

Effectively increase sample turnover and boost data confidence using triple quadrupole ICP-MS

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Goal

To highlight the benefits of triple quadrupole ICP-MS for the analysis of toxic metals in foodstuffs.

Introduction

Toxic elements such as arsenic, cadmium, mercury, or lead should not be part of our daily diet, whereas other elements are added intentionally to foodstuffs to maintain a consistent level of important nutrients in a population. Verification that both types are tracked and controlled in all the food and beverages we consume is a key task for laboratories in the Food Safety market. Food analysis includes not only contaminants in a given product, but also extends to other aspects, such as verification of geographic origin using trace elemental or isotopic fingerprints or investigation of the effect of contact of the product with packaging materials under different conditions.



If lower limits of detection are required, ICP-MS is the preferred analytical solution. Modern instruments offer comprehensive interference removal and innovative solutions to increase sample throughput. Moreover, ICP-MS can be coupled to different chromatographic techniques, such as ion chromatography (IC). For some elements, speciation analysis is required to determine the chemical form in which an element is present.

Single quadrupole ICP-MS systems are commonly used for screening a wide range of samples for both toxic as well as nutritional elements, combining consistent interference removal with short measurement times.

This is especially true when complemented by a secondary interference removal mechanism, such as an automated low mass cut off¹. Interference removal is accomplished by using a collision/reaction cell (CRC) flushed with helium to remove the most common polyatomic interferences. In some cases, reactive gases, such as hydrogen, oxygen, or ammonia are used to eliminate certain interferences (e.g., H₂ for reduction of ⁴⁰Ar₂⁺ on ⁸⁰Se), but often, the formation of new interferences caused by these gases in the collision cell is a serious issue, as other ions present in the ion beam can lead to unwanted side reactions.

One way to overcome the challenges of interferences is to use triple quadrupole ICP-MS (TQ-ICP-MS) instrumentation², such as the Thermo Scientific™ iCAP™ TQe ICP-MS. TQ-ICP-MS instruments eliminate interferences through the use of reactive gases flushed into the CRC (often also referred to as quadrupole 2 (Q2), independent of its constructional shape). Interference removal is accomplished as analyte and interference react differently with the collision/reaction gas and can be separated from each other in the analyzing quadrupole (Q3). The occurrence of side reactions is effectively suppressed through a mass filtration step prior to the CRC in the first quadrupole (Q1), added to the mass analyzer axially in front of the CRC (Q2).

Experimental

An iCAP TQe ICP-MS system was used for all analysis³. On each day of measurement, performance of the instrument was verified in an automatic report and tuned using the autotune routines in case performance criteria were not met. The optimized parameters for the analysis of food samples are summarized in Table 1. Complementary measurements using hydrogen as a reactive gas were accomplished using a Thermo Scientific™ iCAP™ RQ ICP-MS.

The selection of the optimum measurement mode for each analyte can be easily achieved using the Reaction Finder Method Development Assistant included in the Thermo Scientific™ Qtegra™ ISDS Software. For single mode analysis, settings proposed by Reaction Finder were modified manually.

Table 1. Instrument configuration and operating parameters

Parameter	Value
Nebulizer	Borosilicate glass MicroMist (Glass Expansion, Australia), 400 μL·min ⁻¹ , pumped at 40 rpm
Spraychamber	Quartz cyclonic spraychamber cooled at 3 °C
Injector	2.5 mm quartz
Interface	Ni sampler and Ni skimmer with 3.5 mm insert
Forward power	1550 W
Nebulizer gas	1.00 mL·min ⁻¹
TQ-O ₂	O ₂ gas at 0.34 mL·min ⁻¹
SQ-KED	He gas at 4.3 mL·min ⁻¹ with 3 V KED

Results and discussion

Kinetic energy discrimination (KED) allows analysis of elements over the full mass range (lithium to uranium), enabling removal of polyatomic interferences in the most affected mass range (*m/z* 40–100) without significantly compromising detection limits (over the so-called standard (no cell gas) mode). However, there are certain elements, which, if present in sample, can lead to the formation of interferences not removable using KED. False positive results caused by the presence of interferences can present a significant disruption to the daily workplan in a busy laboratory, as they require troubleshooting and re-analysis, during which time the instrument affected will have to stop productive analysis. To illustrate the process of interference removal on a triple quadrupole ICP-MS, Figure 1 contains an overview on the analysis of ⁷⁵As and ¹¹¹Cd, demonstrating the two potential pathways of measurement: A mass shift reaction (the analyte is reactive to a specific gas), or an on-mass reaction (the interference reacts while the analyte is detected on its original *m/z* ratio).

A key interference for the often-critical analytes arsenic and selenium can arise from the presence of rare earth elements (REE), such as gadolinium (Gd), samarium (Sm), or neodymium (Nd). These elements readily form doubly charged ions (M⁺⁺) in the plasma, which cause false positive results on arsenic (from ¹⁵⁰Sm⁺⁺ and ¹⁵⁰Nd⁺⁺) and selenium (¹⁵⁴Gd⁺⁺, ¹⁵⁶Gd⁺⁺ and ¹⁶⁰Gd⁺⁺). This is because mass spectrometers detect the mass to charge ratio of a given ion rather than detecting its mass directly. To illustrate this, a comparison of results for two standard reference materials, NIST 1515 (apple leaves) and NIST 1573 (tomato leaves) is shown in Table 2. NIST 1515 contains approximately 17 mg·kg⁻¹ of neodymium and 3 mg·kg⁻¹ of

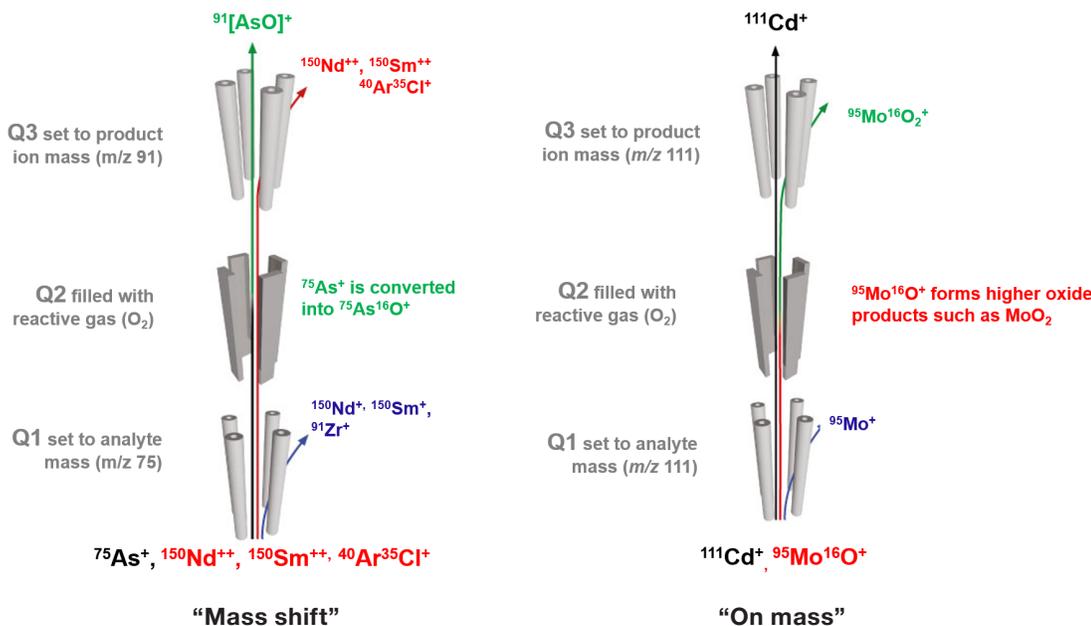


Figure 1. Interference removal using a mass shift reaction (e.g. ^{75}As) or an on-mass reaction (e.g. ^{111}Cd) on a triple quadrupole ICP-MS

gadolinium (dry weight), which translate to approximate concentrations of $85 \mu\text{g}\cdot\text{L}^{-1}$ and $15 \mu\text{g}\cdot\text{L}^{-1}$, respectively in the measured solution (assuming a 200-fold dilution through sample preparation).

Table 2. Comparison of results for NIST SRM 1515 (apple leaves) and 1573 (tomato leaves), showing severe false positive results obtained in KED mode

	Analysis mode	Measured [$\text{mg}\cdot\text{kg}^{-1}$]	Certified [$\text{mg}\cdot\text{kg}^{-1}$]
Arsenic (^{75}As)	KED	0.469 ± 0.012	0.038 ± 0.007
	TQ- O_2	0.036 ± 0.003	
Selenium (^{78}Se)	KED	1.272 ± 1.87	0.050 ± 0.009
	TQ- O_2	0.052 ± 0.006	

Cadmium, another critical contaminant, can be interfered by molybdenum if present in only slightly elevated concentrations (above $30\text{--}50 \mu\text{g}\cdot\text{L}^{-1}$) in the analyzed solution. This could be the case for sample types containing naturally higher amounts of molybdenum, such as cereals, legumes, or soy and soy products, even considering the dilution effect during sample preparation. Again, an elevation of the signal of the commonly analyzed ^{111}Cd isotope (through $^{95}\text{Mo}^{16}\text{O}^+$ interference) would result in an undiscovered false positive result. As a single quadrupole ICP-MS would not distinguish between isobaric $^{111}\text{Cd}^+$ and $^{95}\text{Mo}^{16}\text{O}^+$, even small contributions from the interference alongside a genuine cadmium signal could lead to a false positive result. The results of the analysis of

cadmium in the presence of molybdenum are summarized in Table 3. Please note that also other relevant isotopes of cadmium would be similarly affected by MoO interferences (e.g. ^{110}Cd , ^{112}Cd , and ^{114}Cd).

Table 3. Results obtained for the analysis of cadmium in the presence of varying amounts of molybdenum in different modes of analysis

Mo concentration	^{111}Cd (SQ-KED) [$\mu\text{g}\cdot\text{L}^{-1}$]	^{111}Cd (TQ- O_2) [$\mu\text{g}\cdot\text{L}^{-1}$]
$0.1 \text{ mg}\cdot\text{L}^{-1}$	0.030	<0.001
$1 \text{ mg}\cdot\text{L}^{-1}$	0.322	<0.001
$10 \text{ mg}\cdot\text{L}^{-1}$	2.932	0.001

Another opportunity for improvement over what KED operation can achieve is the suppression of the background created by argon based polyatomic interferences on elements such as ^{56}Fe (through $^{40}\text{Ar}^{16}\text{O}^+$) and ^{80}Se (through $^{40}\text{Ar}_2^+$). To overcome these interferences, reactive gases such as hydrogen can be used in a method, providing typically lower detection limits for these elements, but extending the method runtime. Table 4 shows a comparison of the analytical figures of merit comparing calibration curves obtained in SQ-KED, SQ- H_2 and TQ- O_2 modes. As can be seen, the use of hydrogen helps to improve detection limit significantly, but with no solution to the above mentioned false positive results caused by the presence of neodymium and gadolinium. Using oxygen as a reactive gas in conjunction with a triple quadrupole mass analyzer, these interferences are fully removed and identical detection limits are achieved (Table 4).

Table 4. Analytical performance for the analysis of selenium using different modes

	⁷⁸ Se (SQ-KED)	⁷⁸ Se (SQ-H ₂)	⁸⁰ Se (TQ-O ₂)
IDL [ng·L ⁻¹]	17.5	0.7	0.7
BEC [ng·L ⁻¹]	10.1	2.5	0.3
BEC in sample containing REE [µg·L ⁻¹]	6.3*	4.7**	0.00*

* Solution containing 10 µg·L⁻¹ of all REE (Ce-Lu)

** Solution containing 1000 µg·L⁻¹ of all REE (Ce-Lu)⁴

Although the use of O₂ on a single quadrupole ICP-MS would lead to equally unaffected results in the presence of rare earth elements, its main limitation is again the lack of suppression of unwanted side reactions. Other elements present in the sample (e.g., molybdenum in the case of selenium) could contribute to the signal observed on the new product ion mass (⁹⁶Mo vs. ⁹⁶[⁸⁰Se¹⁶O]⁺). Although molybdenum is reactive to oxygen as well (forming MoO and MoO₂ readily), its contribution to *m/z* 96 can only be eliminated through mass filtration in Q1, and therefore a triple quadrupole mass spectrometer is required.

Impact on sample throughput

Another common challenge in food testing laboratories is the need to analyze a high number of samples to keep up with the backlog and achieve return on investment. TQ-ICP-MS systems are therefore less commonly found in analytical testing laboratories, as each specialized set of measurement parameters (e.g., for multiple reactive gases) adds to the total method runtime. In contrast, SQ-ICP-MS allows for the analysis of samples using one or two acquisition modes only.

However, a potential alternative to achieve both high throughput and full interference removal is the use of a single mode based on triple quadrupole technology (enabling pre-filtration of the ion beam prior to the CRC) and oxygen as a reactive cell gas. In this case, the iCAP TQe ICP-MS is operated in a single mode for all elements, with the use of O₂ as a reactive gas. This allows for effective removal of all interferences, including polyatomic species and doubly charged rare earth element ions, across the entire mass range.

A total of 40 individual isotopes were monitored (simulating an ample set of common analytes plus appropriate internal standards) using different methods typically used on single and triple quadrupole ICP-MS. In all cases, an identical sample delivery system was used (a standard autosampler) with identical uptake and rinse times (30 seconds each).

Table 5. Comparison of runtime, batch runtime, and interference removal capability for different ICP-MS methods

	SQ-ICP-MS		TQ-ICP-MS TQ-O ₂	
	KED Single Mode	KED and H ₂	TQ-O ₂ Single Mode	SQ-KED and TQ-O ₂
Analysis time per sample including uptake/wash [s]	200	239	200	217
Total runtime [min] and time saving for 100 samples	333 + 0 min	398 + 65 min	333 + 0 min	362 + 31 min
Polyatomic interferences	Yes	Yes	Yes	Yes
Doubly charged interferences removed (e.g., REE)	No	No	Yes	Yes
Confidence all interferences are under control	No	No	Yes	Yes

As can be seen from the data in Table 5, a single mode analysis has a clear potential for the realization of time savings, especially compared to a method combining the use of KED with H₂. Here, the sample turnover time is not only extended because of the need to evacuate and flush the CRC with two different gases (He for KED operation, and H₂), but additionally through the longer duration of this process when adding a gas with a high flow rate (often in the range of 7 to 10 mL·min⁻¹ for H₂) and a high diffusion coefficient. Whereas a single mode analysis using KED mode would be able to overcome the most challenging polyatomic interferences, a single mode analysis combining pre-filtration of the ion beam for each analyte and the use of O₂ as a reactive gas would enable identical sample turnover times to be achieved with the certainty that also other, often unexpected, interferences are fully eliminated.

A comparison of the detection limits for a variety of common analytes is shown in Table 6. As can be seen, for elements commonly analyzed using KED, there is no significant negative impact on the achievable detection limits. In contrast, most elements can be detected at a similar concentration level, whereas several can be detected at even lower levels in the TQ-O₂ mode. The reason for the little to no impact observed is found in the applied bias potentials between the CRC and the analyzing quadrupole. Whereas in KED mode, a positive bias potential of typically around 3 V is used, the bias potentials in reactive gas modes are usually set to a negative difference of up to 7 V, allowing part of the signal loss (due to kinetic energy loss on collisions of the target ions with the cell gas) to be offset.

Table 6. Comparison of detection limits obtained in SQ-KED mode and TQ-O₂ mode (elements benefitting from superior interference removal, such as arsenic and selenium are not considered in this comparison). In the 'Comparison' row, the symbol + denotes an improvement of TQ-O₂ mode vs. KED mode in the resulting LOD, whereas O denotes equivalent performance.

Element	¹¹ B	²³ Na	²⁴ Mg	³⁹ K	⁵⁵ Mn	⁵⁹ Co
LOD [$\mu\text{g}\cdot\text{L}^{-1}$] KED mode	0.4	4	1	3	0.003	0.011
LOD [$\mu\text{g}\cdot\text{L}^{-1}$] TQ-O ₂ single mode	0.4	0.92	0.20	0.17	0.006	0.003
Comparison	O	+	+	+	O	+

Element	⁶⁰ Ni	⁶³ Cu	⁶⁶ Zn	⁸⁵ Rb	⁸⁸ Sr	⁹⁸ Mo
LOD [$\mu\text{g}\cdot\text{L}^{-1}$] KED mode	0.023	0.09	0.03	0.004	0.002	0.003
LOD [$\mu\text{g}\cdot\text{L}^{-1}$] TQ-O ₂ single mode	0.005	0.02	0.04	0.005	0.009	0.008
Comparison	+	O	O	O	O	O

Element	¹¹¹ Cd	¹²¹ Sb	¹³⁸ Ba	²⁰⁸ Pb	²³⁸ U
LOD [$\mu\text{g}\cdot\text{L}^{-1}$] KED mode	0.001	0.001	0.002	0.001	0.001
LOD [$\mu\text{g}\cdot\text{L}^{-1}$] TQ-O ₂ single mode	0.0004	0.003	0.006	0.005	0.0003
Comparison	+	O	O	O	+

Conclusion

As demonstrated in this note, the use of TQ ICP-MS with a combination of helium and oxygen as collision/reaction gases is a powerful approach to address the challenges caused by the presence of rare earth elements and their associated interferences. With this technology, existing and established methods can be transferred and extended for improved interference removal on key analytes and new options become available. In addition as shown, a reduction in analysis time of between 10% and 20% compared to methods based on either single or triple quadrupole ICP-MS using different collision/reaction gases is possible, without an impact on detection limits.

The iCAP TQe ICP-MS enables complete removal of many commonly encountered interferences, providing not only significantly reduced detection limits for key analytes, but also increasing confidence in data quality. With no additional investment in laboratory infrastructure on top of what is required for a single quadrupole instrument (only the common gases helium and oxygen are required for interference removal), unnecessary interruptions to the daily laboratory routine caused by unexpected false positive results can be avoided.

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