26	2.05	5.07	HR-ICP-MS, J. Anal. At. Spectrom, 18, 1443, 2003
BaF^+	4,073	0.23	0.027	ICP-QQQ, O_2 mode, this work
$BaF(NH_3)_3^+$	929	0.17	0.043	ICP-QQQ, NH_3 mode, this work
$BaF(NH_3)_4^+$	67	0.087	0.031	ICP-QQQ, NH_3 mode, this work

ICP-QQQ with Oxygen Reaction Mode for Accurate Trace-Level Arsenic Analysis in Complex Samples

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Keywords

arsenic, zirconium, doubly-charged ion interferences, oxygen mass-shift

Introduction

Arsenic (As), with its high first ionization potential and single isotope at mass 75, is one of the most difficult elements to measure accurately by ICP-MS, particularly in complex matrices. The polyatomic interferences from $ArCl^+$ and $CaCl^+$ that overlap As^+ at mass 75 can be removed effectively using quadrupole ICP-MS (ICP-QMS) in helium collision mode, but collision mode cannot resolve the doubly-charged ion interferences from $^{150}Nd^{++}$ and $^{150}Sm^{++}$. A quadrupole mass spectrometer separates ions based on their mass to charge ratio (*m/z*), so doubly-charged ions appear at half their true mass; $^{150}Nd^{++}$ and $^{150}Sm^{++}$ therefore give an apparent overlap on As at mass 75.

Oxygen reaction mode (O_2 mode) offers a solution to these doubly-charged ion overlaps, since As can be converted to a reaction product ion $^{75}As^{16}O^+$, measured at *m/z* 91, where it is separated from the doubly charged Nd and Sm, which do not form such product ions. However, the new mass of the AsO^+ product ion is also overlapped by an isotope of zirconium ($^{91}Zr^+$). The presence of Zr in a sample may therefore cause an error in the results for As measured as AsO^+ using O_2 reaction mode on ICP-QMS.

ICP-QQQ solves this problem, as MS/MS mode allows all masses apart from *m/z* 75 (including the $^{91}Zr^+$ ions) to be rejected by the first quadrupole (Q1), ensuring that the AsO^+ product ions can be measured free from overlap. ICP-QQQ with MS/MS therefore allows the accurate determination of As in complex samples that contain any combination of Cl, Ca, Nd, Sm and Zr.

Experimental

Reagents and sample preparation: All of the sample matrices used for this work were prepared using single-element stock solutions (Spex CertiPrep, Claritas grade). The acid matrix and elemental standard concentrations are shown in the caption for each spectrum and are representative of the acid matrix (dilute HNO_3/HCl) and matrix levels commonly found in ICP-MS samples.

The sample matrices investigated were:

- Dilute nitric acid (1% HNO_3)
- Dilute hydrochloric acid (5% HCl)
- Calcium (100 ppm)
- Neodymium and samarium (1 ppm each element)
- Zirconium (0.5 ppm)

Instrumentation: Agilent 8800 #100.

Plasma conditions and ion lens tune: Preset plasma/General purpose, Soft extraction tune: Extract 1 = 0 V, Extract 2 = -170 V.

Acquisition conditions: Four operational modes were used, to investigate the different interference removal performance provided by the different cell modes:

- Single Quad (SQ); no gas
- Single Quad (SQ); collision mode (using helium (He) cell gas at a flow rate of 4 mL/min)
- Single Quad (SQ); reaction mode (using oxygen (O_2) cell gas at a flow rate of 0.2 mL/min).
- MS/MS; reaction mode (using O_2 cell gas at a flow rate of 0.2 mL/min)

KED bias voltage was +5 V in no gas and He mode, and -8 V in O_2 mode.

The three "Single Quad" modes represent the performance available on conventional ICP-QMS operating in collision or reaction mode. MS/MS mode is unique to the tandem mass spectrometer configuration of the 8800 ICP-QQQ.

Results and discussion

Figures 1a, 1b and 1c illustrate how Single Quad mode with He cell gas is effective at removing the common $ArCl^+$ and $CaCl^+$ polyatomic interferences on As^+ at *m/z* 75, but is ineffective against the Nd^{++}/Sm^{++} interferences.

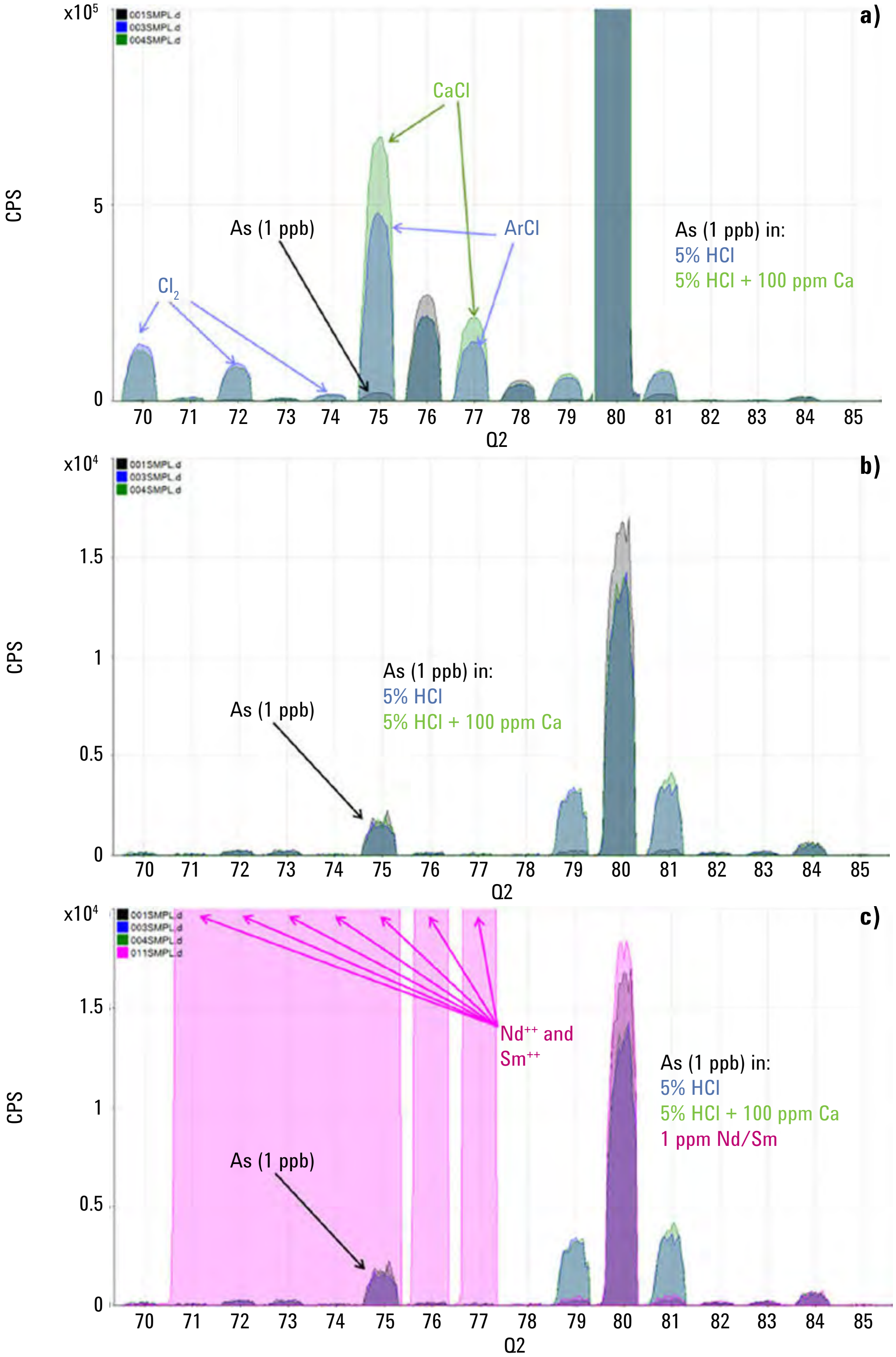

Figure 1. a) As^+ (*m/z* 75) in no gas mode, showing polyatomic interferences from $ArCl^+$ and $CaCl^+$; **b)** $ArCl^+$ and $CaCl^+$ polyatomics are removed in He collision mode; **c)** He collision mode fails to remove Nd^{++} and Sm^{++} interferences at *m/z* 75.

Figures 2a and 2b show how Single Quad mode with O_2 reaction gas successfully avoids the doubly-charged Nd and Sm interferences by mass-shifting the As to the new AsO^+ product ion mass at *m/z* 91; but O_2 reaction mode on ICP-QMS cannot remove the $^{91}Zr^+$ overlap on the AsO^+ product ion.

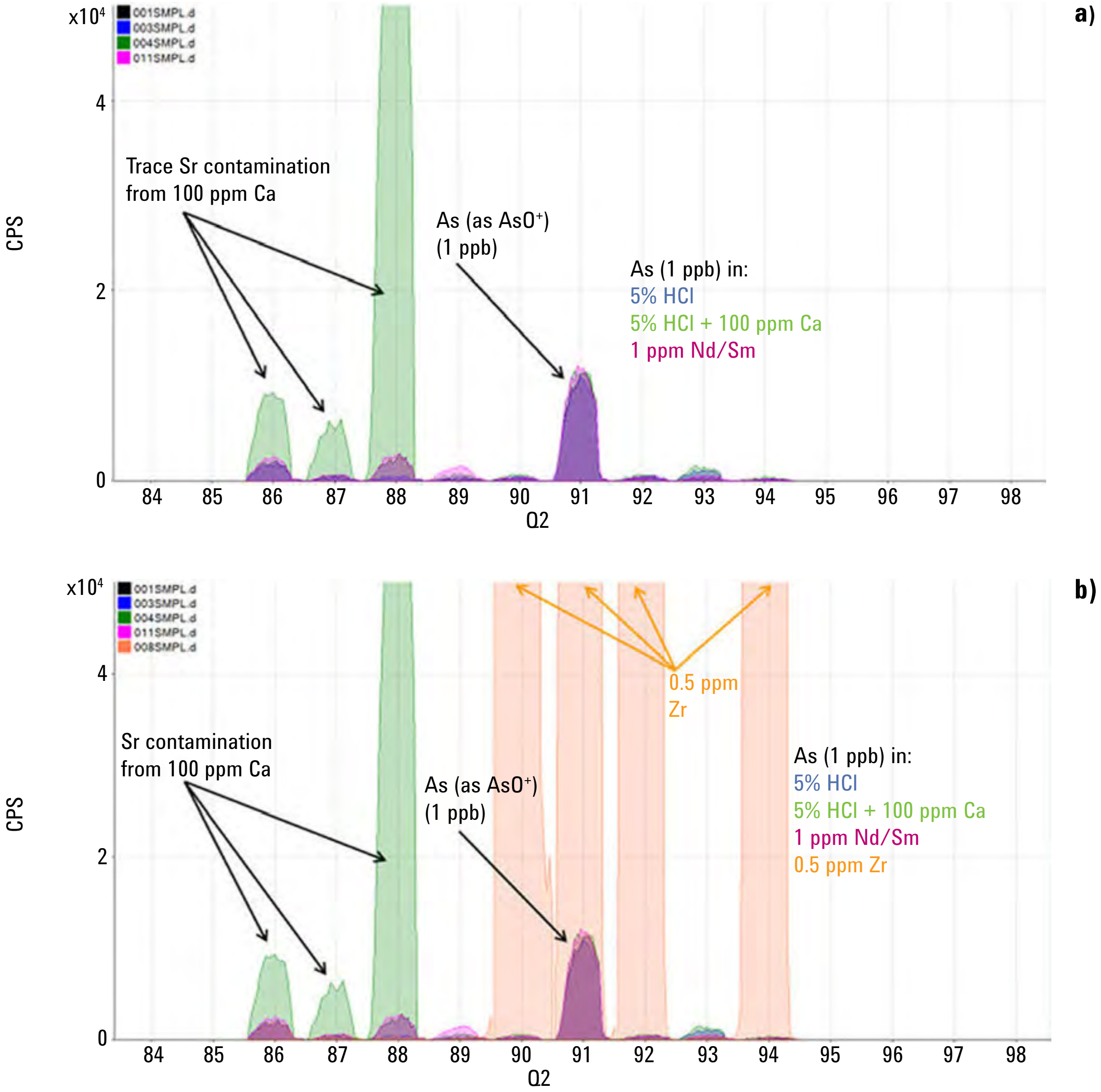

Figure 2. a) Nd^{++} and Sm^{++} interferences at *m/z* 75 are avoided in SQ O_2 reaction mode, by measuring As as the AsO^+ product ion at *m/z* 91; **b)** SQ O_2 reaction mode fails to remove $^{91}Zr^+$ overlap on the AsO^+ product ion.

Figure 3 shows that the 8800 ICP-QQQ in MS/MS mode with O_2 reaction gas provides reliable and consistent measurement of As (as AsO^+) in all matrices. All the original polyatomic and doubly-charged interferences at *m/z* 75 are avoided by mass-shifting the As to *m/z* 91; and in MS/MS mode the $^{91}Zr^+$ ion is removed by Q1, so the potential overlap on the AsO^+ product ion at *m/z* 91 is also removed.

Conclusions

With the combination of O_2 reaction mode and MS/MS operation, the 8800 ICP-QQQ provides a reliable approach to the accurate measurement of As in complex samples. All the polyatomic and doubly-charged interferences that affect As measurement at its native mass (*m/z* 75) are avoided by using O_2 mode to mass-shift the As to its AsO^+ product ion, measured at *m/z* 91. Furthermore, uniquely to the 8800 ICP-QQQ, MS/MS mode also eliminates potential native ion overlaps at *m/z* 91, as they are rejected by Q1 that is set to *m/z* 75 when measuring As.

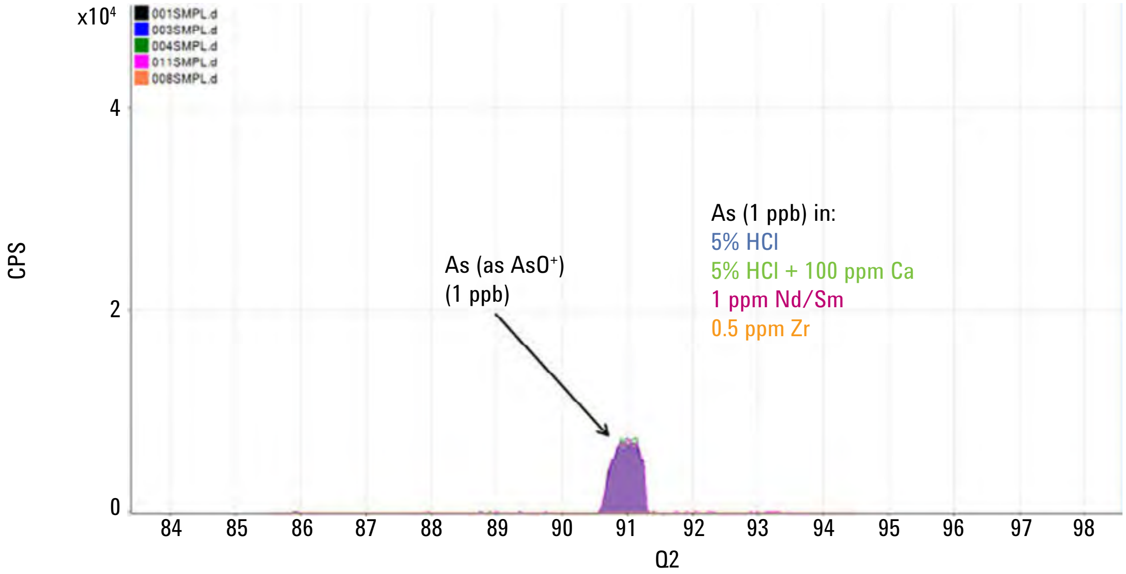

Figure 3. MS/MS mass-shift with O_2 reaction mode provides consistent, interference-free measurement of As as AsO in all the matrices.

Avoidance of Spectral Overlaps on Reaction Product Ions with O_2 Cell Gas: Comparison of Quadrupole ICP-MS and ICP-QQQ

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Keywords

titanium, reaction chemistry, oxygen mass-shift

Introduction

The 8800 ICP-QQQ opens up many new analytical possibilities and novel methodologies for interference removal based on reaction chemistry. The major benefit provided by the 8800 ICP-QQQ is its unique tandem mass spectrometer configuration, which permits operation in MS/MS mode. In MS/MS, the first quadrupole (Q1) operates as a 1 amu mass filter, providing precise selection of the ions that can enter the reaction cell, and therefore control of the reaction processes that occur. This level of reaction process control is fundamentally different to the operation of conventional quadrupole ICP-MS (ICP-QMS) when using these same reaction chemistries, as ICP-QMS has no way to reject ions before they enter the cell, and so cannot select which ions are involved in the reactions.

This difference is apparent in many reaction chemistries, including both on-mass measurements (where the interfering ions are reactive and are moved away from the analyte ions, which are then measured at the natural mass), and mass-shift methods (where the analyte ions are reactive and are moved to a new product ion mass that is free from the original overlap). Overlaps on analyte product ions commonly occur in ICP-QMS and can give severe errors in results, especially in cases where the sample matrix or co-existing analyte levels vary from sample to sample.

Table 1. Potential native ion overlaps on TiO^+ product ions in O_2 reaction mode

Precursor ion (Q1)	Product ion (Q2)	Potential overlaps from other analytes		
Ti	**TiO**	**Ni**	**Cu**	**Zn**
46	62	^{62}Ni	–	–
47	63	–	^{63}Cu	–
48	64	–	–	^{64}Zn
49	65	–	^{65}Cu	–
50	66	–	–	^{66}Zn

In this note, we compare the performance of ICP-QMS (the 8800 ICP-QQQ operated in Single Quad mode with Q1 as a bandpass filter) and ICP-QQQ (the 8800 ICP-QQQ operated in MS/MS mode) for the measurement of titanium (Ti) as TiO^+ product ions, using oxygen reaction mode (O_2 mode).

The native ion overlaps that could affect the measurement of TiO^+ product ions with oxygen reaction gas are shown in Table 1. It should be noted that these native ion overlaps cannot be rejected by the cell bandpass settings of a conventional quadrupole ICP-MS, because they occur at the same mass as the analyte product ion being measured.

Experimental

For the spectral comparison, scan data were collected for the mass range from *m/z* 60 to 69, covering the TiO^+ product ions formed from Ti in O_2 reaction mode.

Instrumentation: Agilent 8800 #100.

Plasma conditions and ion lens tune: Preset plasma/General purpose, Soft extraction tune: Extract 1 = 0 V, Extract 2 = -180 V.

CRC conditions: Cell gas = O_2 gas at 0.3 mL/min, Octopole bias = -5 V, KED = -7 V.

Acquisition parameters: Scan range = *m/z* 60 to 69; points per peak = 20; integration time per mass = 1 sec.

Results and discussion

The comparative results for TiO^+ measured in Single Quad (SQ) mode and MS/MS mode are shown in the overlaid spectra in Figures 1 and 2. In both cases, the TiO^+ ions at mass 62, 63, 64, 65 and 66 (from the 5 isotopes of Ti at 46, 47, 48, 49 and 50, respectively) are shown, measured using the same O_2 reaction mode conditions for both modes. The four solutions measured for the overlaid spectra are:

1. 1 ppb Ti in 1% HNO_3
2. 1 ppb Ti + 10 ppb Ni in 1% HNO_3
3. 1 ppb Ti + 10 ppb Cu in 1% HNO_3
4. 1 ppb Ti + 10 ppb Zn in 1% HNO_3

The overlaid spectra in Single Quad mode, shown in Figure 1, show that the peaks for the five TiO^+ isotopes match the theoretical isotopic template in the 1 ppb Ti sample. However, in the other samples containing the elements Ni, Cu and Zn, all of the TiO^+ product ions suffer significant overlap from the native Ni (*m/z* 62), Cu (*m/z* 63 and 65) and Zn (*m/z* 64 and 66) ions. Unexpected or variable levels of these common elements would lead to an error in the reported results for Ti measured as TiO^+ using quadrupole ICP-MS in O_2 reaction mode.

In contrast, the overlaid spectra for MS/MS mode, shown in Figure 2, demonstrate consistent measurement of all five TiO^+ product ions in all four solutions. The presence of the other elements Ni, Cu and Zn has no impact on the TiO^+ peaks and all five TiO^+ product ion isotopes could be used to give reliable results for Ti in these variable samples. This illustrates how MS/MS mode on the 8800 ICP-QQQ can simplify method development, because consistent cell conditions, acquisition parameters and isotope selection can be used for a range of variable sample types. A further benefit is that interferences are removed from all isotopes under the same cell conditions, so secondary (or qualifier) isotopes become available for data confirmation or isotope analysis.

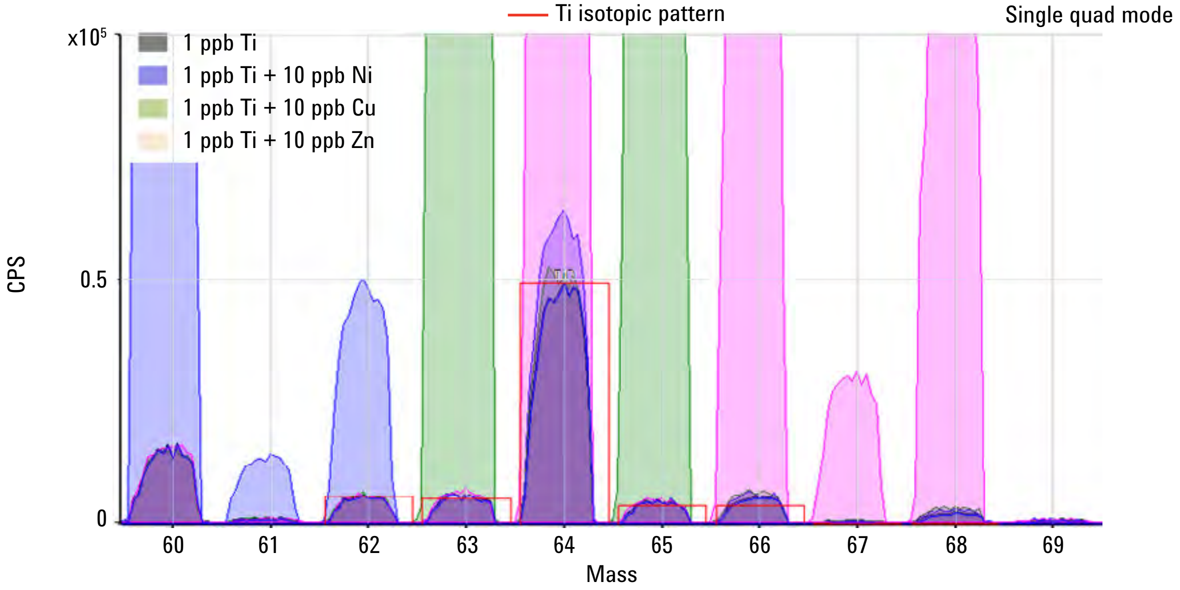

Figure 1. Overlaid spectra for TiO^+ product ions in variable samples measured using SQ mode (see text for sample composition).

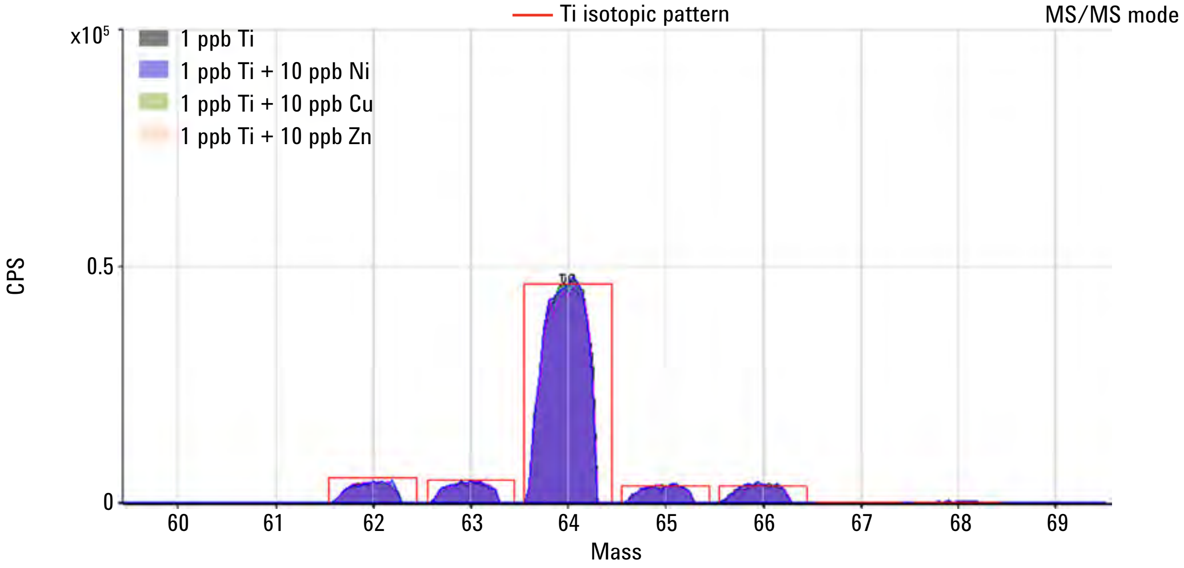

Figure 2. Overlaid spectra for TiO^+ product ions in variable samples measured using MS/MS mode (see text for sample composition)

Conclusions

The comparative spectra presented in this note illustrate the improved accuracy and consistency delivered by ICP-QQQ operating in MS/MS mode, compared to a conventional quadrupole ICP-MS using a reaction cell with bandpass filter. By rejecting non-target native ions that would occur at the same mass as analyte product ions, potential interferences can be eliminated by MS/MS. This allows simpler, more consistent method development, as well as improving accuracy for interfered elements in complex and variable samples.

Removal of Complex Spectral Interferences on Noble Metal Isotopes

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Keywords

Platinum Group Elements, gold, silver, ore exploration, geochemical, environmental, catalytic converter, ammonia

Introduction

The precise determination of the noble metals, comprising the Platinum Group Elements (PGEs: Ru, Rh, Pd, Os, Ir and Pt), Au and Ag, is of great interest in areas such as ore exploration and geochemical studies, and these metals are increasingly used for industrial applications including advanced materials and alloys, medical devices, and catalysts for pharmaceutical manufacturing. Environmental monitoring is also required as some of these elements are used in automobile catalytic converters. ICP-MS is widely used for these applications due to its high sensitivity and multi-element capability. However, the analysis is challenging because the metal concentrations are often low and they are subject to severe spectral overlaps.

Table 1 summarizes the interferences and abundance (%) of each isotope of the elements (the isotopes highlighted in yellow represent the recommended isotope for determination by ICP-MS). Several methods have been developed to resolve the interferences, such as mathematical correction, matrix removal and high-resolution magnetic sector (HR-)ICP-MS. However the mass resolution required to separate some of the interferences is beyond the capability of current commercial HR-ICP-MS. For example separation of $^{103}Rh^+$ from $^{87}Sr^{16}O^+$, $^{105}Pd^+$ from $^{89}Y^{16}O^+$, and $^{109}Ag^+$ from $^{93}Nb^{16}O^+$ requires mass resolution (M/ΔM) of 102900, 27600 and 31500, respectively; commercial HR-ICP-MS instruments

Table 1. Abundance (%) of each isotope of noble metals and the interference on each isotope

m		96	97	98	99	100	101	102	103	104	105	106	107	108	109	110
Element	**Ru**	5.54		1.87	12.76	12.6	17.06	31.55		8.62						
	Rh								100							
	Pd							1.02		11.14	22.33	27.33		26.46		11.72
	Ag												51.84		48.16	
Interference	Atomic	Zr, Nb, Mo		Mo		Mo						Cd		Cd		Cd
	MH			MoH	MoH		MoH									
	MO, MOH	SeO, BrOH		SeO		SrO	RbO	SrO	SrO, RbO	SrO	YO, SrOH	YOH, ZrO	ZrO	ZrO, MoO	NbO	ZrO, MoO
	Argide			NiAr		NiAr	NiAr	NiAr	CuAr	ZnAr	CuAr	ZnAr	ZnAr	ZnAr		
	others			CuCl	ZnCl	CuCl	ZnCl	CuCl, ZnCl	ZnCl, Pb^{++}	ZnCl	ZnCl					

m		184	185	186	187	188	189	190	191	192	193	194	195	196	197	198
Element	**Os**	0.02		1.59	1.96	13.24	16.15	26.26		40.78						
	Ir								37.3		62.7					
	Pt							0.014		0.782		32.97	33.83	25.24		7.163
	Au														100	
Interference	Atomic	W		W	Re									Hg		Hg
	MH				WH											
	MO, MOH			YbO	YbO	YbO	YbO	YbO	LuO	YbO, LuD, HfO	HfO	HfO	HfO	HfO	TaO, HfOH	Wo, TaOH
	Argide	NdAr	NdAr	NdAr	SmAr	SmAr, NdAr	SmAr	SmAr, NdAr	EuAr	SmAr	EuAr	SmAr, GdAr	GdAr	GdAr	GdAr	GdAr
	others															

are limited to a maximum resolution of 10,000. To remove the multiple, complex interferences on noble elements, the Agilent 8800 ICP-QQQ was used in MS/MS mode, using ammonia as the reaction gas.

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/Low matrix.

Ion lens tune: Soft extraction tune: Extract 1 = -3 V, Extract 2 = -200 V.

CRC conditions: NH_3 (10% NH_3 in He) was used as CRC gas in MS/MS mode.

Following a preliminary optimization study, three different NH_3 gas flow rates (low (L), medium (M) and high (H)) were used. Cell conditions are given in Table 2. No gas mode was also applied for comparison purposes.

Table 2. CRC conditions

	No gas	NH_3-L	NH_3-M	NH_3-H
Cell gas	na	NH_3	NH_3	NH_3
Gas flow rate (mL/min)	na	2.0	3.0	5.0
Octopole bias (V)	-8	-5	-10	-12
KED (V)	+5	-8		
Cell exit (V)	-90			
Deflect lens (V)	20	10	6	2
Plate lens (V)	-110			

Method

The BECs of the noble metals were determined in a series of synthetic-matrix samples, using an external calibration method. Indium (In) internal standard (ISTD) was mixed online with the sample via the standard ISTD mixing T-connector. An integration time of 1 s per isotope was used with 3 replicates (7 replicates for blank).

Samples and sample preparation

Standards and matrix samples were prepared from single element stock solutions purchased from Kanto Chemical Co., Inc. (Saitama, Japan) and a REE mixture standard, XSTC-1 purchased from Spex certiPrep. All solutions were diluted into a final acid mix of 1% HNO_3 and 3% HCl.

Results

Matrix interference study

Tables 3 and 4 summarize the results of the spectral interference study obtained by analyzing individual synthetic matrix blank solutions. Table 3 shows the observed interferences, expressed as BEC (ppb), in each matrix blank measured using no gas mode. As expected from Table 1, the synthetic matrices caused significantly elevated BECs (>> 1 ppb) on all the primary and secondary isotopes of all the analytes except for Ru; Rh suffered a relatively minor increase in BEC of ~0.5 ppb in the 10 ppm Pb/1 ppm Hg matrix.

Table 4 shows the results obtained using NH_3 reaction mode. The optimum gas flow rate for NH_3 for each element was investigated and three gas flow rates (Low: 2.0, Medium: 3.0, and High: 5.0 mL/min) were used. The best isotope and method is highlighted in bold in the Table. It can clearly be seen that NH_3 reaction mode effectively removes the interferences on all the analytes, giving BECs of << 0.1 ppb for the preferred isotope/cell mode in all the matrices. The mechanism for the removal of each interference using the MS/MS capability of the 8800 ICP-QQQ is as follows:

- **Ru:** slight interferences from Zn and Mo were resolved using on-mass method with NH_3-M.
- **Rh:** Pb^{++} interference was resolved using on-mass method with NH_3-M.
- **Pd:** significant interferences from $SrOH^+$ and YO^+ were seen on ^{105}Pd, the only isotope free from atomic isobar. On-mass method with NH_3-H removed the interferences.
- **Ag:** significant ZrO^+ interference on both ^{107}Ag and ^{109}Ag was resolved using on-mass method with NH_3-H.
- **Os:** YbO^+ interference was observed on both $^{188}Os^+$ and $^{189}Os^+$. Since Os^+ sensitivity in NH_3 mode is low, but Os^+ forms a product ion of $OsNH^+$, NH_3-L with mass-shift gave the best result.
- **Ir:** LuO^+ and HfO^+ interfere with $^{191}Ir^+$ and $^{193}Ir^+$ respectively. NH_3-M with mass-shift method worked for $^{191}Ir^+$ as Ir^+ forms a product ion of $IrNH^+$.
- **Pt:** $^{195}Pt^+$ suffers a significant interference from HfO^+. While the overlap is less significant on $^{198}Pt^+$, $^{198}Pt^+$ suffers an atomic isobar interference from $^{198}Hg^+$. However Hg^+ is effectively neutralized by NH_3 so $^{198}Pt^+$ can be measured free from interference.
- **Au:** significant interferences by TaO^+ and $HfOH^+$ are resolved by mass-shift method with NH_3-M. Au^+ forms a product ion of $Au(NH_3)_2^+$.

Table 3. Summary of spectral interferences in no gas mode, showing analyte BECs (ppb) in each matrix blank. Matrix overlaps that made a significant contribution to the analyte BECs are indicated in red (BEC > 10 ppb) and orange (BEC > 1 ppb).

	Ru		Rh	Pd	Ag		Os			
Isotope	99	101	103	105	107	109	188		189	
NH_3 flow rate mL/min	NA									
Method	on-mass	on-mass	on-mass	on-mass	on-mass	on-mass	on-mass		on-mass	
Mass pair	99-99	101-101	103-103	105-105	107-107	109-109	188-188		189-189	
10 ppm Cu Zn	0.058	0.041	0.138	0.328	0.064	0.061	0.000		0.000	
10 ppm Sr Rb	0.000	0.034	0.150	4.39	0.005	0.001	0.000		0.000	
10 ppm Ni	0.007	0.019	0.000	0.022	0.012	0.016	0.000		0.000	
10 ppm Mo	0.059	0.018	0.000	0.004	0.000	0.018	0.000		0.000	
10 ppm Pb, 1 ppm Hg	0.000	0.000	0.472	0.002	0.033	0.034	0.000		0.000	
10 ppm Zr Nb	0.000	0.000	0.000	0.022	21.9	1.59	0.000		0.000	
10 ppm REE	0.004	0.000	0.009	165	0.147	0.005	2.78		2.99	
10 ppm Ta	0.008	0.000	0.000	0.004	0.003	0.000	0.000		0.000	
10 ppm Hf	0.000	0.000	0.000	0.004	0.312	0.026	0.000		0.000	
10 ppm W	0.000	0.000	0.000	0.003	0.001	0.001	0.000		0.000	

Table 3. continued

	Ir				Pt				Au	
Isotope	191		193		195		198		197	
NH_3 flow rate mL/min	NA									
Method	on-mass		on-mass		on-mass		on-mass		on-mass	
Mass pair	191-191		193-193		195-195		198-198		197-197	
10 ppm Cu Zn	0.003		0.002		0.000		0.279		0.001	
10 ppm Sr Rb	0.002		0.000		0.001		0.310		0.004	
10 ppm Ni	0.009		0.004		0.002		0.444		0.011	
10 ppm Mo	0.000		0.000		0.000		0.295		0.000	
10 ppm Pb, 1 ppm Hg	0.002		0.002		0.000		1293		0.000	
10 ppm Zr Nb	0.002		0.775		1.98		3.17		0.417	
10 ppm REE	123		0.712		0.788		2.17		0.138	
10 ppm Ta	0.000		0.000		0.244		114		284	
10 ppm Hf	0.071		28.1		70.9		2.34		14.1	
10 ppm W	0.001		0.000		0.000		19.6		0.002	

Table 4. Summary of spectral interferences in MS/MS NH$_3$ reaction cell mode, showing analyte BECs (ppb) in each matrix blank. Matrix overlaps that made a significant contribution to the analyte BECs are indicated in red (> 10 ppb) and orange (> 1 ppb).

	Ru		**Rh**	**Pd**	**Ag**		**Os**			
Isotope	99	**101**	**103**	**105**	107	**109**	188		**189**	
NH$_3$ flow rate mL/min	3.0		3.0	5.0	5.0		2.0			
Method	on-mass	**on-mass**	**on-mass**	**on-mass**	on-mass	**on-mass**	on-mass	mass-shift	on-mass	**mass-shift**
Mass pair	99-99	101-101	103-103	105-105	107-107	109-109	188-188	188-203	189-189	189-204
10 ppm Cu Zn	0.000	0.000	0.000	0.001	0.061	0.057	0.000	0.000	0.001	0.002
10 ppm Sr Rb	0.000	0.005	0.016	0.033	0.000	0.000	0.000	0.000	0.002	0.000
10 ppm Ni	0.000	0.000	0.000	0.000	0.010	0.009	0.000	0.000	0.000	0.000
10 ppm Mo	0.005	0.001	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.000
10 ppm Pb, 1 ppm Hg	0.000	0.000	0.000	0.001	0.033	0.035	0.000	0.000	0.001	0.000
10 ppm Zr Nb	0.000	0.000	0.000	0.000	0.003	0.000	0.000	0.000	0.002	0.001
10 ppm REE	0.000	0.000	0.000	0.014	0.004	0.004	2.79	0.003	5.85	0.010
10 ppm Ta	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.003	0.000
10 ppm Hf	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.058	0.000
10 ppm W	0.000	0.000	0.000	0.001	0.001	0.001	0.000	0.000	0.000	0.000

Table 4. continued

	Ir				**Pt**				**Au**	
Isotope	**191**		193		195		**198**		**197**	
NH$_3$ flow rate mL/min	3.0				5.0		3.0		3.0	
Method	on-mass	**mass-shift**	on-mass	mass-shift	on-mass	mass-shift	on-mass	**mass-shift**	on-mass	**mass-shift**
Mass pair	191-191	191-206	193-193	193-208	195-195	195-229	198-198	198-232	197-197	197-231
10 ppm Cu Zn	0.004	0.000	0.003	0.004	0.003	0.000	0.002	0.000	0.000	0.000
10 ppm Sr Rb	0.002	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000
10 ppm Ni	0.004	0.000	0.001	0.004	0.000	0.000	0.000	0.002	0.000	0.000
10 ppm Mo	0.000	0.000	0.000	0.000	0.000	0.000	0.003	0.000	0.000	0.000
10 ppm Pb, 1 ppm Hg	0.002	0.001	0.000	0.000	0.000	0.000	0.005	0.001	0.000	0.000
10 ppm Zr Nb	0.017	0.000	0.679	0.066	0.031	0.009	0.003	0.001	0.000	0.000
10 ppm REE	44.3	0.019	1.56	0.019	0.031	0.002	0.000	0.000	0.044	0.003
10 ppm Ta	0.000	0.000	0.000	0.000	0.004	0.000	0.261	0.009	4.11	0.046
10 ppm Hf	0.690	0.095	21.4	2.40	0.904	0.115	0.141	0.070	0.070	0.003
10 ppm W	0.001	0.000	0.000	0.000	0.001	0.000	0.479	0.000	0.001	0.000

Analysis of complex synthetic matrix sample using optimized NH_3 reaction mode

A complex synthetic matrix sample containing 10 ppm each of Cu, Zn, Sr, Rb, Ni, Mo, Pb, Zr, Nb, REEs, Ta, Hf, W and 1 ppm Hg was prepared, and this matrix was spiked with 1 ppb each of Ru, Rh, Pd, Ag, Os, Ir, Pt and Au as analytes. The concentration of the noble metals was determined in two modes: No gas mode and NH_3 reaction cell mode, and the spike recovery results are displayed in Figure 1 for each mode. The results demonstrate that MS/MS mode with NH_3 reaction cell gas successfully removes multiple interferences on all the noble metals, providing accurate results for these analytes even in a complex and challenging matrix.

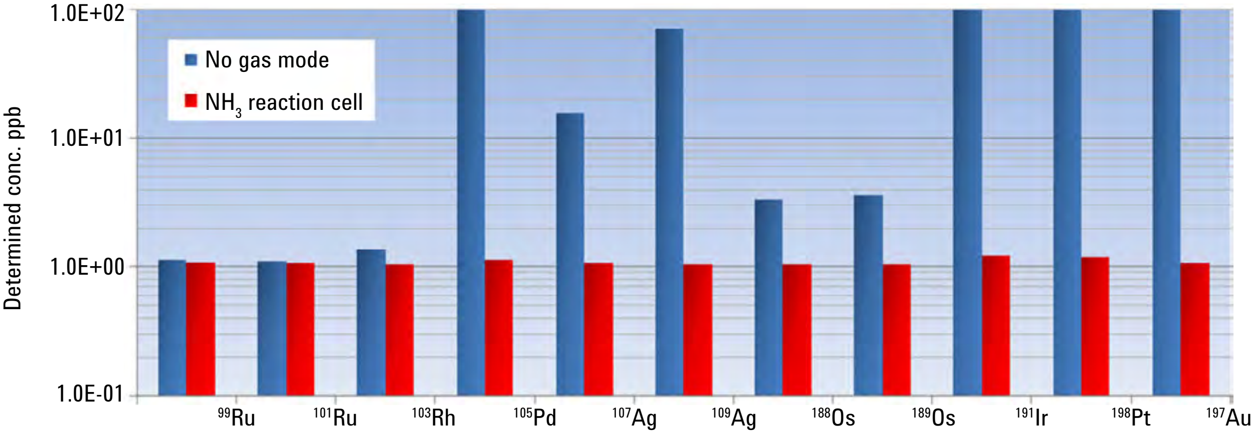

Figure 1. Result of synthetic matrix sample test. 1 ppb noble metals were measured in a multi-matrix sample containing 10 ppm of each Cu, Zn, Sr, Rb, Ni, Mo, Pb, Zr, Nb, REEs, Ta, Hf, W and 1 ppm Hg

Routine Soil Analysis using the Agilent 8800 ICP-QQQ

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Keywords

soil, sediment, routine analysis, As, Se, HMI, matrix tolerance, robustness

Introduction

Quadrupole ICP-MS is widely used in inorganic testing laboratories, due to its high sensitivity, low detection limits, wide dynamic range, and high speed multi-element analysis. The technique is well suited to the analysis of elemental contaminants present in soil and sediment samples. Helium (He) collision cell technology can be used successfully to remove many common matrix-based polyatomic interferences. He mode is less effective for the removal of interferences caused by doubly charged ions though. For example, interferences on arsenic (As) and selenium (Se) by doubly charged ions of rare earth elements (REEs). Typically, the REE content of environmental samples is low. However, all interferences, including the doubly charged ions of REEs on As and Se, can be removed using oxygen mass-shift mode of Agilent's ICP-QQQ. This approach provides a high level of confidence in the analysis of unknown samples. Agilent's ICP-QQQ instruments also offer the same robustness and matrix tolerance of Agilent's single-quadrupole ICP-MS systems.

This study demonstrates the robustness of the Agilent 8800 ICP-QQQ for routine soil analysis.

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/HMI-4. The ICP-MS MassHunter software automatically sets robust plasma tuning conditions that are suitable for soil/sediment analysis.

Method: the method was based on a preset method for soil (EPA 6020). It was modified to include O_2 mass-shift mode for sulfur (S), As, and Se. All other elements were measured in He mode. After the calibration standards and initial QC samples had been analyzed, 13 sample blocks were analyzed. Each block consisted of 10 samples (two each of Soil A, Soil B, Estuarine Sediment, River Sediment A, River Sediment B). A Periodic Block consisting of Continuing Calibration Blank (CCB) and Continuing Calibration Verification (CCV) samples was automatically inserted into the sequence after each set of 10 samples.

Samples: Five soil and sediment CRMs bought from High-Purity Standards Inc. (Charleston, SC, USA) were analyzed in this study. These included CRM River Sediment A, CRM River Sediment B, CRM Estuarine Sediment, CRM Soil A, and CRM Soil B.

Results and discussion

The total number of analyses of calibration standards, QC samples, and soil samples was 177 over ~12 hours. The internal standard (ISTD) stability plot, shown in Figure 1, met EPA 6020 requirements of between 70 and 120% of the value of the initial calibration standard.

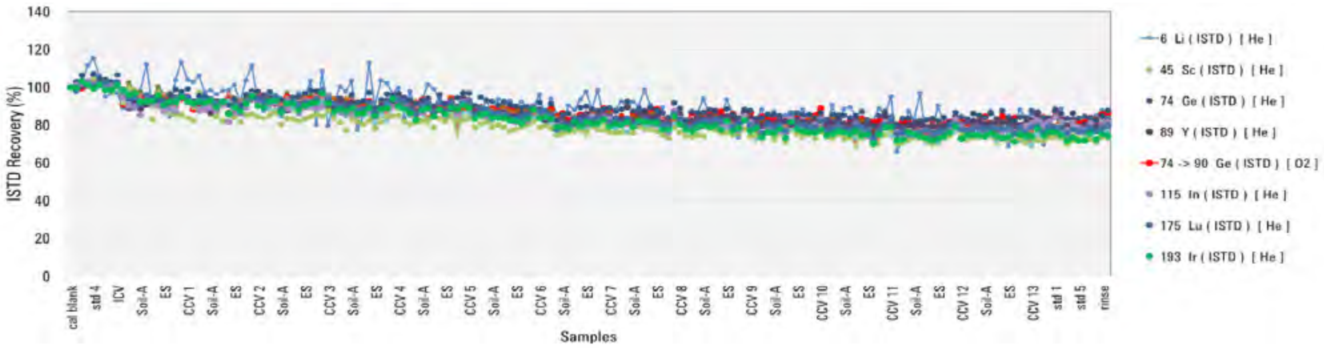

Figure 1. ISTD signal stability plot over 12 hours

The accuracy of the method was evaluated by analyzing the soil and sediment CRMs as unknown samples. Each CRM was measured 26 times in the batch. The mean concentrations and relative standard deviations (%RSD) were calculated and compared to the certified value, as shown in Table 1. The mean concentration for all elements was in good agreement with the certified value, with most RSDs well below 5% over the 12-hour analysis.

Conclusions

The Agilent 8800 ICP-QQQ with HMI offers the robustness and matrix tolerance required for the routine analysis of the widest range of trace and major elements in high matrix samples, such as soil and sediments. Doubly charged REE interferences that can affect arsenic and selenium measurement at trace levels were avoided using MS/MS mass-shift mode with O_2 cell gas. Most other elements were measured in He mode, proven to remove common matrix-based polyatomic interferences in complex and variable matrices. Not all soils, sediments, and food products contain significant concentrations of REEs. However, the presence of REEs in samples that are analyzed using single quadrupole ICP-MS can lead to false positive results for As and Se. The use of the ICP-QQQ with MS/MS improves confidence in the results for these two important elements. Furthermore, method development is simplified with the use of preset methods and autotuning, ensuring reproducible performance from day-to-day and irrespective of operator experience.

More information

Routine soil analysis using an Agilent 8800 ICP-QQQ, Agilent application note, 2015, 5991-6409EN.

Table 1. Mean recovery % of three soil/sediment CRMs

Element	Integration time (s)	MDL (ppb)	River Sediment A			Estuarine Sediment A			Soil A		
			Mean conc. (ppb)	RSD (%)	Mean recovery (%)	Mean conc. (ppb)	RSD (%)	Mean recovery (%)	Mean conc. (ppb)	RSD (%)	Mean recovery (%)
^{9}Be	3	0.06	< MDL			2.1	5.5	106	< MDL		
^{23}Na	0.1	0.98	5191	2.6	104	20862	2.4	104	7292	2.6	104
^{24}Mg	0.1	0.73	7292	2.6	104	10553	2.7	106	7341	2.6	105
^{27}Al	0.1	1.00	25862	2.4	103	70884	2.7	101	51034	2.5	102
^{31}P	1	3.20	< MDL			520	2.4	104	1042	2.0	104
^{32}S	1	4.10	< MDL			< MDL			< MDL		
^{39}K	0.1	7.50	15623	2.2	104	15568	2.7	104	20678	2.3	103
^{44}Ca	0.1	2.70	28860	2.1	96	7760	3.2	97	33670	1.8	96
^{51}V	0.3	0.021	26	2.6	105	103	2.9	103	10.4	3.4	104
^{52}Cr	0.3	0.04	29792	2.7	99	83	3.0	104	< MDL		
^{55}Mn	0.3	0.062	809	2.2	101	399	2.9	100	10.9	3.0	109
^{56}Fe	0.1	0.45	120085	2.7	100	35335	3.3	101	20215	2.2	101
^{59}Co	0.3	0.017	11	2.9	106	10.8	2.8	108	0.33	3.1	
^{60}Ni	0.3	0.049	52	2.8	103	30.7	3.2	102	30.2	2.6	101
^{63}Cu	0.3	0.021	102	2.9	102	20.2	3.1	101	30.2	2.4	101
^{66}Zn	0.3	0.063	1499	2.5	100	151	2.9	101	101	2.3	101
^{75}As	1	0.024	60	3.6	100	10.5	3.6	105	20.4	3.0	102
^{78}Se	3	0.049	2.0	3.6	101	4.9	3.0	99	1.0	6.2	99
^{95}Mo	0.3	0.022	0.19	10.5		< MDL			< MDL		
^{107}Ag	0.3	0.015	0.15	9.0		0.015	16.4		0.038	17.3	
^{111}Cd	3	0.012	10.3	2.0	103	0.11	4.5		0.37	2.9	125
^{121}Sb	0.3	0.011	50.8	2.1	102	0.58	4.4		3.2	3.5	106
^{135}Ba	0.3	0.055	50.9	2.1	102	1.5	5.4		513	2.6	103
^{201}Hg	1	0.003	< MDL			< MDL			0.018		
^{205}Tl	0.3	0.008	0.97	2.0	97	< MDL			< MDL		
^{208}Pb	0.3	0.009	719	2.1	103	30.7	2.6	102	41	2.4	101
^{232}Th	0.3	0.007	2.1	3.1	106	10.4	2.5	104	10	2.2	103
^{238}U	0.3	0.09	1.0	2.4	104	< MDL			1.0	2.5	102

HPLC-ICP-MS/MS: Fluorine Speciation Analysis

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Keywords

BaF+, fluorine speciation analysis, fluoride, fluoroacetate, trifluoroacetate, HPLC-ICP-QQQ

Introduction

Fluorine is often used in the form of organofluorine compounds in applications such as pharmaceuticals, agrochemicals, and materials. This usage has resulted in the accumulation of large quantities of unknown organofluorine compounds in the environment [1, 2]. Fluorine is a difficult element to determine by ICP-MS. Its high ionization potential (17.423 eV) results in a low yield of F^+ ions in the plasma, leading to low sensitivity.

Fluorine can be determined, however, by mixing barium and fluorine solutions and measuring the polyatomic ion BaF^+ by triple quadrupole ICP-MS (ICP-QQQ) [3]. Because ^{138}Ba is the most abundant isotope, the highest sensitivity would be achieved for $^{138}Ba^{19}F^+$ at *m/z* 157. Mechanisms for the formation of BaF^+ are shown in equations 1 and 2.

(1) $^{138}Ba^+ + {}^{19}F^0 \quad {}^{138}Ba^{19}F^+$

(2) $^{138}Ba^{++} + {}^{19}F^- \quad {}^{138}Ba^{19}F^+$

While this approach resolves the low ionization yield issue for F, the formation of potential interfering ions at *m/z* 157 from $^{138}Ba^{18}O^1H^+$, $^{138}Ba^{16}O^1H_3^+$, and $^{138}Ba^{17}O_2H^+$ also need to be considered. These interferences can be reduced by operating the ICP-QQQ in MS/MS mode, using oxygen as the reaction gas. This approach was used for development of an online HPLC-ICP-QQQ speciation method for the determination of F.

Experimental

Instrumentation: Agilent 8800 ICP-QQQ with Micromist nebulizer and s-lens.

Operating conditions: Table 1 summarizes the plasma, ion lens, and cell tuning conditions.

Acquisition parameters: MS/MS mode with O_2 on-mass. Integration time per *m/z* for BaF^+ = 1 sec. .

HPLC system: Agilent 1290 with Metrosep A Supp 5 (150 mm x 4.0 mm) separation column and Metrosep RP Guard/3.5 column. Buffer = 3.2 mM sodium carbonate and 1.0 mM sodium bicarbonate (pH 10); flow rate = isocratic 0.7 mL/min of 70% buffer solution; sample injection = 100 µL.

A transfer capillary was used to connect the chromatographic column to the nebulizer of the ICP-QQQ system via a T-pin, which allowed the mixing of Ba with F solution. The parameters were optimized in a previous study [4].

Table 1. ICP-QQQ operating conditions

Parameter	Unit	Value
Plasma		
RF power	W	1500
Sampling depth	mm	8.0
Carrier gas flow rate	L/min	1.00
Makeup gas flow rate	L/min	0.36
Lenses		
Extract 1	V	-150.0
Extract 2	V	5.0
Deflect	V	-48.0
Cell		
Oxygen flow rate	mL/min	0.75
Octopole Bias	V	-60.0
Octopole RF	V	200
Energy discrimination	V	-10.0
Wait time offset	msec	2
Sample uptake rate	mL/min	0.33
32 mg/L Ba uptake rate	mL/min	0.22

Results and discussion

Figures 1 and 2 show the chromatograms and calibration curves for fluorine speciation analysis of three different fluorine compounds: fluoride, fluoroacetate (FAA), and trifluoroacetate (TFA). All compounds were baseline separated within 10 minutes. The sensitivity of F is similar for each sample, indicating the method is compound independent and fluorine specific.

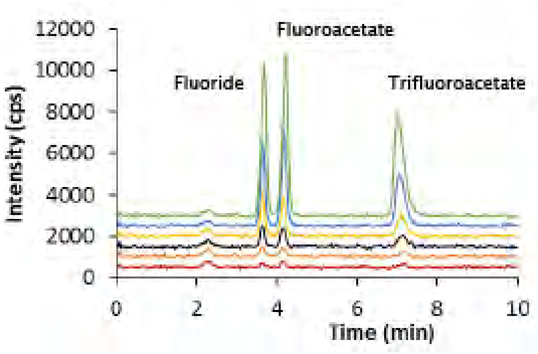

Figure 1. HPLC-ICP-QQQ chromatogram of fluoride, fluoroacetate, and trifluoroacetate at different F concentrations: 0.1, 0.25, 0.5, 1.0, 2.5, and 5.0 mg/L (as indicated by red to green colored lines).

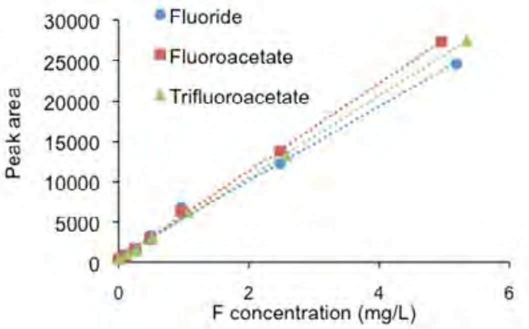

Figure 2. HPLC-ICP-QQQ calibration curves of fluorine compounds: fluoride, fluoroacetate, and trifluoroacetate.

The limits of detection (LOD) of the HPLC-ICP-QQQ method were 0.012 mg/L, 0.073 mg/L, and 0.12 mg/L for fluoride, FAA, and TFA, respectively. Table 2 shows the LOD results for F from this study compared to data reported in the literature.

Conclusions

For the first time, coupling an HPLC directly to an ICP-QQQ enabled the speciation analysis of fluorine-containing compounds through the formation of the polyatomic ion BaF^+ [4]. The method was not only able to detect fluorine specifically but also has a comparable low LOD, which opens up possibilities for future non-targeted fluorine speciation analysis in environmental samples.

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4. N. L. A. Jamari, J. F. Dohmann, A. Raab, E. M. Krupp, J. Feldmann, Novel non-target analysis of fluorine compounds using ICP-MS/MS and HPLC-ICP-MS/MS. J. Anal., At. Spectrom., 2017, 32, 942-950.

Table 2. Limit of detection (LOD) of F analysis obtained by different methods

Method	Analyte ion	LOD (mg/L)	Reference
IC-ICP-MS (indirect determination)	Al^+ (AlF^+ complex)	0.0001	Analyst, 1999, 124, 27–31
HR-ICP-MS	F^+	5.1	J. Anal. At. Spectrom., 2003, 18, 1443–1451
ETV-ICP-MS	F^+	3.2	J. Anal. At. Spectrom., 2001, 16, 539–541
ICP-MS/MS	BaF^+	0.027	Agilent, 2015, 5991-2802EN
		0.043	J. Anal., At. Spectrom., 2017, 32, 942-950
HPLC-ICP-MS/MS	BaF^+ for fluoride	0.012	This work
	BaF^+ for fluoroacetate	0.073	This work
	BaF^+ for trifluoroacetate	0.12	This work

Nuclear

Geology

Analysis of Radioactive Iodine-129 Using MS/MS with O_2 Reaction Mode

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Keywords

radionuclide, iodine, ^{129}I, environmental, nuclear, xenon, NIST 3231 Level I and II, abundance sensitivity, oxygen on-mass

Introduction

Iodine-129 is a long-lived radionuclide (half-life of 15.7 My) which has been released into the environment as a result of human activities such as nuclear weapons testing, accidents at nuclear power plants and especially by emissions from spent nuclear fuel reprocessing plants. The determination of iodine-129 in environmental samples is very difficult by ICP-MS due to the element's relatively low sensitivity, the very low concentrations at which ^{129}I must be determined, relative to potentially high levels of ^{127}I, the high background caused by ^{129}Xe impurities in the argon plasma gas, and possible polyatomic interference from $^{127}IH_2^+$. Iodine analysis is further complicated by the fact that it is rapidly volatilized from samples prepared using the acid digestions that are normal for ICP-MS analysis, so an alternative, alkaline sample solubilization and stabilization strategy is required. The isobaric interference from $^{129}Xe^+$ can be significantly reduced using ICP-QMS with an Octopole Reaction Cell operated in O_2 reaction mode, resulting in a measured ratio for $^{129}I/^{127}I$ of 10^{-7} in NIST 3231 SRM Level I[1]. However, the problem of potential overlap due to tailing from ^{127}I and ^{127}IH remains, as the relative abundance of the ^{129}I to ^{127}I will typically exceed 10^{-7}, which is of the same order as the abundance sensitivity (ability to separate adjacent peaks) of quadrupole ICP-MS (ICP-QMS). In order to overcome these challenges, ICP-QQQ operating in MS/MS mode with O_2 reaction gas was applied to determine ultratrace levels of iodine-129 in aqueous samples.

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/Low matrix.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -190 V.

CRC conditions: O_2 gas at 0.8 mL/min, Octopole bias = -18 V and KED = -1.5V. MS/MS O_2 on-mass mode was applied to measure iodine-127 and iodine-129 (Q1 = Q2 = 127 for iodine-127, Q1 = Q2 = 129 for iodine-129).

Reference materials and calibration standards: Calibration standards were prepared by diluting ^{129}I isotopic standards NIST SRM 3231 Level I and II (NIST, Gaithersburg MD, USA) with 0.5% TMAH in deionized water. The Level I Certified Value for $^{129}I/^{127}I = 0.981\times10^{-6} \pm 0.012\times10^{-6}$, Level II = $0.982\times10^{-8} \pm 0.012\times10^{-8}$. These reference materials were used to check the calibration linearity of the iodine isotopes and to validate the isotopic ratio of iodine-129 and iodine-127.

Results and discussion

Optimization of oxygen cell gas flow

The oxygen gas flow rate was optimized by varying the O_2 flow over the full range of the mass flow controller (0–1.12 mL/min), while monitoring the ^{127,129}I signal and blank intensity, as shown in Figure 1. As the flow rate of O_2 increases, the background signal (due to ^{129}Xe) at m/z = 129 decreases rapidly, and the iodine signal remains high, dramatically improving the DL for ^{129}I.

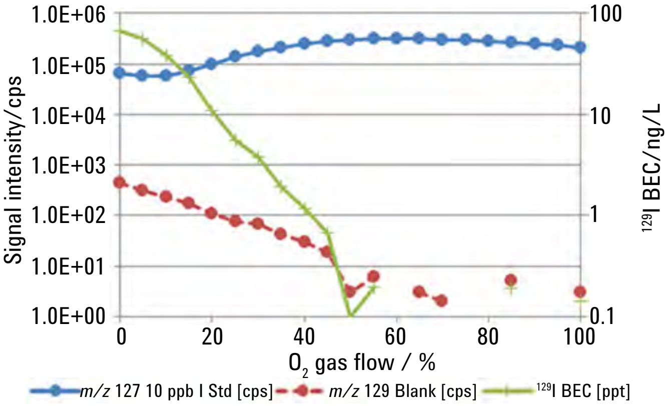

Figure 1. Profile of $^{127}I^+$, $^{129}Xe^+$ signals and estimated ^{129}I BEC. For the BEC calculation, the sensitivity of ^{129}I was assumed to be the same as ^{127}I. Scale of O_2 flow: 100% = 1.12 mL/min.

Abundance sensitivity

Scan spectra over the mass range 127 to 129, covering both ^{127}I and ^{129}I, were acquired for the two SRMs, NIST 3231 Level I and II, using the Agilent 8800 ICP-QQQ in MS/MS on-mass mode with O_2 reaction gas. The overlaid spectra are shown in Figure 2. Excellent abundance sensitivity can be seen, with the sides of the intense (>10^9 cps) ^{127}I peak reaching baseline with no tailing of $^{127}I^+$ or $^{127}IH^+$ on $^{129}I^+$.

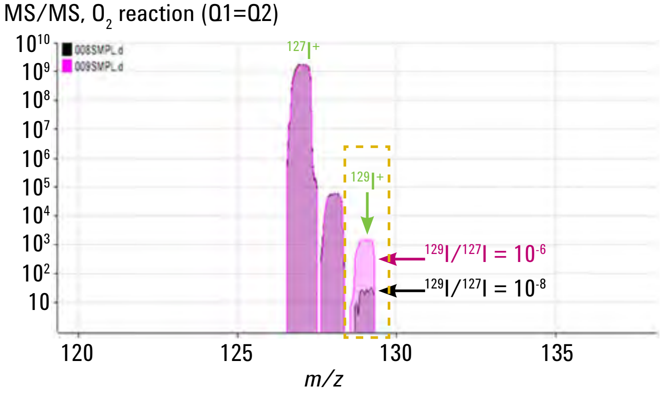

Figure 2. Iodine spectra showing both ^{127}I and ^{129}I acquired using MS/MS on-mass mode with O_2 cell gas. $^{127}IH^+$ remains to some extent while $^{127}IH_2^+$ is completely removed, as noted later.

Calibration curves for ^{127}I and ^{129}I

In order to check the linearity of both iodine isotopes, different concentration solutions of NIST 3231 SRM Level I were prepared in 0.5% TMAH and analyzed as calibration standards, as shown in Figure 3. The BECs for ^{127}I and ^{129}I were 2.9 µg/L and 0.04 ng/L respectively, and the detection limits (3σ, n=10) were 0.26 µg/L for ^{127}I and 0.07 ng/L for ^{129}I.

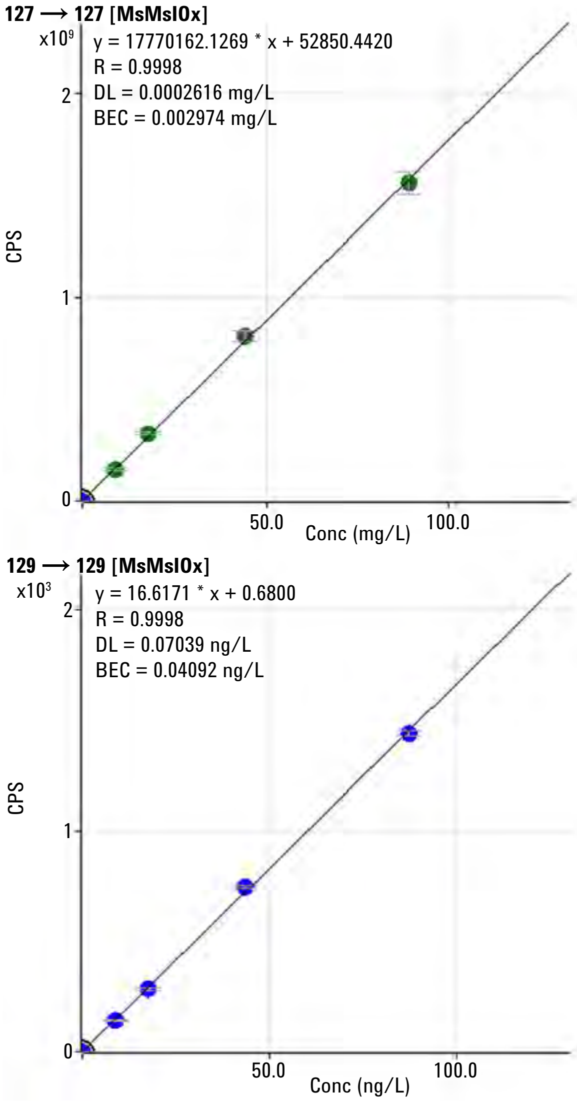

Figure 3. Calibration curve for iodine-127 (top) and iodine-129 (bottom) obtained from multiple dilutions of NIST 3231 SRM.

Analysis of NIST 3231 SRM Level I and Level II

The $^{129}I/^{127}I$ ratio in 10x diluted NIST 3231 SRM Levels I ($^{129}I/^{127}I = 0.981 \times 10^{-6}$) and II ($^{129}I/^{127}I = 0.982 \times 10^{-8}$) was measured using ICP-QQQ in MS/MS on-mass mode with O_2 cell gas. The results are summarized in Table 1. After subtracting the ^{129}I blank, the measured $^{129}I/^{127}I$ ratio of NIST 3231 SRM Levels I and II corresponded well with the certified values of 0.981×10^{-6} and 0.982×10^{-8} respectively. The good agreement with the certified ratio indicates that the potential interference of $^{127}IH_2^+$ on $^{129}I^+$ is completely removed by O_2 reaction with MS/MS mode.

Reference

1. The ultratrace determination of iodine 129 in aqueous samples using the 7700x ICP-MS with oxygen reaction mode, Agilent application note, 5990-8171EN.

Table 1. Analytical results for NIST 3231 Level I and Level II

Sample name	Dilution factor	Q1=Q2=127 CPS	Q1=Q2=129 CPS	$^{129}I/^{127}I$	$^{129}I/^{127}I$ (average n = 5)	RSD (%)
NIST 3231 10^{-6} ($^{129}I/^{127}I = 0.981 \times 10^{-6}$)	10	594,277,896	585.6	0.971×10^{-6}	0.981×10^{-6}	0.8
		592,633,576	597.4	0.994×10^{-6}		
		590,000,723	586.5	0.980×10^{-6}		
		593,387,443	588.5	0.978×10^{-6}		
		592,834,056	588.9	0.979×10^{-6}		
NIST 3231 10^{-8} ($^{129}I/^{127}I = 0.982 \times 10^{-8}$)	10	608,737,949	15.1	1.12×10^{-8}	1.02×10^{-8}	7.2
		608,536,242	14.8	1.07×10^{-8}		
		602,626,536	14.2	0.979×10^{-8}		
		603,091,763	13.9	0.929×10^{-8}		
		603,250,003	14.5	1.03×10^{-8}		
NIST Blank	10	600,444,851	8.3	—	—	—

More information

1. The ultratrace determination of iodine 129 using the Agilent 8800 Triple Quadrupole ICP MS in MS/MS mode, Agilent application note, 5991-0321EN.

Feasibility Study on the Analysis of Radioisotopes: Sr-90 and Cs-137

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Keywords

radioisotopes, radioactive, environmental, nuclear, strontium, ^{90}Sr, zirconium, cesium, ^{137}Cs, barium, abundance sensitivity, oxygen and hydrogen on-mass, nitrous oxide on-mass

Introduction

ICP-MS can be an effective analytical tool for the analysis of long half-life radioisotopes due to its high sensitivity, speed of analysis, low sample consumption, and ease of sample preparation. The challenge for ICP-MS analysis of radioisotopes arises from interferences; not only by polyatomic ions but also atomic isobar ions that cannot be separated even by high-resolution (HR-) ICP-MS.

Trace analysis of the radionuclide ^{90}Sr (half-life = 28.74 years) in environmental samples is of great interest. ^{90}Sr is a main fission product that may be present in the environment following accidental releases from nuclear power plants. Geiger-Muller (GM) detectors or Liquid Scintillation Counters (LSC) are used to measure ^{90}Sr, though both techniques require complex chemical separation prior to analysis, or long integration times. ICP-MS is also used to measure ^{90}Sr, especially when a quick turn-around time is desired. However detection limits of quadrupole ICP-MS are compromised by a spectral overlap from ^{90}Zr; in common with all direct isobaric interferences, the ^{90}Zr overlap is too close in mass to the ^{90}Sr to be resolved using sector field HR-ICP-MS, which is limited to a maximum resolution (M/ΔM) of 10,000. This note describes a method for measuring trace ^{90}Sr in the presence of ^{90}Zr using ICP-QQQ in MS/MS reaction mode. Since it isn't possible to obtain ^{90}Sr, a natural isotope of strontium (^{88}Sr) was used to estimate the DL for ^{90}Sr. A similar approach was applied to ^{137}Cs (half-life = 30.0 years).

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/Low matrix.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -190 V.

CRC and acquisition conditions: The following conditions were used for the analysis of ^{90}Sr and ^{137}Cs:

- For ^{90}Sr: MS/MS on-mass mode (Q1 = Q2 = 90) with $O_2 + H_2$ cell gas: 1 mL/min of O_2 and 10 mL/min of H_2, Octopole bias = -5 V and KED = -13 V.
- For ^{137}Cs: MS/MS on-mass mode (Q1 = Q2 = 137) with N_2O cell gas: 7 mL/min of N_2O (10% N_2O balanced in He, introduced via the 3rd cell gas flow line), Octopole bias = -5 V and KED = -13 V.

Results and discussion

Radioactive Sr-90 ($O_2 + H_2$ on-mass mode)

Figure 1 shows spectra of a solution containing Sr and Zr (natural isotopes) acquired on the 8800 ICP-QQQ operated in Single Quad mode (Q1 operated as an ion guide to emulate conventional quadrupole ICP-MS) with no cell gas (left), and in MS/MS mode with $O_2 + H_2$ cell gas (right). As can be seen in the left hand spectrum, the overlap of $^{90}Zr^+$ on $^{90}Sr^+$ precludes the low-level determination of ^{90}Sr by conventional quadrupole ICP-MS. The spectrum on the right indicates that $^{90}Sr^+$ could be measured on-mass at *m/z* = 90 free from interference by $^{90}Zr^+$, since Zr^+ reacts readily with the $O_2 + H_2$ gas to form ZrO^+ and ZrO_2^+. The signal-to-noise ratio for ^{90}Sr was improved by six orders of magnitude using MS/MS $O_2 + H_2$ reaction cell mode.

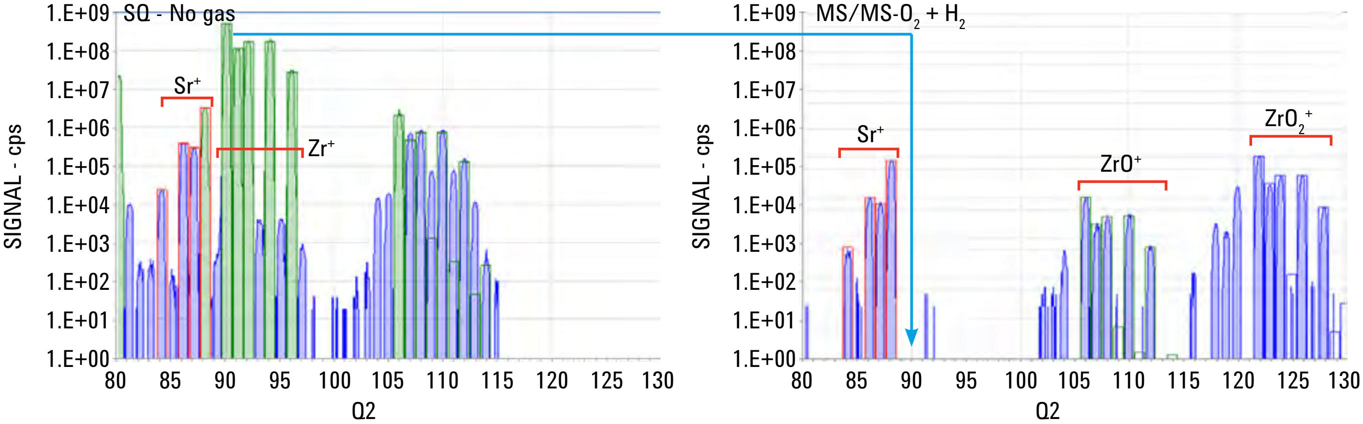

Figure 1. Mass spectra of a solution containing 20 ppb Sr + 5 ppm Zr: (left) SQ no gas mode and (right) MS/MS $O_2 + H_2$ reaction mode.

Figure 2 is a spectrum of 100 ppm Sr acquired using MS/MS on-mass mode with $O_2 + H_2$ reaction gas. The excellent abundance sensitivity (peak separation) of MS/MS mode can be confirmed. The peak sides reach the baseline with no tailing from the intense peak of the natural isotope of $^{88}Sr^+$. In addition, no $^{88}SrHH^+$ at *m/z* = 90 is formed in cell, even in a solution containing 100 ppm natural Sr.

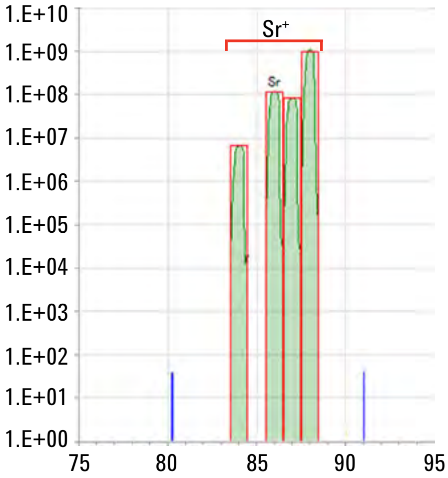

Figure 2. Spectrum of 100 ppm Sr solution acquired using MS/MS $O_2 + H_2$ on-mass mode

Radioactive Cs-137 (N_2O on-mass mode)

Figure 3 shows spectra of a solution containing Cs and Ba (natural isotopes) acquired on the 8800 ICP-QQQ operated in Single Quad mode with no gas mode (left), and in MS/MS mode with N_2O cell gas (right). As can be seen in the left hand spectrum, the $^{137}Ba^+$ overlap on $^{137}Cs^+$ is a problem in conventional quadrupole ICP-MS. As with ^{90}Sr, the right hand spectrum shows that $^{137}Cs^+$ could be measured on mass at *m/z* = 137, free from the $^{137}Ba^+$ interference. Ba^+ reacts readily with N_2O to form BaO^+ and $BaOH^+$ while a part of the Cs^+ analyte ion signal remains at its original mass (as shown by the substantial peak for ^{133}Cs in the right-hand spectrum).

Estimated BEC and DL for Sr-90 and Cs-137

The BEC and DL for two radioisotopes, ^{90}Sr and ^{137}Cs, were estimated from these spectra as summarized in Table 1. This feasibility study demonstrates the potential of ICP-QQQ for the measurement of radioisotopes such as ^{90}Sr and ^{137}Cs.

Table 1. Estimated BEC and DL for ^{90}Sr and ^{137}Cs

Radioisotope	BEC (ng/L)	DL (ng/L)
^{90}Sr	0.08	0.23
^{137}Cs	2.9	15

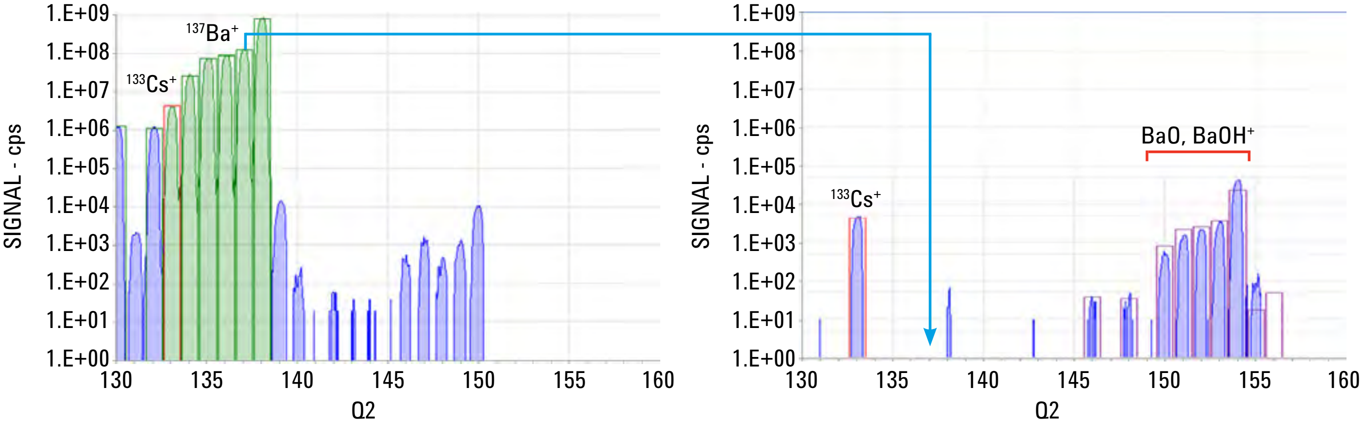

Figure 3. Mass spectra of a solution containing 20 ppb Cs + 5 ppm Ba: (left) SQ no gas and (right) MS/MS N_2O reaction mode.

Determination of Trace ^{236}U as UOO$^+$ using ICP-QQQ Oxygen Mass-shift Method

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Keywords

uranium, uranium-236, O_2 cell gas, mass-shift, extended mass range

Introduction

Uranium-236 is a long-lived radionuclide that is created from the naturally occurring trace isotope ^{235}U (0.72% abundance) by thermal neutron capture. This process leads to a natural abundance of ^{236}U in the range from 10^{-14} to 10^{-13} relative to the major ^{238}U isotope (^{236}U/^{238}U). ^{236}U is also created during the process of uranium enrichment for nuclear fuel or weapons. The ^{236}U/^{238}U ratio is increased up to 10^{-3} in spent nuclear fuel, with background levels in the environment at around 10^{-7} to 10^{-8} as a result of global fallout. The ^{236}U/^{238}U isotope ratio can therefore be used as a sensitive method to trace the accidental release of enriched uranium fuel, spent fuel, and nuclear waste.

The challenges for ICP-MS for this application are the interference on ^{236}U$^+$ by the hydride ion ^{235}UH$^+$, and the contribution at *m/z* 236 from tailing of the ^{235}U$^+$ and ^{238}U$^+$ peaks. The hydride overlap and peak tailing are more problematic in samples that have been enriched, as these samples contain a higher proportion of ^{235}U. Uranium was measured via its dioxide ion, UO_2^+, due to the efficient conversion (almost 100%) of U$^+$ to UO_2^+ with O_2 cell gas.

Experimental

Instrumentation: Agilent 8900 Advanced Applications configuration ICP-QQQ with PFA nebulizer (p/n G3139-65100).

Plasma tuning: RF power = 1550 W, sampling depth = 8.0 mm, nebulizer gas flow rate = 0.80 L/min, makeup gas flow rate = 0.30 L/min, and peristaltic pump = 0.1 rps.

Cell tuning: Octopole bias = 0 V, KED = -10 V, O_2 cell gas flow = 0 to 35% of full scale (0 to 0.53 mL/min).

Sample preparation: Uranium solutions were prepared at suitable concentrations by diluting SPEX multi element standard XSTC-331 (SPEX CertiPrep, Metuchen, NJ, USA) with de-ionized water. All samples, blank, and rinse solutions were spiked with high purity TAMAPURE 100 HNO_3 (Tama Kagaku, Saitama, Japan) to a concentration of 1%.

Results and discussion

UO$^+$ and UOO$^+$ formation as a function of O_2 cell gas flow rate

The rate of formation of UO$^+$ and UO_2^+ was studied as a function of O_2 cell gas flow rate. A solution containing 10 ppb uranium (1000x dilution of XSTC-331) was introduced into the ICP-QQQ. The signals of ^{238}U$^+$, ^{238}U^{16}O$^+$, and ^{238}U^{16}O^{16}O$^+$ were measured via three mass pairs (Q1→Q2) = (238→238), (238→254), and (238→270), and plotted against the O_2 cell gas flow rate. The octopole bias (Octp Bias) voltage was optimized to give the maximum UO_2^+ signal (0 V). Figure 1 shows that UO$^+$ formation reaches a maximum at an O_2 flow rate of 5% of full scale (equivalent to 0.074 mL/min as O_2). Above 0.075 mL/min flow rate, the formation of UO$^+$ decreased, while the formation of UO_2^+ increased, reaching a maximum at an O_2 flow of 22% of full scale (0.33 mL/min). This indicates the conversion of UO$^+$ to UO_2^+ via a chain reaction. The 8900 ICP-QQQ was optimized for highest sensitivity for the UO_2^+ product ion.

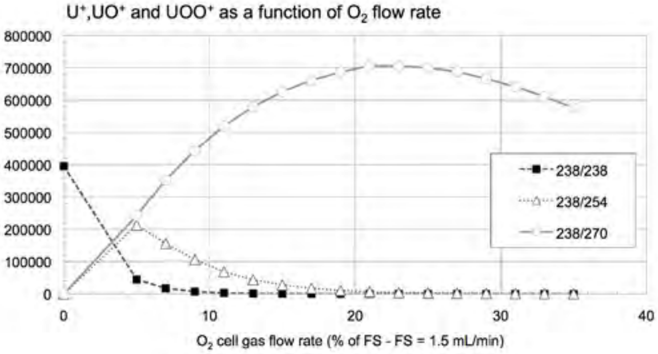

Figure 1. U$^+$ (238 → 238), UO$^+$ (238 → 254), and UO_2^+ (238 → 270) as a function of O_2 cell gas flow rate

Effect of product ion selection on hydride ion formation rate

The hydride ratio was measured at the optimal O_2 flow rate for U^+ and each of the U-oxide product ions: $^{238}UH^+/^{238}U^+$, $^{238}UOH^+/^{238}UO^+$, and $^{238}UO_2H^+/^{238}UO_2^+$.

A sample containing 50 ppb U (200x diluted XSTC- 331) was introduced for the measurement of the hydride formation ratio. 10 replicate measurements were made, with integration times of 1 s and 10 s for the analyte and hydride ions respectively. The results are summarized in Table 1. The data shows that measuring UO^+ decreases the hydride ratio by a factor of ~20, while measuring UO_2^+ leads to more than a three orders of magnitude improvement, reducing the hydride ratio to 10^{-8}.

Uranium detection limit

The detection limit (DL) of U was estimated using the UO_2^+ method. A blank solution was introduced and the signal of the mass pairs (236→268 and 238→270) corresponding to $^{236}U^+ \rightarrow {}^{236}UO_2^+$ and $^{238}U^+ \rightarrow {}^{238}UO_2^+$ were measured using an integration time of 10 s. The results in Table 2 are based on 10 replicate measurements. The DL for ^{236}U was calculated from the concentration equivalent to three times the standard deviation of the background, using the sensitivity of $^{238}UO_2^+$ given in Table 1 and the background for mass pair 236→268 in Table 2. The DL for uranium-236 was calculated to be 0.50 ppq (fg/g).

Conclusions

The Agilent 8900 ICP-QQQ operating in MS/MS mode with O_2 cell gas is suitable for the measurement of U via its reaction product ion UO_2^+. This approach was successful in reducing the contribution from the hydride ion (i.e. ^{235}UH overlap on ^{236}U). The formation of ^{235}UH was decreased by three orders of magnitude compared to direct, on-mass measurement of U^+. MS/MS mode with O_2 cell gas gave a UO_2H^+/UO_2^+ ratio in the 10^{-8} range, without the use of a desolvation system. The results suggest that the approach could be successful in reducing the interference of $^{235}UH^+$ on $^{236}U^+$, even in samples containing enriched U.

More information

Using ICP-QQQ for UO_2^+ product ion measurement to reduce uranium hydride ion interference and enable trace ^{236}U isotopic analysis, Agilent application note, 2016, 5991-6553EN.

Table 1. UH^+/U^+ ratios obtained by measuring uranium as U^+, UO^+, and UO_2^+

	O_2 cell gas flow rate (%)	**U^+ analysis**			**UH^+ analysis**			**UH^+/U^+**
		Mass pair for U^+	Counts	RSD	Mass pair for UH^+	Counts	RSD	
		Q1/Q2	cps	%	Q1/Q2	cps	%	
as U^+	0	238/238	24168974	2.8	239/239	1578.5	0.6	6.53E-05
as UO^+	5	238/254	14152816	4.2	239/255	48.9	4.3	3.46E-06
as UOO^+	22	238/270	40527770	2.0	239/271	2.3	20.8	5.68E-08

Table 2. Uranium background noise

236/268		**238/270**	
Counts	RSD	Counts	RSD
cps	%	cps	%
0.15	90.3	0.18	51.1

Measurement of Neptunium in the Presence of Uranium: Benefits of Low Abundance Sensitivity and Oxygen Reaction Mode

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Keywords

neptunium, radiochemistry, abundance sensitivity, oxygen reaction mode

Introduction

Neptunium is present in the environment at ultratrace levels due to natural neutron capture, nuclear bomb testing, and as a decay product of ^{241}Am. ^{241}Am is used in ionizing smoke detectors, radiography, and a neutron source, among other uses. By far the greatest quantity of Np is formed during energy production within uranium fission reactors. The predominant isotope formed is ^{237}Np, with approximately 50 metric tonnes per annum being produced in nuclear waste. As the half-life of ^{237}Np is ~2.14 billion years, ^{237}Np in existence today is solely from the previously mentioned processes rather than remaining from the formation of the earth. However, the relatively long half-life ensures its persistence. Np will readily form aqueous solutions (more so than any other actinide element). It also attaches to particles and colloids rather than getting trapped in humic media (such as soil and peat). These properties mean that Np is fairly mobile once in the environment. Its high affinity for calcium-rich media causes it to concentrate within concrete and bone etc.

Trace and ultratrace measurement of ^{237}Np is hindered by the presence of uranium within the sample. The biggest potential interference comes from peak broadening of the adjacent ^{238}U isotope. This Abundance Sensitivity (AS) interference is difficult to overcome. AS depends on the fundamental design of the spectrometer – such as the mass separation process (e.g. quadrupole or magnets), vacuum system, and electronics. Furthermore, minor but important polyatomic interferences from the hydrides of lighter U isotopes; ^{236}U^{1}H, ^{235}U^{1}H^{2}, ^{235}U^{2}H, ^{234}U^{1}H^{2}H hinder the measurement of ^{237}Np. Regardless of the interference source, its affect will vary depending on the concentration of uranium (and its isotope ratio), potentially causing false and variable measurements.

Experimental

Instrumentation: An Agilent 8900 Advanced Applications configuration ICP-QQQ was used. The instrument version features Axial Acceleration across the ORS^{4} collision/reaction cell that gives a higher product ion yield when using reaction chemistry.

Tuning: Np was measured under two sets of MS/MS conditions: on-mass (using no gas) and mass-shift (using O_2 reaction gas). In the latter mode, ^{237}Np is shifted away from the UH_x interferences allowing Np to be measured as the product ion NpO_2^+, free from interference, at *m/z* 269.

Calibration: Np was spiked into a 10 mg/L (ppm) U matrix to produce a set of calibration standards at 0.0, 0.19, 0.95, 1.9, 19.0, 95.0 ng/L (ppt).

Results and discussion

The Single Quad mass scan in Figure 1 shows the problem associated with AS when the U concentration is relatively high. As can be seen, the ^{238}U peak overlaps the ^{237}Np peak, impeding the trace level measurement of Np. Conversely when operating the ICP-QQQ in MS/MS mode, the peak overlap on Np is eliminated. This improvement is due to two separate mass separations taking place, improving the AS from ~10^{-7} to <<10^{-10}. The background is significantly reduced under MS/MS mode but not eliminated. Uranium can form various hydride interferences that are not related to (or removed by) AS. However, reaction chemistry can be used to remove interference-based background levels.

To check the reaction efficiency of oxygen as a cell gas for this study, a spiked U matrix was measured under MS/MS mass-shift mode with O_2 reaction gas. The Np spike was 1000x lower than the previous scans at 950 ppq (0.95 ng/L). Figure 2 shows the mass scan of the NpO_2 (and UO_2) product ions. It is worth noting that during quantitative analysis (rather than scanning, as shown in Figure 2), all the U isotopes would be eliminated by Q1, which would be set to *m/z* 237. The conversion efficiency of Np to NpO_2 was found to be 99%. Only 1% of total Np signal converted to NpO.

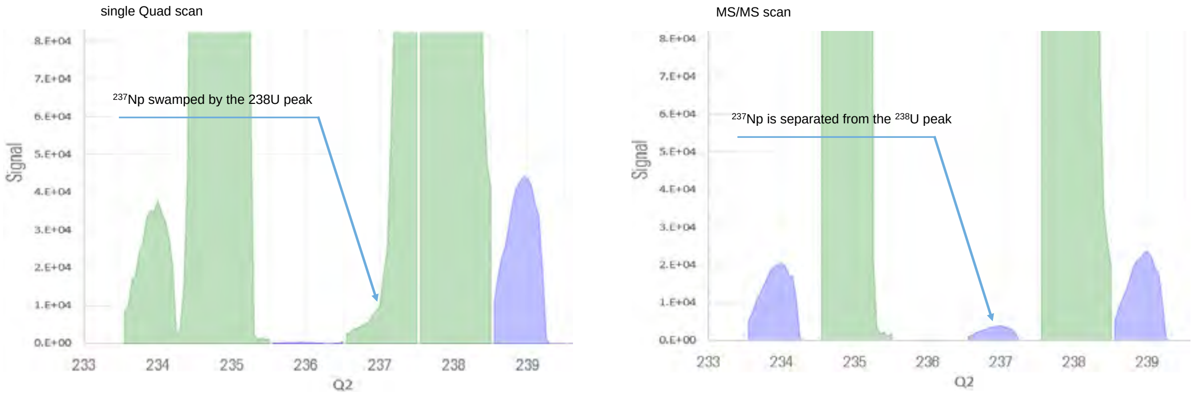

Figure 1. Spectrum of ^{237}Np in presence of 10 ppm U. Left: Single Quad scan and Right: MS/MS mode. MS/MS mode eliminates the peak tail on the low mass side of the intense ^{238}U peak.

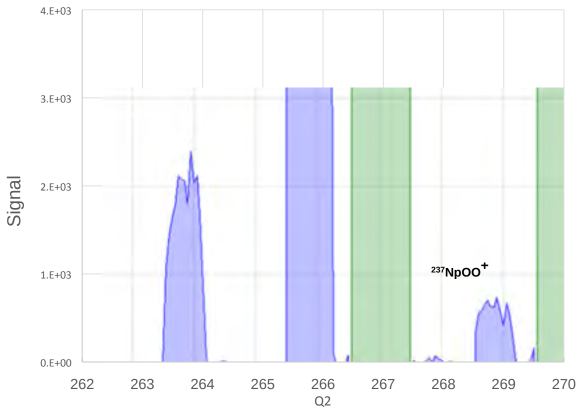

Figure 2. 950 ppt Np in 10 ppm U measured in MS/MS mass-shift mode with O_2 cell gas

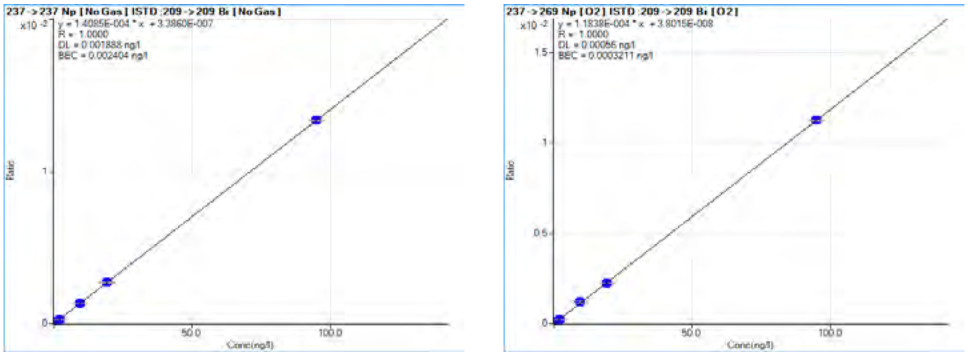

Figure 3. Np calibration in a 10 ppm U matrix. Left: no gas mode. Right: O_2 reaction gas mode – showing a 7.5x reduction in BEC. All UH-based interferences were avoided by measuring ^{237}N as $^{237}Np^{16}O_2$.

Figure 3 shows the calibration graphs for Np in a 10 ppm U matrix generated in no gas mode (left) and oxygen reaction gas mode (right). Identical solutions were analyzed in both cases. The improvement in BEC and DL can be clearly seen in oxygen mass-shift mode. The DL and BEC under no gas conditions were 1.9 ppq and 2.4 ppq. Using O_2 mode and measuring Np as NpO_2 improved the DL to 0.56 ppq and the BEC to 0.32 ppq (pg/L).

Conclusions

The Agilent 8900 ICP-QQQ offers unrivalled abundance sensitivity performance allowing an ultratrace element to be measured in the proximity of a major matrix isotope. For the determination of Np, the removal of uranium-based interferences is essential, as U is present within the environment at significantly higher concentrations than Np. The unique MS/MS capability of the 8900 ICP-QQQ removes peak overlaps and uranium hydride-based interferences.

Lead Isotope Analysis: Removal of ^{204}Hg Isobaric Interference on ^{204}Pb using ICP-QQQ MS/MS Reaction Cell

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Keywords

lead, isotope, ratio, geochronology, dating, mercury, artifacts, precious metals, food, ammonia, on-mass

Introduction

Lead isotope ratio analysis is important as it is used for Pb-Pb dating in geochronology, and to trace the origin of artifacts, precious metals and even foodstuffs. The natural isotopic pattern of lead varies more than any other element in the periodic table, because three of its isotopes are formed from the radioactive decay of uranium ($^{235}U \rightarrow ^{207}Pb$; $^{238}U \rightarrow ^{206}Pb$) and thorium ($^{232}Th \rightarrow ^{208}Pb$). The Pb isotopic pattern can therefore vary depending upon the geology of the rocks and minerals from which the lead was extracted, and the age of the material. In geochronology, the constant rate of U/Th decay allows the Pb/Pb, U/Pb and Th/Pb ratios to be used to date the age of rocks using a so-called geological clock.

When Pb ratios are measured, it is often necessary to correct for the lead naturally present in the sample, and the only non-radiogenic isotope of Pb (^{204}Pb; natural or common lead), is used for this purpose. For Pb-Pb dating, ^{204}Pb is the reference isotope against which the radiogenic isotopes are compared ($^{206}Pb/^{204}Pb$; $^{207}Pb/^{204}Pb$). Unfortunately ^{204}Pb is directly overlapped by an isotope of Hg (^{204}Hg), which makes accurate measurement of ^{204}Pb impossible by ICP-MS. Mass resolution of ^{204}Pb from ^{204}Hg is far beyond the capability of any commercial high-resolution (HR-) ICP-MS system, and until recently there has been no reliable chemical means to remove the Hg interference, so mathematical correction has been employed, which introduces error.

Mercury does however undergo a gas-phase charge-transfer reaction with ammonia gas (NH_3), a reaction that can be utilized in the collision/reaction cell of a suitably equipped ICP-MS as follows:

$$Hg+ + NH_3 \rightarrow Hg^0 + \text{“}NH_3^+\text{”}$$

This reaction offers the potential to remove the ^{204}Hg interference from ^{204}Pb, and could be applied to either solution or laser-based ICP-MS analysis.

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/General purpose.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -170 V.

CRC conditions: NH_3 gas (10% in He) at 1.7 mL/min, Octopole bias = -8 V, KED = -8 V.

Acquisition parameters: Three acquisition modes were compared:

- **No gas:** No reaction cell gas; Single Quad (SQ) mode with Q1 operating as an ion guide
- **NH_3 bandpass:** Ammonia reaction gas; SQ mode with Q1 operating as a bandpass filter
- **NH_3 MS/MS:** Ammonia reaction gas; MS/MS mode with Q1 operating as a mass filter at unit mass resolution

Results and discussion

Removal of $^{204}Hg^+$ interference on $^{204}Pb^+$

A preliminary study showed that Pb is almost unreactive with NH_3 cell gas (<0.5% loss of Pb signal) indicating that on-mass sensitivity for Pb should be maintained. On-mass measurement of Pb in NH_3 cell gas mode was therefore investigated in the presence of Hg at 10 ppb. Figure 1 displays the spectra obtained in no gas (left) and NH_3 cell gas (right) modes. The ^{204}Hg interference on ^{204}Pb can be clearly seen in the no gas spectrum, while it has been completely removed under NH_3 reaction mode with MS/MS. A perfect isotopic pattern match was confirmed for Pb in NH_3 mode.

Effectiveness of MS/MS

The NH_3 reaction that removes the ^{204}Hg interference would also work in the reaction cell of a quadrupole ICP-MS (ICP-QMS), but ammonia is a highly reactive gas and can produce many adduct cluster ions, for example from Rare Earth Elements (REEs), see Table 1. The complex matrix composition of many natural samples means that the results obtained with NH_3 cell gas in ICP-QMS are often extremely unreliable. With the 8800 ICP-QQQ, MS/MS mode allows all the co-existing matrix elements to be rejected by Q1, so only the target ions (^{204}Pb and ^{204}Hg) enter the CRC. The NH_3 reactions are therefore controlled and consistent, and no overlapping reaction product ions are formed from other elements in the sample.

Table 1. Some possible Rare Earth Element cluster ions that can form in the CRC of an ICP-QMS when using NH_3 reaction gas – the list is by no means exhaustive.

Mass	Potential Cluster Ions of REE
204	$Eu(NH_3)_3$; $Yb(NH_3)_2$; $Ce(NH_3)_4$
205	$Yb(NH_3)_2$; $Gd(NH_3)_3$
206	$Yb(NH_3)_2$; $Lu(NH_2)_2$; $La(NH_3)_4$; $Ce(NH_3)_4$; $Gd(NH_3)_3$
207	$La(NH_3)_4$; $Yb(NH_3)_2$; $Gd(NH_3)_3$
208	$Ce(NH_3)_4$; $GdNH(NH_3)_2$; $TbNH(NH_3)_2$; $Yb(NH_3)_2$; $Gd(NH_3)_3$

To check the formation of cluster ions, the ICP-QQQ was operated with NH_3 cell gas; "Single Quad bandpass" and MS/MS modes were compared for the measurement of a 50 ppb REE mix. Figures 2a and 2b display the spectra obtained using bandpass and MS/MS conditions, respectively.

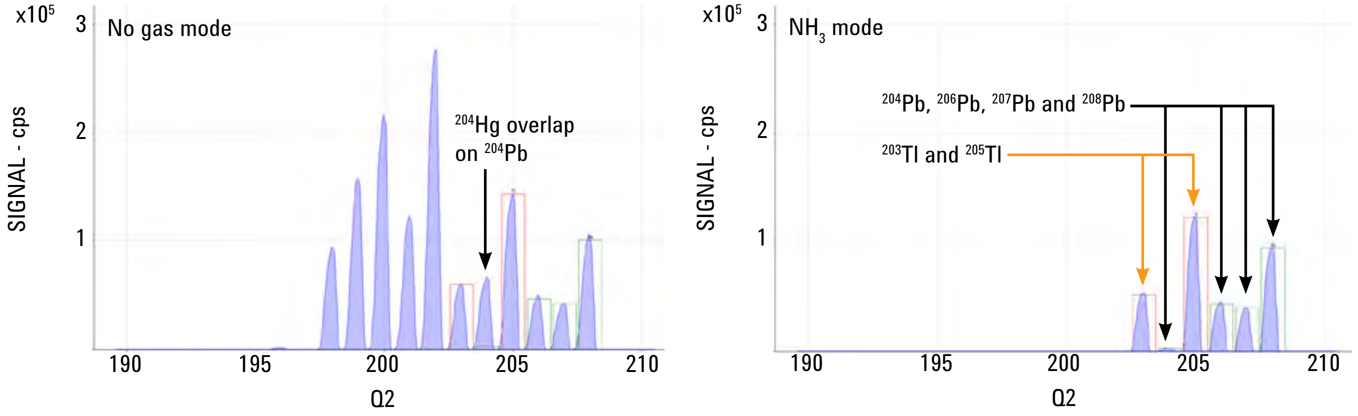

Figure 1. Standard solution (1 ppb each of Pb and Tl) spiked with 10 ppb Hg without cell gas (left) and with NH_3 (right) using MS/MS mode; Note the ^{204}Hg interference on ^{204}Pb in no gas mode.

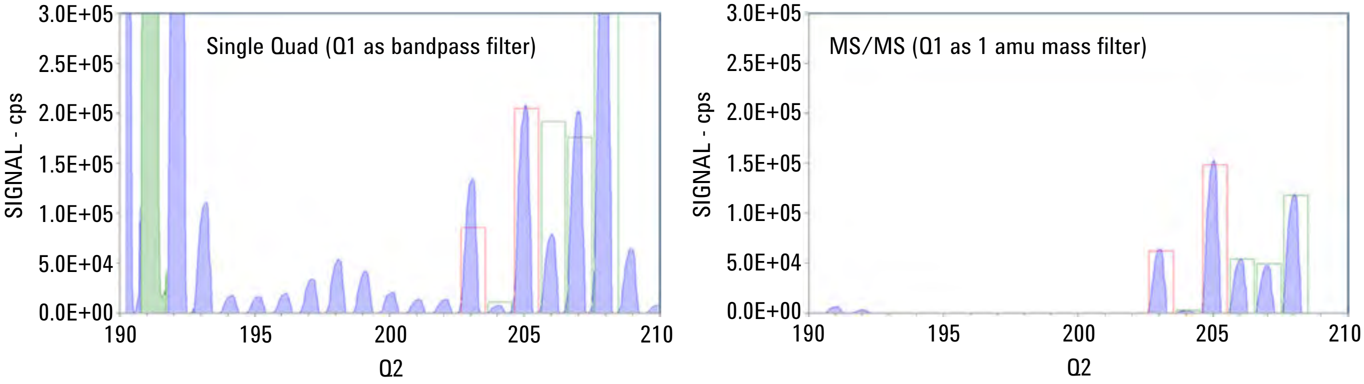

Figure 2. Cluster ion formation for 50 ppb REE standard in ammonia mode. Figure 2a (left): REE cluster ion formation using ammonia cell gas in bandpass mode; REE's are allowed into the cell if Q1 is operated as a bandpass filter. The REE cluster ions can be seen at all masses including those for Hg, Tl, Pb and Bi. Figure 2b (right): The identical sample under the same ammonia conditions but this time with Q1 operated at unit mass resolution (MS/MS mode). The REE's are removed from the ion beam before they can enter the cell and form reaction by-products.

^{204}Pb/^{208}Pb isotope ratio analysis in presence of Hg

To check the effectiveness of the ^{204}Hg removal, the ^{204}Pb/^{208}Pb ratio was measured in a 1 ppb lead solution spiked with increasing Hg concentration. Table 2 displays the measured Pb ratio results (without any mass bias correction), showing that the Pb isotope ratio remained constant, regardless of the Hg content.

Table 2. Uncorrected isotopic ratios measured in 1ppb Pb solutions containing mercury at varying concentrations. The lead isotopic ratio 204/208 is not influenced by the presence of Hg.

	^{204}Pb	^{208}Pb	IR (204/208)
Sample	**CPS**		
Theoretical	NA	NA	**0.02671**
Pb	3518.5	136124.8	**0.02585**
Pb Hg 5 ppb	3510.0	139585.9	**0.02515**
Pb Hg 10 ppb	3439.2	132796.4	**0.02590**
Pb Hg 20 ppb	3464.8	134417.7	**0.02578**

Conclusions

With the successful removal of the ^{204}Hg interference on the natural ^{204}Pb isotope, ICP-QQQ displays great promise for Pb/Pb and U/Pb dating and for other applications where accurate measurement of ^{204}Pb is required.

Fractionation of Sulfur Isotope Ratio Analysis in Environmental Waters

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Keywords

sulfur, sulfur isotope ratio, isotope ratio analysis, fractionation, mass-shift

Introduction

Sulfur isotope ratio (IR) data is a useful indicator in geochemical and biochemical studies [1]. In stable sulfur isotope analysis, the variation in the $^{34}S/^{32}S$ IR is calculated and reported as a deviation or delta (δ) in ^{34}S abundance relative to a standard material, the troilite (iron sulfide) mineral from the Canyon Diablo meteorite. This standard is referred to as δVCDT (Vienna Canyon Diablo Troilite). Natural variations in ^{34}S abundance, expressed in parts per thousand or "per mil" (‰), can be of the order of -50‰ to +40‰ (and occasionally much greater), due to redox reaction [2]. In this study, triple quadrupole ICP-MS (ICP-QQQ) was investigated as a fast and simple technique for S IR analysis. ICP-QQQ is a tandem ICP-MS that can resolve spectral interferences using reaction cell technologies. Using the method described in this paper, ICP-QQQ can measure S at a low concentration (background equivalent concentration < 0.2 ppb in UPW) with high sensitivity (^{32}S > 10000 cps/ppb).

Experimental

Instrumentation: Agilent 8900 Advanced Applications configuration ICP-QQQ with PFA nebulizer. Self-aspiration mode was used for better precision.

Tuning: O_2 mass-shift method. Tuning conditions are summarized in Table 1.

Method: the following procedures were used for the accurate determination of sulfur IRs:

- **Matrix matching:** all samples were diluted by the matrix blank, which contained 50 ppm Ca and 100 ppm NaCl in 1% HNO_3.
- **Concentration matching:** each sample was diluted by the matrix blank to ~0.5 ppm S concentration. This dilution was done to remove any errors caused by signal count differences. For example, NASS 5 was diluted 2000 times and mineral water A was diluted 10 times.
- **Mass bias correction:** to correct mass bias (including mass-bias drift), sample-standard bracketing was applied. IR of 0.5 ppm IAEA-S-1 [3] was measured before and after the IR analysis of each sample. The average of the IRs for the standard was used to correct the mass-bias, and the drift.

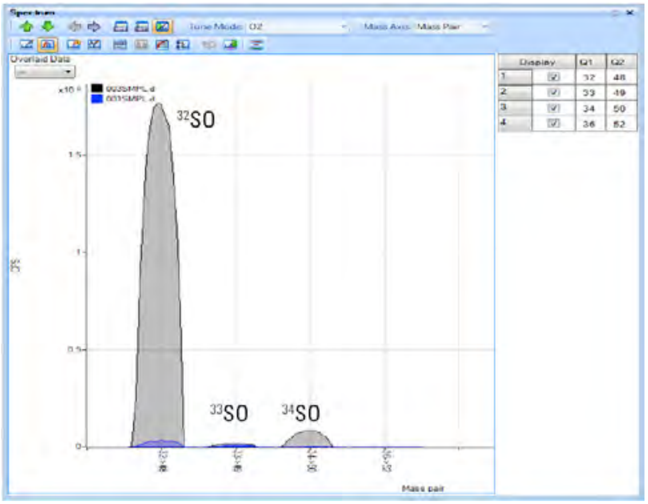
Table 1. ICP-QQQ tuning and method parameters

	Tuning parameter	Unit	Value
Plasma	RF power	W	1550
	Sampling depth	mm	8.0
	Nebulizer gas flow rate	L/min	0.90
	Makeup gas flow rate	L/min	0.30
Lens	Extract 1	V	-80
	Extract 2	V	-150
	Omega	V	10.0
	Omega bias	V	-120
Cell	Octp Bias	V	-5.0
	Axial Acceleration	V	2.0
	KED	V	-8.0
	Cell gas		Oxygen
	Cell gas flow rate	mL/min	0.45

	Method parameter	Unit	Value
Data acquisition	Integration time	s	1 and 5 for ^{32}S and ^{34}S
	Number of sweeps	–	1000
	Number of replicates	–	10
Rinse	1% HNO_3 rinse	s	20
	50 ppm/100 ppm NaCl rinse	s	30
Sample load	Load time	s	30
	Stabilization time	s	30

Results and discussion

Figure 1 shows a spectrum of three sulfur isotopes in a blank and 10 ppb S standard measured by ICP-QQQ in O_2 mass-shift mode. The two spectra show the low BEC of sulfur in the blank, which allows accurate S IR analysis.



	Display	Q1	Q2
1	☑	32	48
2	☑	33	49
3	☑	34	50
4	☑	36	52

Figure 1. Spectra of S isotopes measured in O_2 mass-shift mode. The blank is indicated in blue and the 10 ppb S standard in grey. The spectra show that the BEC of the blank is < 200 ppt.

Synthetic samples were prepared and analyzed. Two standards, IAEA S-1 ($^{34}\delta$ = -0.3‰) and IAEA S-2 ($^{34}\delta$ = +22.6‰), were mixed to make four synthetic samples with a theoretical S IR of $^{34}\delta$ = -0.3, 5.4, 11.2 and 22.6 ‰. Each sample was measured six times, and the average IR and precision (as two times the standard deviation) were calculated. As shown by the linearity of Figure 2, the measured $^{34}\delta$ values were in excellent agreement with the theoretical values.

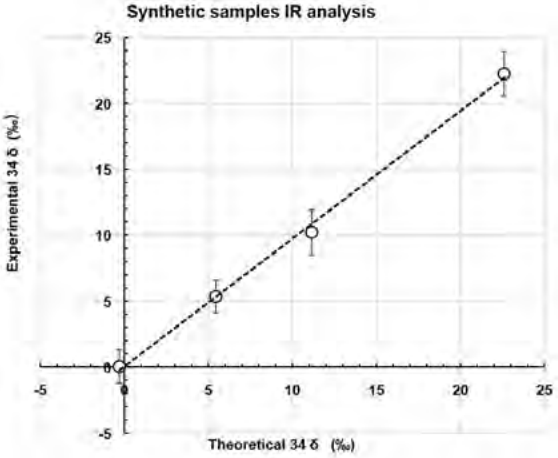


Figure 2. Sulfur IR of four synthetic samples

The developed method was used to analyze seven samples: sulfuric acid (Tamapure AA-100); a Japan river water CRM, JSAC0301; a hot spring water, IKAHO; three mineral waters A, B, and C; and a seawater SRM, NASS-5. The concentration of S was first determined in each sample. The samples were then diluted with the matrix blank (50 ppm Ca + 100 ppm NaCl) to ~0.5 ppm of S. The IR of each sample was measured 10 times to determine the average value and precision (as two times the standard deviation). The results given in Figure 3 show ±1.2 to ±1.7 ‰ error.

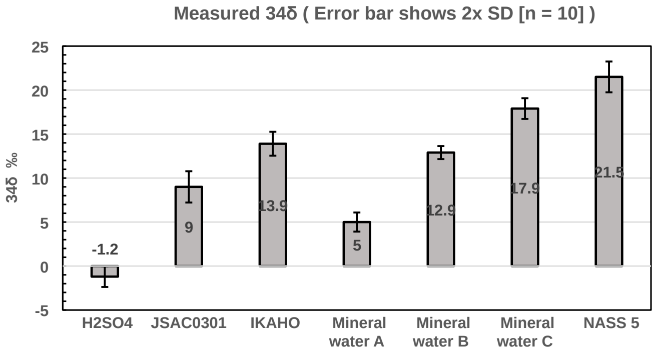


Figure 3. Measured $\delta^{34}S$ of seven samples

Conclusions

The Agilent 8900 Advanced Applications configuration ICP-QQQ is ideally suited to $^{34}S/^{32}S$ isotope ratio analysis. The analysis can provide valuable information for sample characterization in natural systems or to monitor anthropogenic impact. The 8900 ICP-QQQ provides a low background and high sensitivity for sulfur, which enabled a method to be developed that required the sample to be diluted with the matrix blank before analysis. The precision of the IRs achieved was excellent at 1.2–1.7 ‰ (as two times the standard deviation).

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More information

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Direct Strontium Isotopic Analysis of Solid Samples by LA-ICP-MS/MS

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Martín Resano, University of Zaragoza, Spain

Keywords

isotopic analysis, LA-ICP-MS/MS, LA-ICP-QQQ, strontium, geology

Introduction

Strontium has four stable isotopes: ^{84}Sr (0.56%), ^{86}Sr (9.86%), ^{87}Sr (7.0%), and ^{88}Sr (82.58%). ^{87}Sr is either formed during nucleosynthesis with other stable Sr isotopes or via beta decay from ^{87}Rb (half-life of 4.88 x 10^{10} years): $^{87}\text{Rb} \rightarrow {}^{87}\text{Sr} + \beta^- + \bar{\upsilon}$. Consequently, a high ^{87}Sr/^{86}Sr ratio is observed in rocks that are geologically old or which contain a high concentration of Rb (high Rb/Sr ratio). The ^{87}Sr/^{86}Sr ratio has been widely studied and reported in geological studies [1].

Measuring the ^{87}Sr/^{86}Sr ratio using mass spectrometry techniques is challenging because of the isobaric overlap of the signals from ^{87}Rb and ^{87}Sr. Chemical separation can be used to isolate Sr from Rb before analysis by ICP-MS. However, a simpler method uses triple quadrupole ICP-MS (ICP-QQQ) and chemical reaction in the CRC with a reactive gas. In this study, Laser Ablation coupled to ICP-QQQ (LA-ICP-QQQ) in MS/MS mode with CH_3F/He reaction gas was used to resolve the ^{87}Rb interference on ^{87}Sr. This approach allowed the direct Sr isotopic analysis of solid samples [2].

Experimental

A preliminary study showed that better precision was obtained using wet plasma conditions. The experimental setup shown in Figure 1 was used throughout. De-ionized water was continuously aspirated using a standard nebulizer. The sample aerosol that was generated by the LA system was carried by helium gas. Before being delivered to the plasma, the dry aerosol was combined with the liquid aerosol in the spray chamber, which was chilled to 2 °C.

Instrumentation: An Analyte G2 193 nm ArF*excimer-based LA-unit (Teledyne CETAC Technologies, USA) equipped with a HELEX 2 ablation cell was coupled to an Agilent 8800 #100. The ICP-QQQ was fitted with a standard sample introduction system.

Method: Tuning conditions and method parameters are given in Table 1.

Reaction cell method: The CH_3F/He (1:9) cell gas was introduced via the ICP-QQQ's fourth cell gas mass flow channel (0-1 mL/min as O_2). Rb^+ ions do not react with CH_3F, whereas Sr^+ reacts with CH_3F to form SrF^+. Thus $^{86}Sr^+$, $^{87}Sr^+$, and $^{88}Sr^+$ can be measured as the corresponding $^{86}SrF^+$, $^{87}SrF^+$ and $^{88}SrF^+$ reaction product ions, free from interference.

Mass bias correction: The instrumental mass bias was corrected for using a double correction approach: internal correction assuming a constant ^{88}Sr/^{86}Sr isotope ratio (Russell's law, given below), followed by external correction in a sample-standard bracketing (SSB) approach using NIST 612 glass SRM.

$$R^{87Sr/86Sr}_{\text{sample, corrected}} = R^{87Sr/86Sr}_{\text{sample, measured}} \times (m^{87Sr}/m^{86Sr})^f$$

$$f = \ln\,[R^{88Sr/86Sr}_{\text{true}} \,/\, R^{88Sr/86Sr}_{\text{measured}}] \,/\, \ln\,[m^{88Sr}/m^{86Sr}]$$

Samples: Seven geological reference materials (RMs) were analyzed for their Sr isotopic composition. The RMs were selected to cover a wide range of matrix composition, Sr concentration, and Rb/Sr elemental ratio, as summarized in Table 2.

Table 1. LA-ICP-QQQ tuning conditions

Laser Ablation		
Energy density	J/cm^2	3.54
Repetition rate	Hz	40
Scan speed	µm/s	15
Beam size	µm	20-85
He carrier gas flow	L/min	0.42

ICP-QQQ		
RF power	W	1550
Sampling depth	mm	3.5
Nebulizer gas flow	L/min	1.0
Makeup gas flow	L/min	0.33
CH_3F/He cell gas flow	mL/min	0.90
Dwell time per acquisition point	ms	300
Acquisition time per replicate	s	60
Number of replicates		12
Total analysis time per sample	min	15.55

Results and discussion

Removal of ^{87}Rb overlap using MS/MS mass-shift mode with CH_3F/He cell gas

Seven RMs were selected to cover a wide range of Rb/Sr ratios. The ^{87}Sr/^{86}Sr ratio was measured in each RM. For comparison purposes, the analysis was done using a no gas on-mass method and the CH_3F/He mass-shift method. Figure 2 shows the measured ^{87}Sr/^{86}Sr and ^{88}Sr/^{86}Sr ratios obtained with the two methods as a function of the Rb/Sr ratio.

With both methods, a constant ^{88}Sr/^{86}Sr ratio was obtained regardless of the sample type. However, the measured ^{87}Sr/^{86}Sr ratio increased in no gas mode, indicating an interference from ^{87}Rb on ^{87}Sr. In contrast, the ^{87}Sr/^{86}Sr ratio measured in CH_3F/He mode remained constant, regardless of the Rb/Sr ratio, showing that the method was effective at removing the ^{87}Rb isobaric overlap on ^{87}Sr.

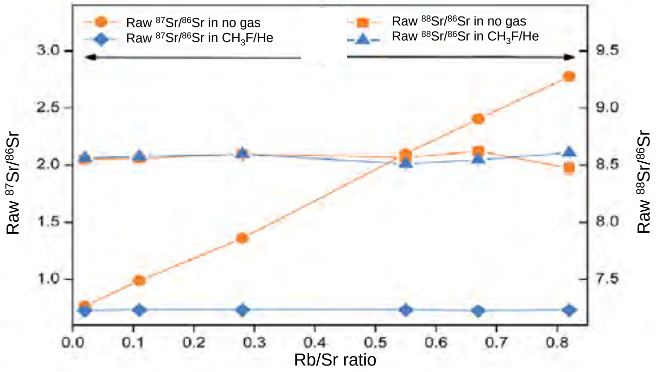

Figure 2. ^{87}Sr/^{86}Sr and ^{88}Sr/^{86}Sr isotope ratios measured using LA-ICP-QQQ in no gas and CH_3F/He cell gas modes.
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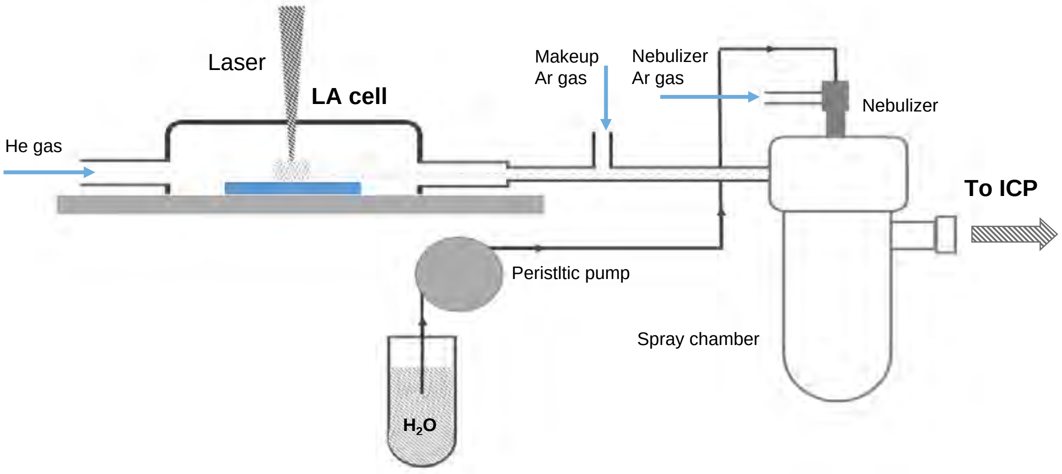

Figure 1. Schematic diagram of LA-ICP-QQQ using wet plasma conditions

Determination of $^{87}Sr/^{86}Sr$ ratio in seven RMs

The method was used to determine the $^{87}Sr/^{86}Sr$ ratio in seven RMs. The results are summarized in Table 2. After mass bias correction, excellent agreement was obtained between the measured $^{87}Sr/^{86}Sr$ ratios and the recommended reference values, even in samples with a high Rb content.

Table 2. $^{87}Sr/^{86}Sr$ isotope ratio results in seven reference materials

Reference material	Type	Rb/Sr ratio	Chemical composition of the reference materials (%)								$^{87}Sr/^{86}Sr$ ratio				
			Al_2O_3	CaO	FeO	K_2O	MgO	MnO	Na_2O	SiO_2	Experimental		Recommended		Error (%)
USGS BHVO-2G	Basalt	0.02	13.6	11.4	11.3	0.51	7.13	0.17	2.4	49.3	0.70351	±0.00034	0.703469	±0.000007	0.006%
USGS NKT-1G	Nephelinite	0.03	10.5	13.4	12.2	1.27	14.2	0.24	3.85	38.9	0.70363	±0.00017	0.703509	±0.000019	0.017%
USGS TB-1G	Basalt	0.11	17.12	6.7	8.67	4.52	3.51	0.18	3.56	54.29	0.70576	±0.00030	0.705580	±0.000023	0.026%
USGS GSD-1G	Basalt	0.55	13.4	7.2	13.3	3	3.6		3.6	53.2	0.70924	±0.00029	0.709416	±0.000050	-0.025%
USGS BCR-2G	Basalt	0.14	13.4	7.06	12.4	1.74	3.56	0.19	3.23	54.4	0.70486	±0.00038	0.705003	±0.000004	-0.020%
MPI-DING T1-G	Diorite	0.28	17.1	7.1	6.44	1.96	3.75	0.127	3.13	58.6	0.70990	±0.00035	0.710093	±0.000017	-0.027%
MPI-DING ATHO-G	Rhyolite	0.67	12.2	1.7	3.27	2.64	0.103	0.106	3.75	75.6	0.70310	±0.00026	0.703271	±0.000015	-0.024%

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Conclusions

LA-ICP-QQQ with wet plasma conditions can be used for the direct determination of the $^{87}Sr/^{86}Sr$ isotope ratio in geological samples. The isobaric interference from ^{87}Rb on ^{87}Sr was overcome using MS/MS mass-shift mode with CH_3F/He cell gas. The Sr^+ ions react in the CRC to form SrF^+ reaction product ions, while Rb^+ ions do not react. $^{87}Sr/^{86}Sr$ ratios were accurately determined in seven reference materials, regardless of the matrix composition, Sr concentration, and Rb/Sr elemental ratio.

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Manganese Analysis in Whole Blood: Expanding the Analytical Capabilities of ICP-MS

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Keywords

manganese, whole blood, iron, abundance sensitivity, helium MS/MS

Introduction

Analysis of clinical samples is challenging due to their complex matrices. While ICP-MS is an immensely powerful multi-element analytical technique, it does suffer from some well-documented spectral interferences. Achieving low detection limits is limited by background signal from low level impurities and the presence of polyatomic interferences, which require the use of CRC technology for their removal. Although the use of CRC-ICP-MS has alleviated many of these analytical challenges, some spectral interferences remain problematic for quadrupole ICP-MS (ICP-QMS). One such interference is the signal overlap on ^{55}Mn due to peak tailing from both ^{54}Fe and ^{56}Fe. Whole blood contains an average of 500 ppm of Fe, and with the level of Mn in whole blood being roughly 10 ppb, analytical results for Mn tend to bias high due to the significant signal tailing and overlap from the adjacent Fe peaks. In this work, we use the superior abundance sensitivity of the 8800 ICP-QQQ to remove any signal overlap from Fe on Mn in whole blood.

Experimental

Instrumentation: Agilent 8800 #100.

Plasma conditions and ion lens tune: Preset plasma/ General purpose with soft extraction tune:
Extract 1 = 0 V.

Method: Samples were analyzed using the 8800 ICP-QQQ in both Single Quad (SQ) mode and MS/MS mode. In this study, the mass range of interest (from *m/z* 50 to 60) was scanned at twenty points per peak in both no gas and helium (He) modes. For the analysis of Mn in blood, MS/MS mode with on-mass measurement (Q2 set to the same mass as Q1) was used, with helium cell gas (typical flow of 4.3 mL/min) to remove polyatomic ion interferences such as FeH^+ and $ArOH^+$.

Sample preparation: A 5 ppb solution of Mn was prepared from a stock of 1000 ppm Mn and either analyzed separately or spiked into “base” whole blood (low level Mn). Whole blood was diluted using an alkali matrix containing ammonium hydroxide, EDTA, Triton X-100, and butanol.

Abundance sensitivity

The abundance sensitivity (AS) of a mass spectrometer is the contribution that the signal at mass M makes to the signals at the adjacent masses (M±1), expressed as a ratio (M-1/M on the low-mass side and M+1/M on the high-mass side). Simply put, AS is the measure of the “peak tailing” to adjacent masses, which will contribute to a false positive signal, such as that seen on ^{55}Mn (present at trace levels) from the large contribution from ^{54}Fe and ^{56}Fe (which exists at very high concentration) in whole blood. The abundance sensitivity of the best quadrupole ICP-MS systems is of the order of 10^{-7}.

Results and discussion

Abundance sensitivity study in SQ and MS/MS mode

SQ and MS/MS spectra for a 500 ppm Fe solution acquired in no gas mode are shown in Figure 1. The spectrum on the right illustrates the superior peak-to-peak resolution of the 8800 ICP-QQQ operated in MS/MS mode. Although no interference removal for polyatomic ions was employed, the elimination of the contribution to mass 55 from adjacent peaks is clearly evident in MS/MS mode. The “flat-top” peak shapes are the result of the logarithmic scale.

Abundance sensitivity plays an important role when samples contain a large concentration of Fe. Figure 1 looks at the contribution of “peak tailing” on ^{55}Mn due to high levels of Fe. The high concentration of Fe together with the ArN^+ and ArO^+ contribution in no gas mode resulted in the signals at 54 and 56 being over the range of the detector, and so they were automatically skipped. However, the signal contribution from ^{56}Fe on mass 55 is clearly visible in the SQ mode (indicated by the red box) while it is absent in the MS/MS mode.

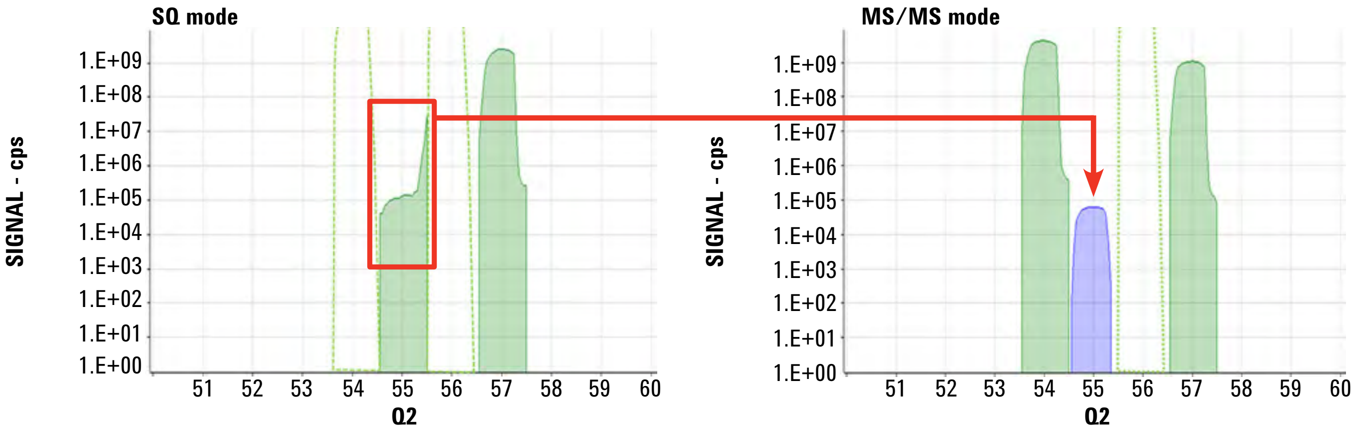

Figure 1. Comparison of no gas mode spectra for 500 ppm Fe solution, measured in SQ mode (left) and MS/MS mode (right). The signal colored blue was obtained in pulse counting while the green signal was obtained in analog mode. The dotted lines indicate over-range peaks (automatically skipped to protect the EM detector).

Figure 2 shows three spectra obtained in MS/MS mode with He cell gas. When He cell mode is used for interference removal, precise and accurate analysis is easily achieved. In He MS/MS mode, all interferences (arising from signal overlap from tailing of adjacent peaks and polyatomic ions isobaric interferences) are removed, yielding unbiased analysis and accurate results.

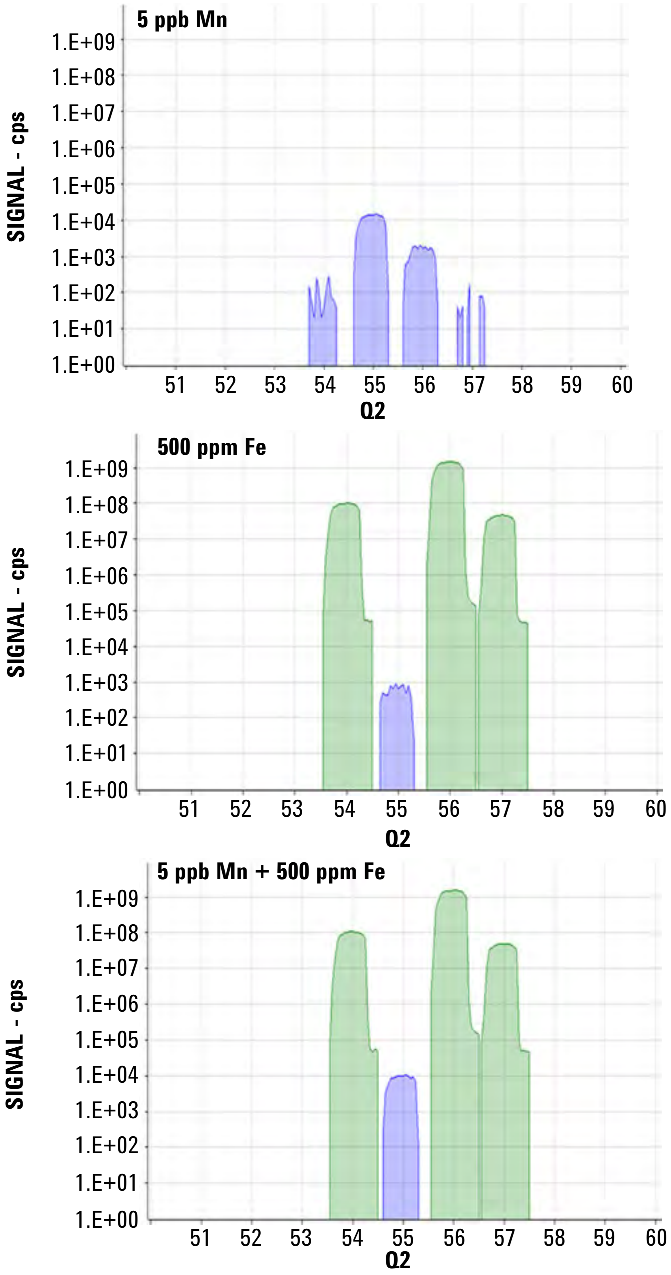

Figure 2. He MS/MS mode spectra: (top to bottm) 5 ppb Mn, 500 ppm Fe, and 5 ppb Mn + 500 ppm Fe

Figure 3 is an overlay of three spectra measured using He MS/MS mode; 1) Blank, 2) 10x whole blood, and 3) 500 ppt Mn spike in 10x whole blood. Table 1 summarizes the results of 10x diluted whole blood analysis and 500 ppt Mn spike recovery test. As shown, very low blank levels were achieved, ^{55}Mn was clearly resolved in the spectrum and good spike recoveries were obtained.

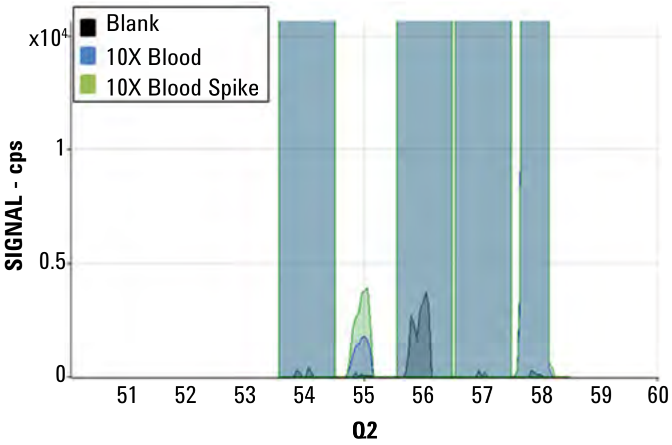

Figure 3. Spectra of three samples: blank, 10x diluted blood and 10x diluted blood spiked with 500 ppt Mn

Table 1. 10x diluted whole blood analysis results for Mn

	Blood sample	Blood sample + 500 ppt Mn	Spike recovery
	µg/L		%
Sample A	0.413	0.983	114
Sample B	0.432	0.924	98

Conclusions

Quadrupole ICP-MS has been almost universally accepted for low level analysis of trace analytes in complex matrices. However, many challenging interferences remain unresolved, especially when trace analytes must be measured close to matrix element peaks in complex samples. The Agilent 8800 ICP-QQQ with MS/MS capability has abundance sensitivity better than 10^{-10}, which enables the analysis of trace analytes (such as Mn) in the presence of a high concentration of adjacent elements (such as Fe).

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Measurement of Titanium in Clinical Samples: Possible Application to Monitoring Patients with Joint Replacements

Glenn Woods
Agilent Technologies (UK) Ltd.

Keywords

titanium, biological, serum, urine, joint-replacement, Seronorm, ammonia mass-shift

Introduction

Although titanium (Ti) has little or no direct biological role, it is widely used in dental, artificial/replacement joints and surgical reconstruction applications due to its high strength, light weight and the fact it is biocompatible. It is also used extensively as a pigment and abrasive polishing agent (as TiO_2) and is often found in foods and toothpaste due to its inert nature (this form is usually passed unaltered in faecal matter and is not normally transported or expressed through body fluids).

More recent applications with certain types of metal-on-metal (rather than ceramic or polymer based) joint replacements can lead to the release of wear metal particles or ions within the body of the patient. These can become highly concentrated in the synovial fluid (lubricating fluid of the joint), pass into the bloodstream and be expressed through urine. Unusually "high" concentrations of Ti can indicate a premature failure of a Ti-based joint and such failure can lead to infection or constant pain for the patient. It is therefore important to reliably determine the concentration of Ti within biological fluids at normal endogenous levels in order to obtain a basal concentration. An increase from this concentration could indicate an imminent failure of the joint.

Experimental

The determination of Ti in biological matrices is challenging for conventional ICP-MS, due to its low natural concentration and the presence of spectral interferences on all the Ti isotopes e.g. sulfur (as SO), P (as PO) and Ca. It is possible to use reaction chemistry with NH_3 cell gas in the CRC of a quadrupole ICP-MS (ICP-QMS), to mass-shift the Ti^+ to a higher mass product ion, leaving the interfering species behind. However, the use of highly reactive cell gases in ICP-QMS is prone to severe errors, as there is no way to control the ions that enter the CRC. This means that the reaction chemistry and the product ions created can change dramatically, with even slight differences in sample matrix or co-existing analyte concentrations. For this application, the 8800 ICP-QQQ was used to provide controlled reaction chemistry with ammonia as the reaction gas and measuring Ti as the $TiNH_2(NH_3)_4^+$ cluster ion at the M + 84 amu transition.

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/General purpose.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -170 V.

CRC conditions: NH_3 gas (10% in He) at 1.7 mL/min, Octopole bias = -8 V, KED = -8 V.

Samples and sample preparation: Certified reference materials of human serum and urine were purchased from Seronorm (Norway). They were prepared in duplicate by 10x dilution into a basic diluent consisting of NH_4OH (0.5%), H_4-EDTA (0.01%), BuOH (2%) & Triton X-100 (0.01%) in ultrapure water. No further matrix matching was applied for the standards.

Results and discussion

Selection of product ion for Ti measurement

In order to select the most appropriate Ti cluster ions in NH_3 mode, a product ion scan was performed for the ^{48}Ti isotope by introducing a 10 ppb Ti solution (Figure 1). Q1 was set to *m/z* 48, allowing only ions at the mass of the target precursor ion to enter the cell; Q2 was scanned over a selected mass range to measure all the product ions formed in the cell by NH_3 reactions with ^{48}Ti. Based upon this scan, the two most abundant cluster ions (Q1 + 84 amu [$TiNH_2(NH_3)_4$] and Q1 + 102 amu [$Ti(NH_3)_6$]) were selected for further study. For each of the two reaction transitions identified above, neutral gain scans

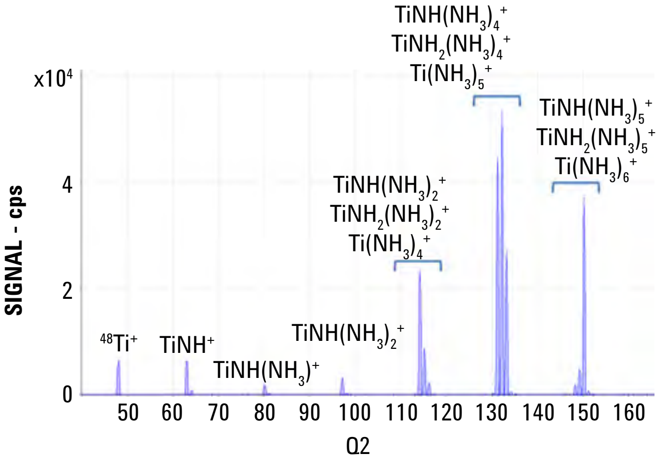

Figure 1. Product ion scan for ^{48}Ti+ in NH_3 mode

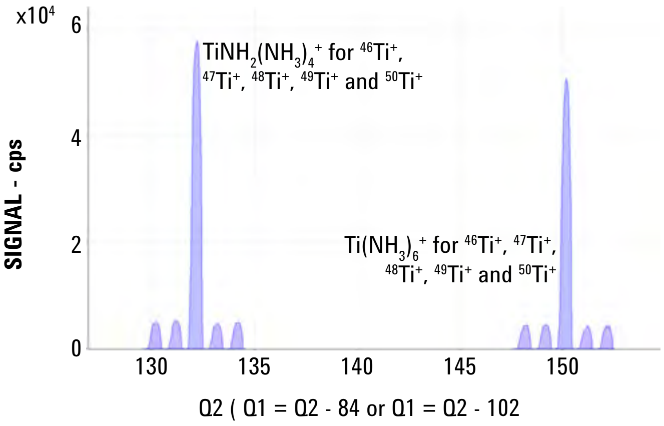

Figure 2. Neutral gain scan for two Ti ⟶ Ti cluster ion transitions: For $TiNH_2(NH_3)_4^+$ cluster ions, Q2 = Q1+ 84 amu, and for $Ti(NH_3)_6^+$ cluster ions, Q2 = Q1+102 amu. The preservation of the natural Ti isotope abundance pattern ($^{46}Ti^+$, $^{47}Ti^+$, $^{48}Ti^+$, $^{49}Ti^+$ and $^{50}Ti^+$) can be seen, confirming that MS/MS mode provides complete control over the complex Ti-NH_3 reaction chemistry.

(where Q1 and Q2 are scanned synchronously, with a set mass difference between them (Q2 = Q1 + 84 and Q2 = Q1 + 102 in this case)) were performed. These scans are shown in Figure 2 confirming the correct natural isotopic abundances for the different Ti isotopes. Without MS/MS capability, it would be impossible to preserve the isotopic information for this element due to the relatively complex nature of the Ti-ammonia adducts. The instrument cell conditions were optimized using simple HNO_3 acidified Ti standards and applied to the analysis of the CRMs.

Table 1 displays the results for both serum and urine sample types measured against a single calibration. The 8800 ICP-QQQ was operated also under no gas and He mode to provide comparative data, and three Ti isotopes were monitored for the same cluster ion transition, to give confirmation of the results.

Conclusions

Titanium was only certified in two of the four materials measured but the 8800 ICP-QQQ data were all comfortably within the measured ranges when operating under ammonia MS/MS mode, in contrast to no gas and He mode data. Importantly, the three Ti isotopes measured under ammonia MS/MS mode all gave equivalent data; this could indicate applicability of the method to the use of isotope-based analysis such as isotope dilution (ID) or isotope tracer analysis. The use of ammonia combined with MS/MS greatly simplifies the analysis of Ti in biological media for several isotopes. Furthermore, because MS/MS mode provides control over the reaction chemistry, no special attention needs to be paid to specific matrix matching regardless of the fluid investigated.

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Table 1. Urine and serum sample recovery (µg/L) for Ti in Seronorm CRM using $TiNH_2(NH_3)_4^+$ cluster

Sample Name	Target	^{47}Ti [No gas]	^{47}Ti [He]	47 -> 131 Ti [NH_3]	48 -> 132 Ti [NH_3]	49 -> 133 Ti [NH_3]
Urine blank	4.6 (2.2-7.0)	1989.79	41.44	2.80	2.79	2.92
Urine blank	4.6 (2.2-7.0)	2004.91	44.30	3.50	2.93	3.33
Urine trace elements		1789.92	51.41	14.81	15.27	14.42
Urine trace elements		1749.13	52.58	14.99	15.49	15.50
Serum L1	1.28 (0.86-1.80)	144.18	3.79	1.21	1.15	1.14
Serum L1	1.28 (0.86-1.80)	128.97	2.95	1.27	1.18	1.09
Serum L2		100.16	3.95	1.76	1.92	1.61
Serum L2		95.65	3.02	1.82	1.64	1.76

Simultaneous Quantitation of Peptides and Phosphopeptides by CapLC-ICP-QQQ

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Keywords

proteins, peptides, phosphorus, phosphopeptides, sulfur, S-containing peptides, heteroatom, isotope ratio, pharmaceutical, clinical, drugs, metabolites, environmental, pesticides, nanotechnology, nanoparticles, oxygen mass-shift

Introduction

LC-MS/MS is used for the quantification of target proteins in pharma/biopharma and clinical research. The approach generally relies on the use of synthetic, isotopically-labeled forms of each target protein and peptide, which are used as internal standards for the specific quantitation of the corresponding target compound. In contrast, the high temperature plasma ionization source used in ICP-MS ensures that elemental response is practically independent of the original form of the compound, which enables non-species-specific (or compound-independent) quantitation of compounds by measuring the signal for an element contained in the target compound. In this way, different proteins and peptides containing the heteroatoms S and P can be quantified using a single S- or P-containing compound as a generic standard. Unfortunately, with conventional quadrupole ICP-MS, the DLs for P and S are compromised by their high ionization potential and by multiple polyatomic interferences. The Agilent 8800 ICP-QQQ can effectively remove those interferences using reaction cell chemistry combined with the unique MS/MS mode, achieving excellent DLs for P and S even in organic solvents. This paper demonstrates the advantage of ICP-QQQ for the determination of proteins and peptides by measurement of P and S heteroatoms.

Experimental

Instrumentation: An Agilent 8800 Triple Quadrupole ICP-MS was used with an Agilent 1260 Series low flow capillary LC system. The standard 2.5 mm internal diameter (id) injector torch was replaced with the narrow injector, 1.5 mm id torch (G3280-80080) used for the analysis of volatile organic solvents. The exit of the LC column was interfaced to the ICP-MS via an Agilent capillary LC interface kit (G3680A) featuring a total consumption nebulizer and micro-volume spray chamber. O_2 gas (20% O_2 in Ar) was supplied to the plasma as an option gas at 0.08 L/min to prevent carbon build-up on the interface cones. Agilent ICP-MS MassHunter chromatographic software was used for integrated control of the LC-ICP-MS system and for data analysis.

CRC conditions: O_2 cell gas flow rate at 0.35 mL/min, Octopole bias = -18 V and KED = -6 V.

Acquisition conditions: MS/MS O_2 mass-shift method was applied for P and S measurement as shown in Figure 1.

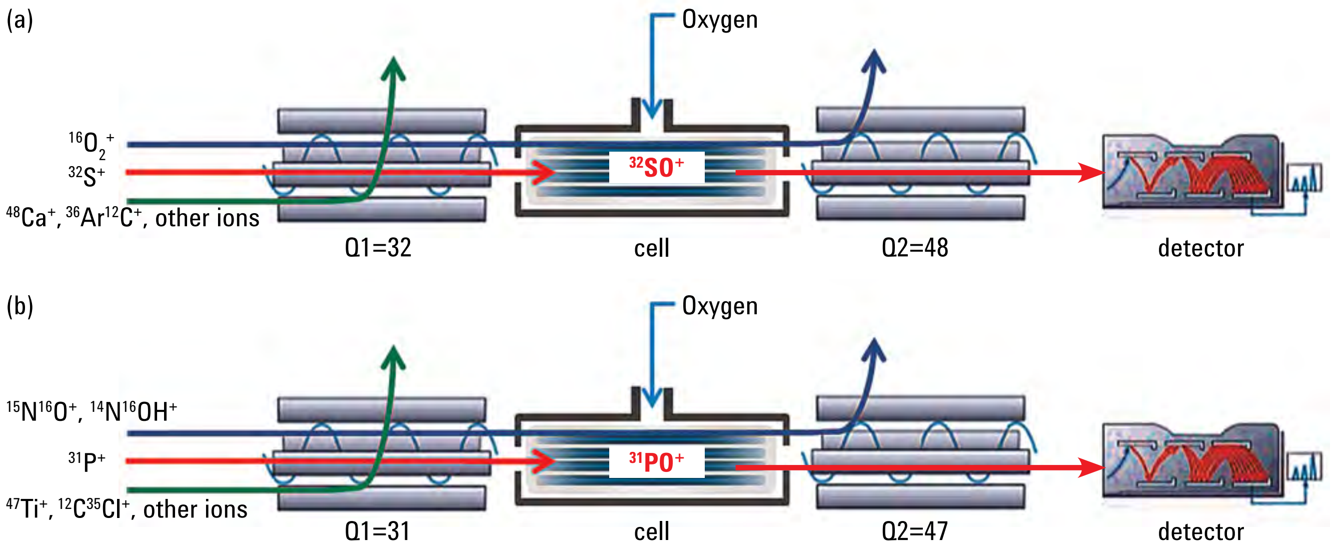

Figure 1. 8800 ICP-QQQ MS/MS operation in mass-shift mode to remove interferences on S (a) and P (b)

LC conditions: An Agilent Zorbax SB C18 (5 µm, 150 x 0.3 mm) reverse phase column was used with a flow rate of 5 µL/min. Mobile phases of water (A) and acetonitrile (B) were used for a gradient elution with the following profile: 0-3 min: 1% B; 3-35 min: 1-60% B linear. Both mobile phases contained 0.1% formic acid and 10 ppb Ge as ISTD and for tuning. The injection volume was 2 µL.

Reagents: Bis-4-nitro-phenyl phosphate (BNPP, 99% purity) and methionine (≥ 99% purity) (Sigma-Aldrich, Steinheim, Germany) were used as calibration standards for phosphopeptides and S-containing peptides respectively. Amino acid sequences of the phosphopeptides were LRRA-pS-LG and KRS-pY-EEHIP, and the S-containing peptides were A-C-TPER-M-AE and VP-M-LK. All peptides were purchased from AnaSpec (Fremont, CA, USA) with purity ≥95%.

Results and discussion

Calibration and DL

Calibration standards containing 25, 50, 100 and 200 ng/mL of both P and S (BNPP and methionine, respectively) were injected and measured. Excellent linearity and RSD of <4% was obtained (see Figure 2).

The chromatogram for the 50 ng/mL standard was used for signal to noise (S/N) and DL calculation. The DL achieved was 0.10 ng/mL for P and 0.18 ng/mL for S. As the injection volume was 2 µL, the DLs in absolute weight were calculated to be 6.6 fmol and 11 fmol for P and S, respectively.

Measurement of phosphopeptide and S-containing peptides

Finally, a sample containing a mixture of phosphopeptides and S-containing peptides was analyzed. The sample was also spiked with the standards methionine and BNPP for non-species-specific calibration. The chromatogram shown in Figure 3 illustrates the excellent peak shape and S/N obtained, demonstrating the exciting potential of ICP-QQQ for quantitative protein and peptide analysis using measurement of P- and S-heteroatoms.

More information

Simultaneous quantitation of peptides and phosphopeptides by capLC-ICP-MS using the Agilent 8800 Triple Quadrupole ICP-MS, Agilent application note, 5991-1461EN.

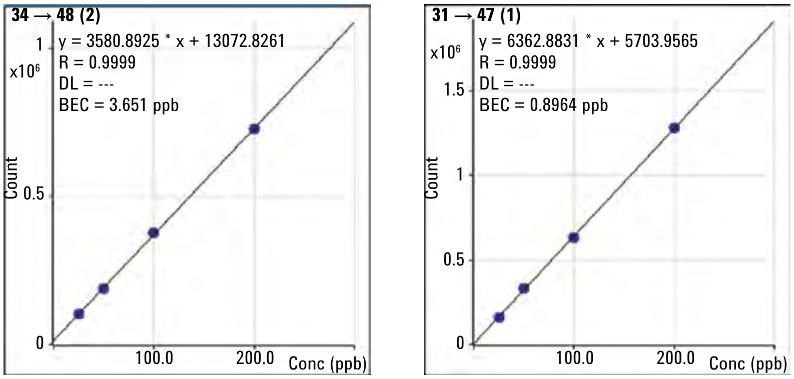

Figure 2. Calibration plots for P and S (in BNPP and methionine, respectively) at 25, 50, 100 and 200 ng/mL (as the element)

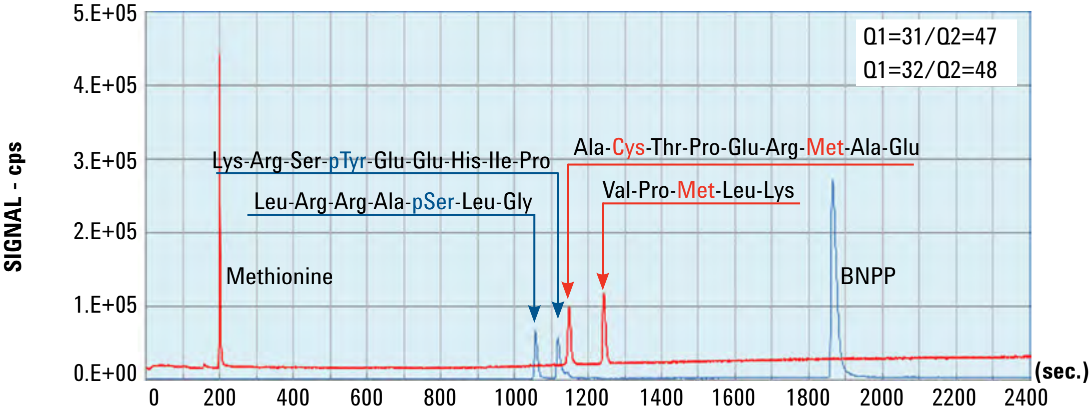

Figure 3. Chromatogram of phosphopeptides and S-containing peptides. Sample: 45 ng/mL of two phosphopeptides and two S-containing peptides, and 105 ng/mL of BNPP and methionine (conc. as P or S)

Analysis of Selenoproteins in Rat Serum using HPLC-ICP-QQQ

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Keywords

selenium, selenoprotein P, Sel P, glutathione peroxidase, eGPx, GPx-3, serum, biological, rat, mouse, hamster, guinea pig, speciation, mass-shift method, oxygen reaction mode

Introduction

Selenium (Se) is an essential micronutrient in animals and is present in several of the key proteins found in plasma. Two selenoproteins which contain Se as selenocysteine (SeCys) in their primary structures, extracellular glutathione peroxidase (eGPx, GPx-3) and selenoprotein P (Sel P), have been detected in animal plasma. Other Se-containing proteins which have Se incorporated into their peptide sequence as selenomethionine (SeMet), are also detected because animals are unable to discriminate SeMet from methionine (Met). The most abundant Se-containing protein in human plasma is albumin. However, some studies have indicated that no or little Se-containing albumin is detected in the blood plasma of experimental animals compared to human plasma [1-3]. This can be explained by the fact that humans ingest Se mainly as SeMet, whereas the major Se species in the feeds given to experimental animals is inorganic Se, such as selenite and selenate.

The three most abundant Se isotopes, ^{80}Se (49.6%), ^{78}Se (23.8%), and ^{76}Se (9.36%), suffer from interference by several polyatomic ions originating from the Ar plasma, namely, $^{40}Ar^{40}Ar^+$, $^{40}Ar^{38}Ar^+$, and $^{38}Ar^{38}Ar^+$, respectively. ^{77}Se is also subject to interference by $^{40}Ar^{37}Cl^+$ when chloride is present in the sample matrix, as is the case with biological samples. Sample matrix components such as S, Ca and K may also contribute polyatomic overlaps on isotopes of Se, for example $^{39}K^{37}Cl^+$ on $^{76}Se^+$, $^{32}S_2{}^{16}O^+$, $^{32}S^{16}O_3{}^+$ and $^{40}Ca_2{}^+$ on $^{80}Se^+$, and $^{79/81}BrH^+$ on $^{80/82}Se^+$.

ICP-QQQ can operate with oxygen cell gas and mass-shift mode, using O-atom addition to move the analyte ions away from the interference for detection at M+16 amu. For example, $^{78}Se^+$ is measured as $^{78}Se^{16}O^+$ at 94 amu; $^{80}Se^+$ is measured at 96 amu; and $^{82}Se^+$ is measured at 98 amu.

The aim of this study is to evaluate the performance of ICP-QQQ for the speciation of Se in rat serum.

Experimental

Instrumentation: Agilent 8800 #100 was used with an HPLC system.

CRC conditions: O_2 cell gas at a flow rate of 0.30 mL/min.

Acquisition conditions: MS/MS O_2 mass-shift method: Se signals were monitored as SeO^+ at *m/z* 94, 96, and 98

LC conditions: A multi-mode gel filtration column, Shodex Asahipak GS-520HQ (7.5 i.d. x 300 mm, with a guard column, 7.5 i.d. x 75 mm, Showa Denko, Tokyo, Japan), was used. A 200 µL aliquot of serum sample was injected onto the column and then eluted with 50 mmol/L Tris-HCl, pH 7.4, at a flow rate of 0.6 mL/min. The eluate emerging from the column was introduced directly into the nebulizer of the ICP-QQQ.

Reagents: The instrument was tuned using an inorganic Se standard. Tris(hydroxymethyl) aminomethane (TRIZMA base and TRIZMA HCl) were purchased from Sigma (St. Louis, MO, USA).

Results and discussion

Elution profiles of Se in rat serum

Blood was collected from the experimental rats after one week; the blood was separated by centrifugation, and the serum samples were stored at -30 °C prior to analysis by LC-ICP-QQQ. Two well-separated Se peaks were detected at retention times of 11.7 and 14.3 min (Figure 1). The former and latter peaks were assignable to eGPx and Sel P, respectively, per a previous study [4]. It was reported that albumin was eluted at the retention time of 15.0-16.0 min on this column [5]. However, we did not detect a Se peak at a retention time of 15.0-16.0 min, suggesting that SeMet was not incorporated into albumin in place of Met.

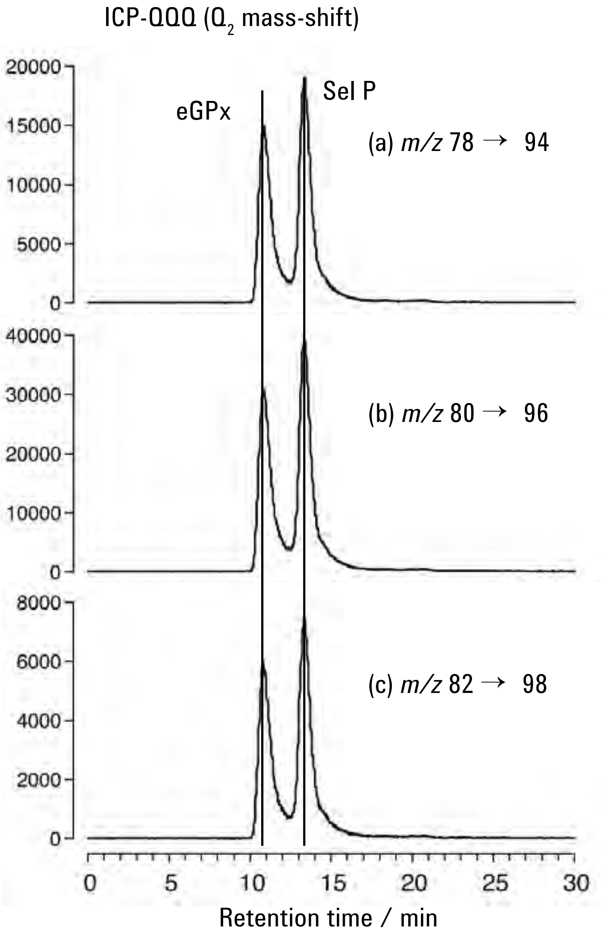

Figure 1. Elution profiles of Se in rat serum. A 200-µL aliquot of a rat serum sample was injected into a GS-520HQ column and the eluate was monitored by ICP-QQQ (a-c) at *m/z* 94 (a), 96 (b), and 98 (c).

Conclusions

Two major selenoproteins, eGPx and Sel P, in rat serum were well separated on an HPLC column. ICP-QQQ was a more accurate detector for the speciation of serum selenoproteins than conventional quadrupole ICP-MS, because the ICP-QQQ analysis was completely free of interferences originating from the Ar plasma source and any matrix elements.

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More information

Analysis of selenoproteins in rat serum by Triple Quadrupole ICP-MS, Agilent application note, 5991-2750EN.

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Absolute Quantification of Intact Proteins without Specific Standards by capLC-ICP-QQQ

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Keywords

proteins, sulfur, isotope dilution analysis, absolute quantification, proteomics, venomics

Introduction

ICP-MS has become a feasible alternative to molecular MS-based proteomic workflows, which commonly require specific (mostly isotopically enriched) standards for each target protein. The introduction of triple quadrupole ICP-MS (ICP-QQQ) has boosted the applicability of ICP-MS-based methods for quantitative proteomic studies. This development is due to the sensitive interference-free detection of heteroelements, such as sulfur (S), and the possibility of generic quantification without the need for specific standards. This paper demonstrates the capacity of capillary reverse phase (RP)-LC-ICP-QQQ for the absolute quantification of intact protein standards using post-column isotope dilution (ID) analysis. The method was used for the individual quantification of up to 27 different proteins present in a relatively complex sample of snake venom.

Experimental

Instrumentation: Capillary LC separation was performed using an Agilent 1200 series HPLC equipped with a BIOshell A400 (3.4 µm, 150 mm x 0.3 mm) reverse-phase column (Sigma-Aldrich, Germany). The exit of the column was coupled to the Agilent 8800 ICP-QQQ using an Agilent Capillary LC interface kit (G3680A). The kit comprised a total consumption nebulizer with single pass spray chamber. Enriched ^{34}S was added post-column. Sulfur isotopes were measured using an oxygen mass-shift MS/MS method and the S content of the proteins was determined by ID. BOC-L-methionine was used as the internal standard to correct for any injection errors.

Reagents: Pure standard BOC-L-methionine (Sigma, Germany) was used as a standard for quantification. Cytochrome C, bovine serum albumin (BSA), β-casein, transferrin (Sigma-Aldrich, Germany), and intact mAb (Waters, USA) were used as protein standards in the recovery study. The venom sample analyzed in the study was extracted from a Tanzanian *Naja mossambica* (Valence, France).

Results and discussion

Protein standards analysis

Absolute quantification of proteins was achieved through the measurement of sulfur with post-column ID. The individual protein samples (BSA, cytochrome C, and transferrin) were spiked with a non-species-specific sulfur-containing standard, BOC-L-methionine, in this case. Quantitative (mass purity) data obtained for cytochrome C (94±2%), BSA (96±2%), and transferrin (94±2%) were in excellent agreement with the theoretical values supplied by the manufacturer, ≥95%, ≥98% and ≥95%, respectively.

Quantification of 27 proteins in snake venom

The method was applied to the analysis and quantification of the proteins present in a snake venom sample. The sample was spiked with BOC-L-methionine. capLC-ICP-QQQ was then used to monitor the sulfur present in each protein and to quantify the concentration via ID analysis. Figure 1 shows the chromatogram (22-39 min) for the snake venom sample.

Parallel capLC-ESI-MS analysis was used to identify the proteins. By identifying the proteins, it was possible to know the S-to-protein stoichiometry of each peak. This information was then used to translate sulfur mass into individual protein quantities, in µmol protein per gram of venom sample. The quantified results are summarized in Figure 2.

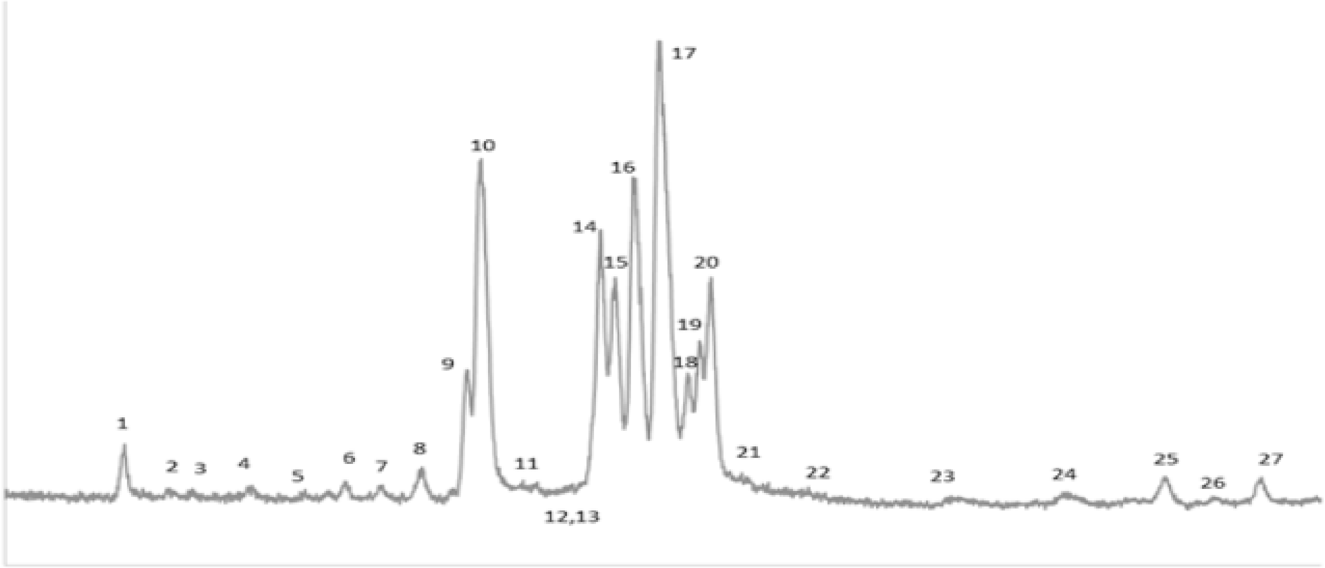

Figure 1. Chromatogram (22–39 min) of snake venom sample (S detection).
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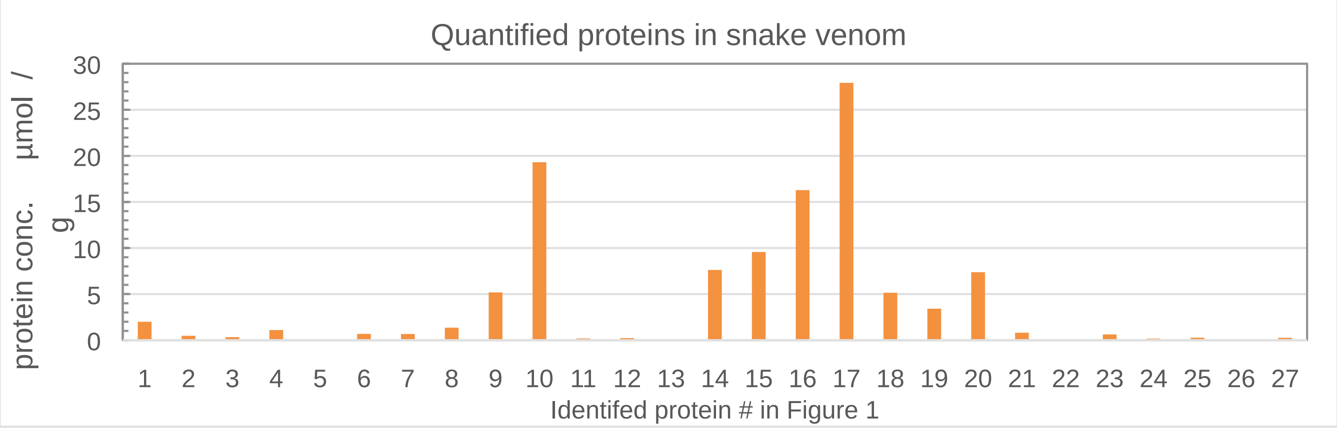

Figure 2. Quantified proteins in snake venom.
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Conclusions

The capLC-ICP-QQQ method is suitable for the absolute quantification of intact proteins without the need for specific standards. If quantitative chromatographic recoveries can be assured, it is even possible to quantify nonpure protein samples using this method. The potential of the methodology for the quantification of intact proteins present in relatively complex samples was demonstrated by analyzing 27 proteins in snake venom.

More information

Francisco Calderón Celis, Elemental Mass Spectrometry for Absolute Intact Protein Quantification without Protein-Specific Standards: Application to Snake Venomics, Anal. Chem., 2016, 88 (19), 9699–97.

Measurement of Selenium in Clinical Samples in the Presence of Gadolinium-Based Magnetic Resonance Imaging Contrasting Agents

Glenn Woods
Agilent Technologies (UK) Ltd.

Keywords

selenium, enzyme, blood, serum, urine, MRI contrasting agents, gadolinium, molybdenum, zirconium, neutral gain scan, oxygen mass-shift

Introduction

Selenium is an important micronutrient for human, mammalian, bacterial and plant life and is contained within several co-factors and enzyme systems. It is monitored in blood, serum and urine as part of human health, and a deficiency can indicate an illness (particularly if the levels change suddenly), such as cancer, diabetes and tuberculosis (TB).

For cancer patients, determining the location of the tumour often requires the use of Magnetic Resonance Imaging (MRI). However, for some soft tissues such as the brain, a "contrasting agent" is needed to effectively show the location of the tumour or problem area. There are several contrasting agents which are salts or chelates of gadolinium (III) (Gd(III)), trade names are given in brackets:

Gadodiamide (Omniscan), Gadobenate (MultiHance), Gadopentetate (Magnevist), Gadoteridol (ProHance), Gadofosveset (Ablavar, formerly Vasovist), Gadoversetamide (OptiMARK), Gadoxetate (Eovist), Gadobutrol (Gadavist)

Unfortunately Gd has a relatively low second ionization potential (12.09 eV) meaning it can form Gd^{++} ions in the plasma. These Gd^{++} ions appear at half their original mass (as a quadrupole measures ions based on their mass to charge ratio or m/z) and form interferences on all of the main analytical isotopes of Se. This is complicated to a greater extent as Gd has several odd-mass isotopes which form Gd^{++} interferences at half-mass (e.g., $^{155}Gd^{++}$ would appear at m/z 77.5). This makes the spectrum in the mass region of the Se isotopes quite complex when Gd is present in the sample. In a typical patient's sample, the Gd concentration can vary between zero to several thousand parts per billion (µg/L). Because of the variability from patient-to-patient (which is also time-dependant on a sample-to-sample basis due to the contrasting agent's half-life in the body) a simple mathematical correction cannot always be made or a constant "background" be assumed.

Experimental

In order to remove the Gd-based interference, Se^+ can be reacted with oxygen cell gas in the collision/reaction cell to produce SeO^+ as a product ion. The Se-O reaction is slightly endothermic ($\Delta Hr = 0.71$ eV) which means that the reaction yield for SeO^+ would be relatively low. However the bias voltage on the ORS can be adjusted to increase the ion energy improving reaction yield significantly over a more "thermalized" approach. These conditions are referred to as high ORS bias conditions.

Instrumentation: Agilent 8800 #100.

Plasma conditions: Preset plasma/General purpose.

Ion lens tune: Soft extraction tune: Extract 1 = 0 V, Extract 2 = -170 V.

CRC conditions: O_2 gas at 0.3 mL/min, Octopole bias = -15 V, KED = -8 V.

Results and discussion

O_2 mass-shift method

Using O_2 mass-shift, the analyte is measured at M +16 amu (e.g. $^{78}Se^+$ is measured as $^{78}Se^{16}O^+$ at 94 amu). With conventional quadrupole ICP-MS, any ^{94}Mo or ^{94}Zr present in the sample would interfere with the measurement at this mass. However, with MS/MS mode, ^{94}Mo or ^{94}Zr are removed by Q1 as it is set to the mass of the Se^+ precursor ion at 78 amu, and $^{156}Gd^{++}$ is eliminated as Q2 is set to the SeO^+ product ion mass of 94 amu. Even if Gd did form GdO^{++} this would also be eliminated by Q2 as the apparent mass (*m/z*) of $^{156}Gd^{16}O^{++}$ is 172/2 (86 amu). Figure 1 is a graphical representation of the MS/MS setup.

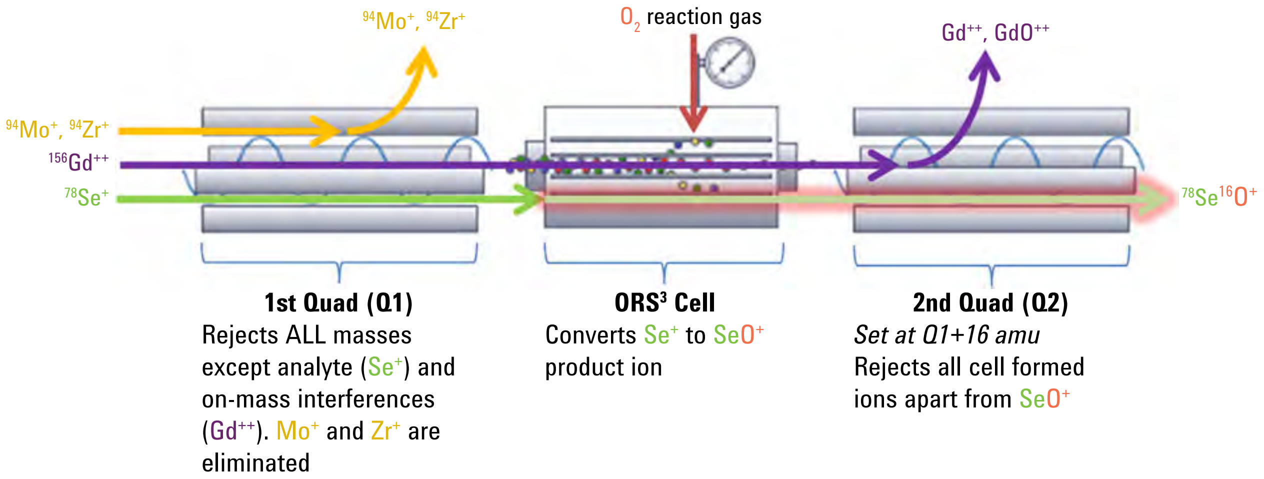

Figure 1. Representation of ICP-QQQ setup with Q1 set to 78 amu and Q2 set to 94 amu. Mo and Zr-based interferences are eliminated by Q1 and Gd^{++} is eliminated by Q2 allowing the measurement of ^{78}Se as $^{78}Se^{16}O^+$

To check for efficient conversion of Se^+ to SeO^+, a neutral gain scan covering the mass range of all the SeO^+ product ions was performed for a 5 ppb Se solution. Figure 2 displays the isotope pattern of the + ^{16}O-atom transitions for all the Se isotopes, showing a perfect match with the theoretical isotopic fit.

Se measurement in human serum

Instrument cell conditions were optimized using a Se standard in a simple HNO_3 matrix. A pooled human serum sample was prepared by 10x dilution into a basic diluent consisting of NH_4OH (0.5%), H_4-EDTA (0.01%), BuOH (2%) & Triton X-100 (0.01%) in ultrapure water. The sample was prepared unspiked and also spiked with Gd equivalent to 250, 500 and 1000 µg/L in the original sample, and analyzed using the 8800 ICP-QQQ in no gas and O_2 mass-shift modes of operation for comparison. The data is summarized in Table 1. The results show that, under no gas conditions, the apparent Se concentration is influenced by the variable Gd^{++} interference. Recovery based upon the original unspiked sample demonstrates an over-recovery of almost 130% for the no gas data when Gd is at a concentration of 1000 µg/L. In contrast, the Se data measured with MS/MS mass-shift mode remains essentially constant at all levels of Gd matrix. This would indicate that the O_2 mass-shift reaction is independent of the Gd concentration and is highly applicable to this relatively difficult and important application.

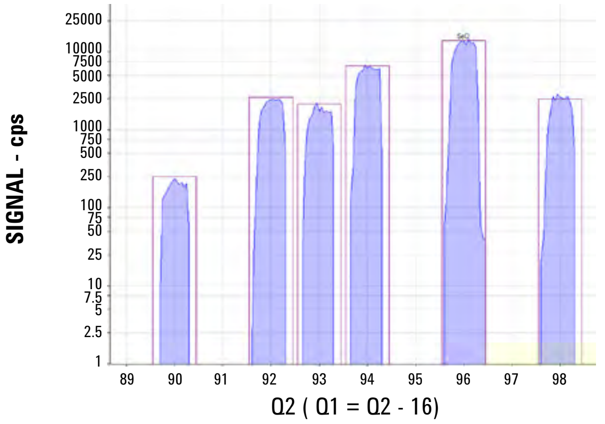

Figure 2. Neutral gain scan for 5 ppb Se solution. Note the excellent spectral fit. The six peaks corresponded to SeO^+ product ions formed from the Se isotopes: ^{74}Se, ^{76}Se, ^{77}Se, ^{78}Se, ^{80}Se and ^{82}Se.

Table 1. Serum sample data and recovery for Se with variable Gd concentration. Recovery is calculated based on determined Se concentration in unspiked serum sample. All data is dilution corrected.

	No gas mode		O_2 mass-shift	
	Conc. ppb	Recovery %	Conc. ppb	Recovery %
Serum	93.64	NA	91.42	NA
Serum with 250 µg/L Gd	99.97	106.7	91.38	100.0
Serum with 500 µg/L Gd	112.1	120.0	91.70	100.3
Serum with 1000 µg/L Gd	121.1	129.3	91.78	100.4

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Quantitative Analysis of Active Pharmaceutical Ingredients using Heteroatoms as Elemental Labels

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Keywords

protein, heteroatom, API, monoclonal antibody, mAb, sulfonamide, sulfur, zoledronic acid hydrate, phosphorus, clonidine hydrochloride, chlorine, mass-shift, oxygen reaction mode, hydrogen reaction mode

Introduction

Organic molecules and proteins can be detected and quantified indirectly by using ICP-MS to measure a heteroatom “tag” element contained within the targeted compound. For example a large number of Active Pharmaceutical Ingredients (API) contain sulfur (S), phosphorus (P) or halogens. Unfortunately, S, P and the halogens have high first ionization potentials so they are poorly ionized in the ICP-MS plasma, leading to low sensitivity. S, P and chlorine (Cl) are also difficult to measure by conventional quadrupole ICP-MS (ICP-QMS) due to intense spectral interferences. As a result, accurate analysis of S, P, and the halogens at the analytical ranges that are relevant to pharmaceutical molecules is nearly impossible to achieve by ICP-QMS. However, ICP-QQQ operating in MS/MS reaction cell mode can be applied to resolve these spectral interferences, allowing the quantification of S, P and Cl at far lower levels (biologically relevant concentrations) than was previously possible by ICP-QMS.

In this study, five APIs and a monoclonal antibody (mAb) were analyzed using ICP-QQQ. The targeted compounds included small (m = 250–320 Da) and large (m = 146 kDa for the mAb) molecules.

Experimental

Instrumentation: An Agilent 8800 ICP-QQQ #100 was coupled to an Agilent 1260 Infinity Bio-inert HPLC system with quaternary pump (G5611A) and autosampler (G5667A). An HPLC flow rate of 0.4 mL/min and an injection volume of 20 µL were applied throughout the study.

CRC conditions: O_2 at 0.3 mL/min. H_2 flow at 3.0 mL/min. Octopole bias = -4 V and KED = -8 V.

Acquisition conditions: MS/MS O_2 mass-shift method for S and P measurement and H_2 mass-shift method for Cl measurement.

LC conditions: Two types of columns were used: an Agilent ZORBAX plus C18, 2.1 x 100 mm, 3.5 µm (Agilent # 959793-902) was used for the analysis of the small molecules, and an Agilent Bio SEC-3 300 Å, 4.6 x 150 mm, 3 µm (Agilent # 5190-2514) was employed for the mAb analysis.

Reagents: Sulfamethizole, sulfamethazine, sulfamethoxazole, zoledronic acid hydrate and clonidine hydrochloride were purchased from Sigma Aldrich (St. Louis, MO, US). The monoclonal antibody (IgG2a) was obtained from Agilent Technologies (Agilent #200473).

Results and discussion

Sulfur-containing API

Three sulfonamide APIs, sulfamethizole, sulfamethazine and sulfamethoxazole, were dissolved separately in methanol or methanol/water. Each sample was filtered, diluted with the LC mobile phase of 13% acetonitrile with 0.1% formic acid, and injected into the HPLC using an isocratic separation. The resulting overlaid chromatograms are shown in Figure 1. The method detection limit (MDL) for the compound sulfamethizole was calculated to be 23 nM (6.3 ppb as the compound and 1.5 ppb as S).

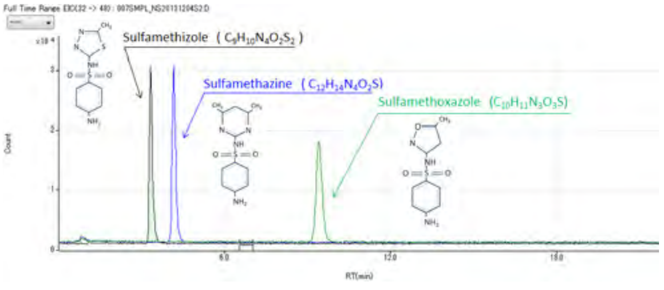

Figure 1. Overlaid chromatograms of three sulfur-containing APIs. The concentration of S in all 3 APIs injected is 100 ppb.

Antibodies are glycoproteins that contain about 1% sulfur and are therefore excellent targets for quantification via sulfur determination by ICP-QQQ. A mAb (IgG2a) obtained from Agilent was diluted with UPW and injected into the HPLC. An isocratic mobile phase of 50 mM phosphate buffer adjusted to pH 7.0 was used. Figure 2 shows the overlaid chromatograms obtained for two different concentrations of IgG2a. The MDL was calculated to be 14 nM (40 ng) as the compound.

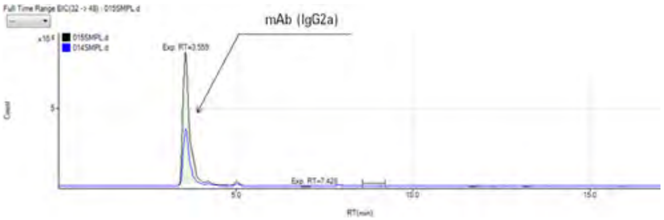

Figure 2. Overlaid chromatograms of 0.5 mg/mL and 1.0 mg/mL mAb (IgG2a) obtained by HPLC-ICP-QQQ.

Phosphorus-containing API

ZOMETA® is a commercial drug that is used for the treatment of hypercalcemia (high levels of blood calcium). It contains zoledronic acid monohydrate ($C_5H_{10}N_2O_7P_2 \cdot H_2O$), which acts as an inhibitor of osteoclastic bone resorption and an inducer of osteoclast apoptosis. A 5 mL vial of commercially supplied ZOMETA® (containing 4.264 mg of the API) was prepared by diluting the drug 2000-fold with the LC mobile phase to give a final API concentration of 426.4 µg/L. The isocratic mobile phase consisted of a 70:30 mixture of A: 6 mM tetra-butyl-ammonium bromide and 5 mM acetic acid adjusted to pH 6.5 with NH_3(aq), and B: 95% MeOH. A calibration curve was prepared using zoledronic acid monohydrate standards, and the API in the sample was quantified based on the response for P compared to the external calibration. The concentration of the API in the sample was determined to be 433 ng/mL, which is a recovery of 102%. The MDL for the drug compound was calculated to be 25 nM (144 pg; 7.2 ppb as compound and 1.5 ppb as P).

Chlorine-containing API

Catapres® is a commercial drug that is used for the treatment of hypertension. It contains clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$) which acts in the brain to suppress secretion of noradrenaline, lowering blood pressure. A tablet of Catapres® (containing 75 µg of the API) was dissolved in 50 mL water and sonicated for 60 minutes. The solution was then filtered and analyzed by HPLC-ICP-QQQ. A calibration curve was prepared by analyzing clonidine hydrochloride standards, and the API in the sample was quantified by external calibration. The isocratic HPLC method used a mobile phase consisting of 20% acetonitrile with 0.1% formic acid adjusted to pH 7.0 by NH_3(aq). The calibration curve for Cl measured as $^{35}ClH_2^+$ at *m/z* 37 and the chromatogram of clonidine hydrochloride measured in the Catapres® sample are presented in Figure 3. The concentration of the API in the sample was determined to be 1444 ppb, which is a recovery of 96%. The MDL of the compound was 146 nM (780 pg; 39 ppb as compound and 15 ppb as Cl).

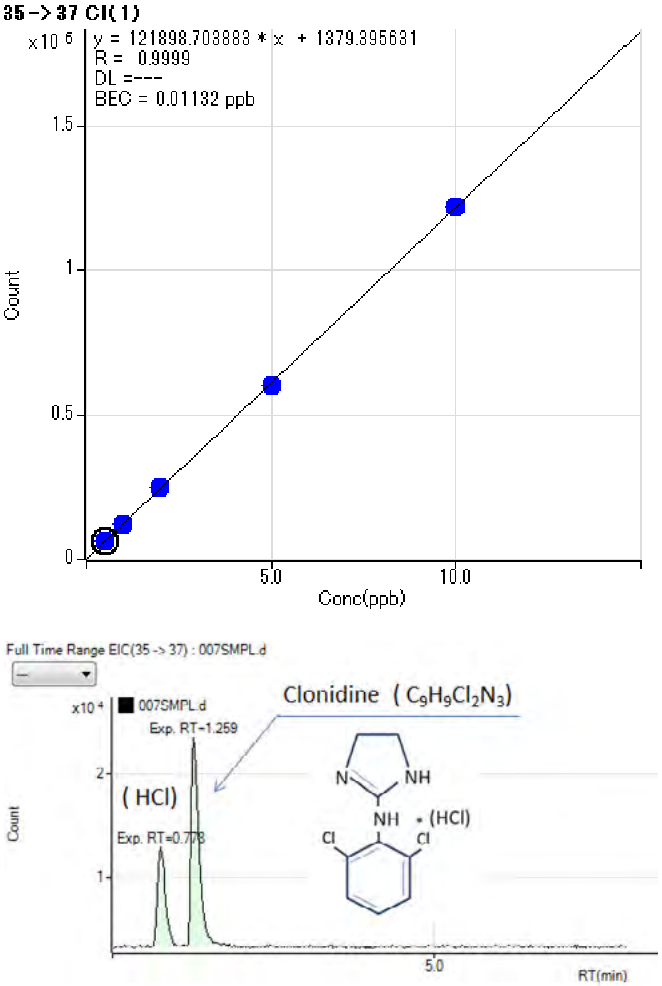

Figure 3. (Top) Calibration curve for Cl (measured as $^{35}ClH_2^+$) in clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$) standards. (Bottom) Chromatogram of clonidine hydrochloride in Catapres® sample

Conclusions

The advanced capability of the Agilent 8800 ICP-QQQ operating in MS/MS mode has been successfully applied to the analysis of APIs and mAb, based on the measurement of the heteroatoms S, P and Cl — an analysis that is normally carried out using molecular-MS techniques. These preliminary studies are presented here in order to demonstrate the potential use of HPLC-ICP-QQQ in drug development and post manufacturing QA/QC control.

More information

Using heteroatoms as elemental labels in the quantitative analysis of active pharmaceutical ingredients by HPLC-ICP-QQQ, Agilent application note, 5991-5445EN.

Fast and Accurate Absolute-quantification of Proteins and Antibodies using ID-ICP-QQQ

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Keywords

proteins, antibody, absolute-quantification, isotope dilution, ICP-MS/MS, ICP-QQQ

Introduction

Triple quadrupole ICP-MS (ICP-QQQ) dramatically improves the efficiency and reliability of removing spectral interferences on a wider number of elements than conventional ICP-MS. Challenging elements such as sulfur (S), which suffer intense spectral overlaps, can be analyzed at low levels by ICP-QQQ. Furthermore, the effective removal of spectral overlaps allows access to multiple isotopes of elements, enabling quantification of metalloproteins and peptides using isotope dilution mass spectrometry (IDMS) analysis. IDMS is an absolute quantification technique that eliminates the requirement for compound-specific calibration standards. It allows accurate quantification without the need for a reference standard, which is a major benefit of ID-ICP-MS/MS for life science research, where many compounds are unknown.

In this study, we evaluated an Agilent 8800 ICP-QQQ and isotope dilution analysis (ID-ICP-QQQ) of sulfur, for the quantification of NIST Bovine Serum Albumin (BSA) 927e standard reference material (SRM) [1] and a monoclonal antibody, trastuzumab.

Experimental

Instrumentation: An Agilent 8800 #100 was used.

Acquisition conditions: two sulfur isotopes, ^{32}S and ^{34}S, were measured in MS/MS mass-shift mode with oxygen (O_2) reaction gas.

Plasma conditions: RF power =1550 W, nebulizer gas flow rate = 0.25 L/min, and dilution gas flow rate of 0.85 L/min.

Double isotope dilution method: in a simple ID method, a sample containing an unknown amount of S, which is primarily composed of the major ^{32}S isotope (94.93% abundance), is spiked with a known amount of a certified enriched isotopic standard solution containing ^{34}S. An aliquot of the resulting solution is analyzed, and the ratio of ^{34}S to ^{32}S is measured. From the measured ratio and the known amount of ^{34}S, it is possible to calculate the amount of ^{32}S and therefore the total S concentration (based on natural isotopic abundances) in the original sample.

However, as the $^{34}SO_4^{2-}$ spiking solution used in this study was prepared by oxidation of a powder of ^{34}S sulfur, the exact concentration of ^{34}S present in the spike was unknown. Therefore, a high accuracy technique known as double IDMS was employed in this study per Equation 1. The concentration of ^{34}S in the $H_2{}^{34}SO_4$ solution was determined by reverse IDMS. A National Institute of Standards and Technology (NIST) certified solution of SO_4, with a natural sulfur isotopic abundance, was used as the reference standard.

Equation 1. The double IDMS equation used in this study

$$w_x = w_z \cdot \frac{m_y \cdot m_z}{m_x \cdot m_{y'}} \cdot \frac{R_y - R_{xy}}{R_{xy} - R_x} \cdot \frac{R_{zy} - R_z}{R_y - R_{zy}}$$

- x refers to the sample
- y and y' refer to the $^{34}SO_4$ spiking solution
- z refers to the NIST SO_4 standard solution
- w_x is the sulfur mass fraction (µg/g) in the sample
- w_z is the sulfur mass fraction (µg/g) in the NIST SO_4 standard solution
- m_i is the mass of sample, standard, or spiking solution
- R_i is the $^{34}S/^{32}S$ ratio measured by ICP-QQQ in the unspiked and spiked solutions
- R_x is the $^{34}S/^{32}S$ ratio measured in the sample solution
- R_y is the $^{34}S/^{32}S$ ratio measured in the spiking solution
- R_z is the $^{34}S/^{32}S$ ratio measured in the SO_4 standard solution
- m_x is spiked with my and ratio R_{xy} is measured
- m_z is spiked with my' and ratio R_{zy} is measured

Samples: sample solutions were prepared for microwave digestion. First, an amount of sample (BSA standard and trastuzumab solution) estimated to contain approximately 50 µg sulfur was weighed into a disposable glass tube. 50 µg of ^{34}S (as $H_2{}^{34}SO_4$) was added, followed by 2 mL of 69% HNO_3, 0.5 mL of 37% HCl, and 1 mL of 30 % H_2O_2. Once the microwave digestion program had finished, the digest was transferred and diluted to 50 mL with H_2O. The concentration of S in solution was about 1 ppm.

A standard was also prepared for the double IDMS method. 50 µg of a 1000 mg/L sulfur ICP-MS standard (natural isotopic abundance) was weighed into another glass tube. The above procedure was then carried out.

Results and discussion

Six samples of NIST BSA 927e were quantified using the ID-ICP-MS/MS method. The average recovery to the certified value (67.38 ±1.38 g/L as S) was 101.26 % and the RSD of six analyses was 0.22%.

Matrix effects were also investigated. The same amount of BSA was spiked with different formulation ingredients. The solutions were then digested and analyzed. The results in Figure 1 show good recoveries were obtained for S in all matrix solutions.

Trastuzumab is a monoclonal antibody (mAb) that interferes with the human epidermal growth factor receptor 2 (HER2/neu receptor). The mAb in solution was quantified using the developed method. The average recovery to expected value (21 mg/mL as S) was 97.8% and the RSD of three analyses was 0.02%.

Conclusions

The Agilent 8800 ICP-QQQ with MS/MS mode provides high analytical sensitivity and effective interference reduction for the determination of multiple sulfur isotopes. This capability allows the accurate analysis of biological molecules that contain sulfur, using isotope dilution analysis. The ID-ICP-QQQ method is suitable for the accurate and precise quantitative analysis of biological molecules, such as pure proteins and antibodies, without the need for compound-specific calibration standards.

References

1. National Institute of Standards & Technology SRM 927e certificate

2. P. De Raeve, J. Bianga, Agilent publication, 2015, 5991-6118EN

More information

Fast and accurate absolute-quantification of proteins and antibodies using Isotope Dilution-Triple Quadrupole ICP-MS, Agilent application note, 2015, 5991-6118EN.

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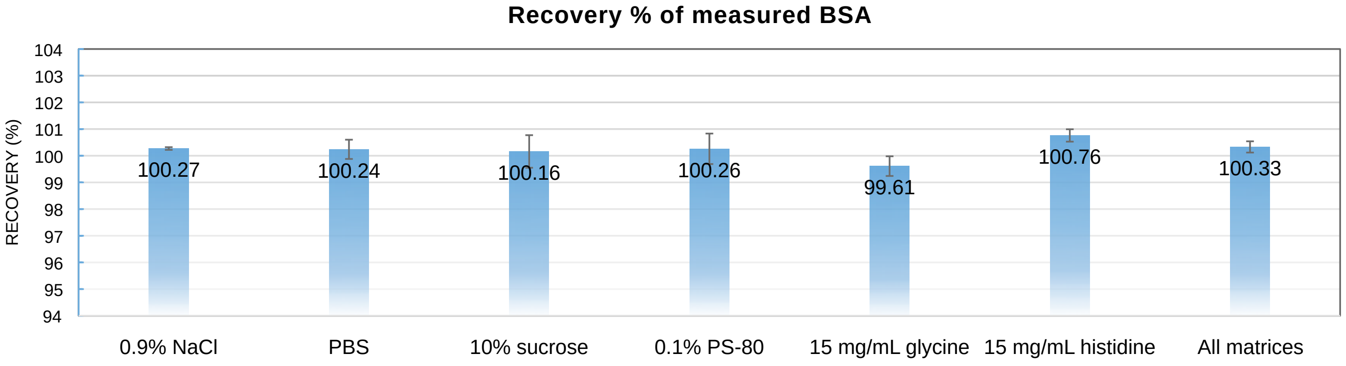

Figure 1. Recovery % (average of n = 3) of measured BSA in various matrix solutions. The error bars show the standard deviation of the three analyses.

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Glossary

A

Acquisition conditions	Parameters including: Peak profile, mass, integration time, scan number and replicate.
Ammonia, NH_3	A reaction gas used in the collision/reaction cell. NH_3 is a very reactive gas, which is used both in on-mass methods and mass-shift methods to remove/avoid interferences.
amu	Atomic mass unit. An obsolete, non-SI unit that is still in common use in its abbreviated form "amu", meaning the same thing as "unified atomic mass unit" (u) or dalton (Da). All are used to indicate the atomic mass of ions, atoms or molecules, based on the carbon 12 standard.
API, Active Pharmaceutical Ingredient	An API is a compound in a drug which has remedy effects on the target disorder.
AS, abundance sensitivity	The measure of an analyzer's ability to separate adjacent peaks differing greatly in intensity. Agilent ICP-QQQ with MS/MS operation delivers unmatched peak separation (abundance sensitivity $<10^{-10}$), as the resolution performance is the product of the abundance sensitvitiy of the two quadrupoles.
ASX-520	Autosampler suitable for medium to high sample throughput applications, with rack configurations providing up to 360 vial positions (up to 720 with the extended rack XLR-8 version).
Axial Acceleration	A function of the ion guide to accelerate/decelerate ions along the axis of the ion guide.

B

BED, Background Equivalent Diameter	BED is the diameter equivalent to the background noise in single particle analysis.
Bandpass	Mode of operation of a multipole ion guide, where both a low-mass cut-off and high-mass cut-off are applied, rejecting ions below and above a certain *m/z*. A bandpass filter passes a "window" of masses (typically covering a 20-30 *m/z* range) through the ion guide, and is therefore distinct from a mass filter, which is capable of unit mass resolution (single *m/z* mass selection).
Batch	The acquisition batch contains all the information required for a sample analysis or experiment, including peripump program, tuning conditions, acquisition parameters, sample list and data analysis (calibration) parameters. The data analysis (DA) batch contains the measured results for the batch of samples, and includes the calibration plots, internal standard signals and QC flags
BEC, Background equivalent concentration	The magnitude of a signal in a blank, expressed as a concentration.

C

CRGS, Carrier gas	Carrier gas is an Ar gas supply flowing through the nebulizer to convert a liquid sample into a fine aerosol. It is a tuning parameter of the plasma.
CRC conditions (collision/ reaction cell)	Parameters that affect collision/reaction cell performance such as cell gas, cell gas flow rate, octopole bias voltage, KED bias and deflection lens.
Charge transfer	A reaction mechanism that relies on the exchange of charge between ions and cell gas molecules, e.g., $Ar^+ + NH_3 \rightarrow Ar + NH_3^+$
Collision mode	A cell mechanism to remove interferences either by collisional dissociation or by kinetic energy discrimination (KED). With KED, ions entering the collision/reaction cell collide with the cell gas (such as helium). Since polyatomic ions have a larger ionic cross-section than mono-atomic analyte ions at the same mass, the polyatomic ions undergo more collisions than the analyte ions, and so lose more energy. By the cell exit, the lower energy ions (the polyatomics) can be separated from the higher energy (analyte) ions by applying a bias voltage "step". This is knows as kinetic energy discrimination (KED).
Cool plasma	A technique used to reduce interferences. Under low temperature plasma (cool plasma) conditions, the formation of interferences such as Ar^+, ArO^+ and ArH^+ is suppressed, allowing the detection of Ca^+, Fe^+ and K^+ at the trace level. Typical RF power for cool plasma is 600-900 W.
CRC	Abbreviation of Collision Reaction Cell.

D

DL	Abbreviation of Detection Limit. Also called LOD (limit of detection). It is the concentration that is equivalent to 3 times the standard deviation (SD) of the background signal.
Desolvation system	A device to remove solvent from the aerosol generated by the nebulizer.
Dynamic range or analytical working range	The range of linearity of an analytical instrument. Agilent ICP-QQQ instruments are fitted with an advanced, dual-mode, discrete dynode electron multiplier (DDEM) that provides a full nine orders dynamic range under standard operating conditions.
DiGS, Dilution gas	Argon gas flow added to the carrier gas via a dilution gas port located between the torch and the spray chamber. A dilution gas is used for Aerosol Dilution with HMI or UHMI. The gas supply used for the DiGS can also be switched automatically to add the gas flow to the spray chamber instead (known as makeup gas or MUGS). It is a tuning parameter of the plasma.
Dwell time	The period of time that the analytical instument accumlates the signal.

E

Enthalpy of reaction, ΔHr	Amount of energy (heat) absorbed or released by a reaction. When ΔHr is positive (ΔHr > 0), the reaction is endothermic, meaning energy is required (absorbed) for the reaction to occur. When ΔHr is negative (ΔHr < 0), the reaction is exothermic, meaning energy is released by the reaction, which is spontaneous.

G

GC Interface kit	Agilent's GC-ICP-MS interface features a fully heated inert transfer line and separately heated inert torch injector that provides reliable separation of volatile compounds.

H

HMI, High Matrix Introduction	HMI Aerosol Dilution technology is standard on Agilent ICP-QQQ, extending the TDS range to % level, while eliminating the added cost, time and potential errors of conventional liquid dilution.
UHMI, Ultra High Matrix Introduction	Agilent’s second generation aerosol dilution system, which allows the direct analysis of 25% NaCl solutions.
Hard extraction	A tuning condition when a negative voltage is applied to the extraction lens. Hard extraction provides higher sensitivity at lower plasma temperature than soft extraction. Cool plasma conditions require hard extraction.
Helium mode, He mode	See collision mode.
HR-ICP-MS, high-resolution ICP-MS	Also known as magnetic sector, sector field or double focusing. Magnetic sector based ICP-MS instruments are capable of resolution (M/ΔM) of up to 10,000 and are able to resolve most polyatomic species from analytes at the same nominal mass.

I

I-AS, Integrated Auto sampler	Integrated, covered auto sampler with pumped rinse station; ideal for ultra-trace analysis and small sample volumes (as low as 0.5 mL). Flexible rack configurations offer a maximum capacity of 89 vials, plus 3 rinse vials.
ICP	Inductively coupled plasma, generated by applying a high-power radio frequency (RF) field to a flow of argon gas. The plasma is a high temperature ion source, up to 10,000 K maximum and around 7,500 K in the central channel.
ICP-MS	Inductively coupled plasma mass spectrometer or spectrometry.
ICP-QQQ	Abbreviation for triple quadrupole ICP-MS.
IDA, ID, ID-MS	Isotope Dilution Analysis or Isotope Dilution Mass Spectrometry is a highly accurate method to quantify elements based on the change in isotope ratio that results from the spiking of an unknown sample with a spike enriched in one isotope of the target analyte. Because each sample result is based on the measurement of the change in ratio in that sample, rather than relative to a response in a separate calibration standard, IDMS results are also directly traceable to certified standards, which reduces uncertainty.
Inert Sample Introduction kit	O-ring-free and manufactured from PFA for the lowest contamination levels. Demountable torch with Pt or sapphire injector options. HF resistant, and suitable for high-purity reagents.
Interferences - spectral	Direct overlap from a different element with an isotope at the same nominal mass (isobar), or overlap from a polyatomic ion, or doubly-charged ions resulting from the loss of two electrons instead of just one. Because the quadrupole separates ions based on m/z (mass over charge ratio), a doubly-charged ion (M^{2+}) will appear at mass M/2.
Ion guide	Operation of an ion lens where no mass rejection is performed. Applies to simple electrostatic ion lenses, and also to multipole ion guides operated with no low- or high-mass cut-off.
IP, Ionization potential	The first ionization potential of the element is the energy required to remove one electron from a neutral atom and is specific for each element. Most elements are largely converted (>90%) to singly-charged ions in an argon plasma. Elements with a low second IP will also form some doubly-charged ions.
IR, isotope ratio	Ratio of abundance of two isotopes of an element.
Isobar	Refers to isotopes of different elements that appear at the same nominal mass. These overlaps occur when atoms of two different elements (i.e. different number of protons in the nucleus, so different atomic number) each have an isotope with the same atomic weight (same total number of protons plus neutrons in the nucleus, e.g. ^{204}Pb and ^{204}Hg).
Isobaric interferences	Overlaps that occur at the same mass (see isobar). These overlaps/interferences can be resolved by reaction chemistry (e.g. NH_3 is used to separate Pb from the Hg overlap), but cannot be separated by high-resoluton ICP-MS; separation of ^{204}Pb from ^{204}Hg would require a resolution of around 500,000 (50x higher than can be achieved by any commercial high-resolution ICP-MS).
Isotope	A specific form (atomic weight) of an element. Many elements have atoms with different atomic weights, such as Pb 204, 206, 207 and 208; these are called isotopes. The different isotopes of Pb all have 82 protons in the nucleus (Pb has atomic number 82) but a different number of neutrons, so the atomic weight is different for each isotope.
ISTD, internal standard	Internal standards are commonly used in ICP-MS, particularly where samples vary in composition from the calibration standards. Changes in sample transport, nebulization efficiency and signal intensity (long-term drift) would all lead to errors, which may be corrected if an ISTD element with similar behavior is used as a reference.

K

KED, Kinetic Energy Discrimination	KED is used to discriminate the analyte ion of interest from interfering ion(s) by the difference of kinetic energy. Refer to collision mode. KED is also used as a tuning parameter of CRC conditions: KED = (Q2 bias voltage) - (octopole bias voltage).

L

LA, Laser ablation	Method used for the direct analysis of solid samples using a laser to vaporize the sample before introduction to the plasma.
LC Speciation kits	Sample introduction kits to facilitate LC coupling and provide turn-key methods for common speciation applications. A Capillary-LC connection kit is also available.

M

MUGS, Makeup gas	Makeup gas refers to Ar gas applied to the spray chamber to increase/adjust total injector gas flow rate. It is a tuning parameter of the plasma.
MS/MS mode	Acquisition mode unique to Agilent ICP-QQQ. MS/MS mode operates Q1 as a unit (1 amu window) mass filter and Q2 is also set to the single mass of the target ion or reaction product ion.
Mass balance	Balance between the amount of a substance introduced into the system and excreted from the system.
Mass pair	MS/MS mode requires a mass setting for Q1 and Q2. The selected mass settings for Q1 and Q2 are known as the mass pair. For example when As is measured in O_2 mode, Q1 is set to the precursor ion (As^+) at *m/z* 75 and Q2 is set to the product ion (AsO^+) at *m/z* 91. 75 --> 91 is the mass pair for As in O_2 mode.
Mass filter	Generic term for any mass analyzer cabable of unit mass resolution. Note that the ion guide used in the CRC of some quadrupole mass spectrometers appears physically similar to a quadrupole mass filter. However, these ion guides cannot provide unit mass resolution because of the ion scattering effect at the higher pressures present in the CRC.
Mass spectrum	See spectrum.
Mass-shift method	A method where the analyte ion is reactive and is moved to a new mass free from the original interference. Sometimes referred to as "indirect" measurement, e.g. Se^+ reacts with O_2 in the cell and is converted to SeO^+. It can then be detected free from the original interference of $ArAr^+$.
MH, Mass Hunter software	Software package that provides comprehensive instrument control for the Agilent ICP-QQQ and accessories, and integrated data processing.
m-lens	An optional lens of the Agilent 8900. It provides a low BEC for alkaline elements like K and Na under hot plasma conditions.
Monoclonal antibody, mAb	Antibody produced by identical antibody-forming cell, which binds to a certain antigen.
MSA, Method of Standard Additions (also known as StdAdd)	A calibration solution is spiked at multiple levels directly into the unknown sample, giving a calibration of response against added concentration. MSA eliminates matrix effects by calibrating in the sample matrix.

N

Nanoparticle, NP	Microscale particles with a size range from 1 µm to 100 µm in diameter.
Neutral Gain Scan	Q1 and Q2 scan together, a fixed mass-shift apart. For example Q2 scans at Q1 + 16 amu for O-atom addition reactions.

O

O_2, oxygen	A reaction gas used with the Agilent ICP-QQQ. A number of elements can be measured in mass-shift method using O_2, e.g. Se^+ can be measured as SeO^+ using O_2 cell gas. O_2 is also added to the plasma carrier gas to decompose the carbon matrix when organic solvents are analyzed.
Octopole bias (OctP Bias)	A CRC parameter. It is the bias voltage applied to the octopole ion guide, which determines the collision energy of analyte ions with cell gas molecules.
OIDA, on-line isotope dilution analysis	A very powerful and useful development of traditional isotope dilution, using on-line addition of the isotope spike. Removes the time consuming step of spiking enriched-isotope standards into each separate sample.
On-mass method	A method where reactive interferences are removed to allow an unreactive analyte to be measured at its original mass. Sometimes referred to as "direct" measurement, e.g., the interference of GdO^+ on Yb^+ can be removed by the reaction of GdO^+ with NH_3.
Organics kit	Contains the sample introduction parts needed to run volatile organic solvents. Includes organics torch, solvent-resistant drain kit and uptake tubing.
ORS	Agilent's CRC design is known as the Octopole Reaction System. It is a temperature-controlled collision/reaction cell with octopole ion guide and four cell gas lines as standard on the Agilent ICP-QQQ. Provides maximum flexibility in collision and reaction modes, and uses a small internal volume cell to ensure rapid cell gas switching and high ion transmission.
ORS^4	Fourth generation Octopole Reaction System.
Oxygen atom abstraction or oxygen atom transfer	Reaction mechanism associated with the use of oxygen in the collision reaction cell.

P

Preset method	Preset methods are provided in the ICP-MS MH software. These built-in methods cover a range of predefined operating conditions to suit different applications. Using a preset method, a user can create a new batch with minimum or no customization.
Preset plasma	Preset plasma conditions are a function of ICP-MS MH software. The software provides several predefined plasma conditions that users can select according to the application. This greatly simplifies system optimization by automatically tuning and calibrating the plasma parameters, rather than the user having to set a number of individual plasma tuning parameters. There are three preset plasma conditions that can be selected depending on the sample matrix: Low matrix, general purpose and HMI/UHMI.
Polyatomic, Polyatomic ion	A molecular ion (an ion composed of more than one atom) that arises in the plasma or during ion extraction, and can appear at the same nominal mass as analyte ions. Polyatomics are usually interferences (such as ArO^+).
Precursor Ion Scan	Q1 scans a user set mass range, while Q2 is set to a single fixed mass, measuring all the reaction product ions at that mass, formed from the different ions entering the cell as Q1 scans the mass range.
Product Ion Scan	Q1 is set to a fixed precursor ion mass, while Q2 scans a user set mass range measuring all reaction product ions formed from that single precursor ion.

Q

Quadrupole bias (QP Bias or Qpole Bias)	Bias voltage applied to the Q2 rods. Used in conjunction with the Octopole bias to provide a bias voltage "step" at the cell exit, usually to reject unwanted low energy ions from the ion beam.
Quantitation or quantification	Quantitative results are produced by comparing signal intensities of elements in the sample to those generated by calibration standards.
Q1	First quadrupole in the configuration of the Agilent ICP-QQQ. Q1 is positioned in front of the ORS, to control the ions that are passed to the cell and enable MS/MS operation.
Q2	Second quadrupole in the configuration of the Agilent ICP-QQQ. Q2 filters the ions that emerge from the cell exit, passing only the target analyte ions to the detector.

R

Rare Earth Elements, REEs	Comprise 17 elements: Sc, Y, La, Ce, Pr, Nd, (Pm), Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, and Lu.
Resolution	The ability of a mass filter to separate adjacent masses. Defined as $M/\Delta M$; the mass of the target peak/the mass difference to the nearest adjacent peak that can be separated. Sometimes also quoted as the width of the peak at a given peak height (e.g. 0.75 amu at 10% peak height).

S

SEMI	Semiconductor Equipment and Materials International standards are international standards for materials, chemicals and manufacturing devices used in microelectronics industries.
Single particle (sp) analysis	In this handbook, spICP-MS analysis refers to particle size measurement using the signal generated from a single particle.
Single Quadrupole MS, ICP-QMS	Conventional ICP-MS containing a single quadrupole mass filter.
Single Quad mode, SQ mode	Q1 operates as a wide band mass filter. SQ mode emulates conventional quadrupole ICP-MS.
Speciation measurement	Combination of chromatographic techniques with ICP-MS as a detector to determine the chemical form of elements in the sample.
Spectrum (Mass Spectrum)	After separation by the final mass filter (Q2), the ions are detected by an electron multiplier. The detector electronics count and store the total signal for each mass (m/z), creating a mass spectrum. The spectrum that is produced provides a simple and accurate qualitative representation of the sample. The magnitude of each peak is directly proportional to the concentration of an element in a sample.
STS, ShieldTorch System	A technique to eliminate capacitive coupling between the RF coil and plasma, keeping the plasma potential low and energy distribution of ions narrow. The technique is crucial for cool plasma and collision mode.

T

TDS, total dissolved solids	The total summed concentration of all non-volatile, dissolved inorganic and organic substances in a liquid. The matrix tolerance of Agilent ICP-MS instruments is 0.2–2 % TDS.
Triple quadrupole ICP-MS	ICP-MS with a tandem MS configuration, featuring a quadrupole mass filter (Q1) in front of the collision/reaction cell (CRC) followed by a second quadrupole mass filter (Q2).

U

UPW	Ultra Pure Water, purified by ion exchange to remove trace contaminants. Used for preparation of standards and for sample dilution for ultra-trace analysis

V

Venomics	The study of venomes via genomic, proteomic, and transciptomic approaches.

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