Accurate and Sensitive Analysis of Arsenic and Selenium in Foods

Use the Agilent 8800 Triple Quadrupole ICP-QQQ to remove doubly charged REE interferences

Application Note

Food Testing and Agriculture

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Introduction

Concern about the impact on public health from potentially toxic elements and compounds present in everyday foodstuff has led to new legislative guidance. The inorganic forms of arsenic (As) are known to be toxic and carcinogenic to humans, and food and drink are a potential source of exposure [1]. To reduce the intake of inorganic arsenic from the diet, the U.S. Food and Drug Administration (FDA) proposed a new action level for inorganic arsenic in apple juice of 10 µg/L in 2013 [2,3]. Also, following the eighth meeting of the CODEX Committee on Contaminants in Food, the World Health Organization (WHO) proposed a guideline for inorganic As in polished rice of 0.2 mg/kg [4].

There is a clear need for reliable screening methods to accurately determine the levels of such contaminants in food and drink products. The detection limits required are low, as a 0.2 mg/kg limit equates to a digestate concentration of 2 µg/L (assuming a 100x digestion dilution). Even small errors in the precision and accuracy of the analytical method could result in a food product being wrongly classified as safe. Selenium (Se) is an essential micronutrient 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.

Arsenic and Se can be difficult to quantify accurately at trace levels by conventional quadrupole ICP-MS, 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*), and 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 can take up higher concentrations of these elements [5,6], leading to false positives for As and Se. In this study, we evaluated the capability of the Agilent 8800 Triple Quadrupole ICP-QQQ in MS/MS reaction mode to remove interferences, including REE^{++}, on As and Se.

We studied two National Institute of Standards and Technology (NIST) standard reference materials (SRMs), NIST 1547 Peach Leaves and NIST 1515 Apple Leaves. These SRMs contain low µg/kg levels of As and Se in the presence of mg/kg levels of REEs. Some standard methods for the quantification of As and Se recommend correcting for doubly charged ions using mathematical equations [7]. However, such correction equations are prone to errors in complex natural samples, and give poorer accuracy than quantification at an *m/z* that is free from interference. To fully investigate the effect of doubly charged REEs on the determination of As and Se, we analyzed the two NIST SRMs using various approaches. These included single quadrupole ICP-MS with helium collision mode, hydrogen reaction mode, and ICP-QQQ in mass-shift mode using oxygen/hydrogen reaction gas.

Experimental

Sample preparation

All samples were acid digested using a MARS 6 closed vessel microwave digestion system (CEM, Mathews, NC) operating at 200 °C with a 20-minute ramp and 20-minute hold time. Samples of NIST (Gaithersburg, MD) SRMs 1547 Peach Leaves and 1515 Apple Leaves were prepared in triplicate. First, a 0.25 g sample was digested in 2.5 mL 9:1 HNO_3:HCl acid mix, and the digest was then diluted to a final weight of 25 g. Butanol (5%) 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 1) and high concentrations of REEs. Reference (noncertified) values for Neodymium (Nd), Samarium (Sm), and Gadolinium (Gd) are 7, 1, and 1 mg/kg in NIST 1547, and 17, 3, and 3 mg/kg in NIST 1515, respectively.

Instrumentation

An Agilent 7700x ICP-MS and an Agilent 8800 ICP-QQQ equipped with a concentric nebulizer and Peltier-cooled, double-pass spray chamber were used. Both instruments were fitted with an octopole-based collision reaction cell (CRC) for control of interferences. The 7700x ICP-MS was operated in helium (He) collision mode and hydrogen (H_2) reaction mode using optimized cell gas flow rates of 4.5 mL/min and 6 mL/min, respectively. The 8800 ICP-QQQ was operated in MS/MS mass-shift mode using O_2/H_2 at a gas flow of 35% O_2, which translates to 0.35 mL/min and 1 mL/min H_2 for a total flow of 1.35 mL/min (combined flow rate). Arsenic was detected as $^{75}AsO^+$ at *m/z* 91, and selenium was measured as $^{78}SeO^+$ at *m/z* 94.

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	$^{160}Gd^{++}$, $^{160}Dy^{++}$,	$^{32}S2^{16}O$, $^{32}S^{16}O_3$, $^{40}Ca^{40}Ar$, $^{45}Sc^{35}Cl^+$	$^{40}Ar^{40}Ar^+$, $^{40}Ca^{40}Ca^+$
	82	8.73	$^{164}Dy^{++}$, $^{164}Er^{++}$	$^{45}Sc^{37}Cl^+$	

The ICP-QQQ mass-shift method can be applied to complex matrix samples that can contain zirconium (Zr) or molybdenum (Mo), or both. If this mass-shift mode is used with conventional quadrupole ICP-MS, matrix or coexisting analyte ions such as $^{91}Zr^+$ and $^{94}Mo^+$ can overlap the AsO^+ and SeO^+ product ions. The MS/MS configuration of the 8800 ICP-QQQ prevents these interferences, because the ions that exist at the analyte product ion masses are rejected by the first quadrupole (Q1), which is located before the CRC.

Calibration

Both instruments were calibrated using NIST-traceable standards and traceable second-source calibration checks. The measured values were considered acceptable if their 95% confidence interval overlapped with the 95% confidence range reported on the NIST certificate.

Results and Discussion

Both kinetic energy discrimination and reactive gases are widely used to reduce polyatomic interferences in ICP-MS, but their effect on doubly charged ion interferences is less often reported. Arsenic and Se were determined in NIST SRMs 1547 and 1515. We used the 7700x ICP-MS in both He and H_2 gas modes, and the 8800 ICP-QQQ in O_2/H_2 mass-shift mode, as shown in Table 2. The As results for both SRMs in both gas modes on the 7700x ICP-MS were far above the certified values. This indicated that, while the gas modes can be useful against the commonly encountered polyatomic interferences ($ArCl^+$, $CaCl^+$), they were not effective in removing the doubly charged ion overlaps. Therefore, mathematical equations were required.

After applying interference correction equations for As, accurate results were obtained for both SRM materials in He and H_2 modes. The uncorrected As value of 0.25 mg/kg for NIST 1515 in He mode was above the proposed 0.2 mg/kg guideline for inorganic As in rice. This showed that doubly charged interferences can cause large false positives, which could potentially lead to product rejection or unnecessary further analysis for inorganic As content. After applying interference correction equations, the As results measured in He mode were much closer to the certified ranges. However, the mean measured result for NIST 1515, which has the lowest As level and the highest REE content, showed a very high RSD of the replicate values. This illustrates a problem of using correction equations, when the measured signal is mostly due to the interferent rather than the analyte. Corrected values for As in H_2-reaction mode were not significantly different from the certified values. However, they were at the higher end of each SRM confidence interval, with recoveries of 132% and 124% for NIST 1547 and 1515, respectively.

It was also necessary to use interference correction equations to obtain accurate results for Se in He mode in both SRMs. The corrected value of 0.013 mg/kg for Se in NIST 1515 had an unacceptably high %RSD of 150%. This again demonstrated the problems of applying correction equations when the signal is mostly due to the interference. In this case, the interference on Se arose from doubly charged Gd, which was present at high concentration in the SRM (3 mg/kg). The effect was greater because of the low concentration of Se in NIST 1515, and the low sensitivity of Se in He mode.

Table 2. Analysis of $^{75}As^+$ and $^{78}Se^+$ in NIST 1547 and 1515 in He mode and H_2 mode using ICP-MS (both uncorrected and corrected data are given) and by triple quadrupole ICP-QQQ in MS/MS mode. All concentrations are in mg/kg, and are averages of three replicate sample digests expressed as mean ± standard deviation.

		ICP-MS He mode		**ICP-MS H_2 mode**		**Triple quadrupole ICP-MS 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

Accurate and precise values for Se in both SRMs were obtained in H_2 mode due to high sensitivity for Se, and the lower level of doubly charged interferences in this gas mode. Hydrogen has been shown to eliminate the doubly charged Gd interference on Se in the blood of patients receiving Gd-based MRI contrasting agents [8].

Both SRM digests were also 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 enhanced the reaction of Se with O_2 [9]. The measured values for As and Se in NIST 1547 and 1515 were well within the certified range for both SRMs. This result demonstrated the successful elimination of the REE^{++} interferences in O_2/H_2 MS/MS mode on the 8800 ICP-QQQ. Results were obtained without the need for correction equations (that is, uncorrected).

To confirm that the MS/MS method could be applied to samples that contained high concentrations of Zr and Mo, an aliquot of NIST 1547 was spiked at 1 mg/L Zr and Mo (1,000 ppm). The results are shown in Table 3. The measured values for As (as $^{75}As^{16}O^+$ at *m/z* 91) and Se (as $^{78}Se^{16}O^+$ at *m/z* 94) were the same as for the unspiked samples. MS/MS mode was, therefore, proven to be effective at rejecting isobars of similar mass to the new mass-shifted analytes.

Conclusions

The Agilent 8800 Triple Quadrupole ICP-QQQ with MS/MS was the optimum method for measuring trace As and Se in the presence of high REE concentrations 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 were avoided using O_2/H_2 cell gas and MS/MS mass-shift mode. Arsenic was shifted to its product ion AsO^+, which was measured at *m/z* 91, and Se was 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 $^{91}Mo^+$ and $^{94}Zr^+$, as both ions were 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. Single quadrupole ICP-MS operating in helium mode is suitable for the analysis of As and Se in general routine sample types that might contain a relatively low concentration of REEs. Hydrogen mode is effective at reducing doubly charged species. Compared to the single quadrupole methods, triple quadrupole ICP-QQQ has 10-fold lower detection limits, which makes it particularly suited to low-level analysis of As and Se in complex sample matrices.

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

		Triple quadrupole ICP-MS with O_2/H_2 mass-shift	
SRM NIST 1547	**Certified value**	**Unspiked (n = 3)**	**Spiked with 1 mg/L Zr and 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

More information

For a full account of this application, see Brian P. Jackson, Amir Liba, and Jenny Nelson, Advantages of reaction cell ICP-MS on doubly charged interferences for arsenic and selenium analysis in foods. *J. Anal. At. Spectrom*. **2015**, *30*, 1179-1183.

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References

1. *Toxicological Profile for Arsenic, 2007.* Agency for Toxic Substances and Disease Registry (ATSDR), U.S. Department of Health and Human Services, Public Health Service, Washington, DC.
2. *Guidance for Industry. Arsenic in apple juice: Action level, 2013*. U.S. Food and Drug Admistration, Washington, DC.
3. Anon. FDA sets limit for arsenic in apple juice. *Chemical & Engineering News*, **2013**, *91*, 21.
4. *Report of the Eighth Session of the Codex Committee on Contaminants in Foods, 2014*. CL 2014/11-CF. FAO/WHO Codex Alimentarius Commission, Rome, Italy.
5. Sucharova, J. Optimisation of DRC ICP-MS for determining selenium in plants. *J. Anal. Atom. Spectrom*. **2011**, *26*, 1756-1762.
6. Wang, R-Y.; Hsu, Y-L.; Chang, L-F.; Jiang, S-J. Speciation analysis of arsenic and selenium compounds in environmental and biological samples by ion chromatography-inductively coupled plasma dynamic reaction cell mass spectrometer. *Anal. Chim. Acta*, **2007**, *590*, 239-254.
7. *FDA Elemental Analysis Manual for Food and Related Products, 4.7 ICP-MS Multi-element in Food, Ver. 1.0; 2013*. U.S. Food and Drug Admistration, Washington, DC.
8. Harrington, C. F.; Walter, A.; Nelms, S.; Taylor, A. Removal of the gadolinium interference from the measurement of selenium in human serum by use of collision cell quadrupole inductively coupled plasma mass spectrometry (Q-ICP-MS). *Ann. Clin. Biochem*. **2014**, *51* (3), 386-91.
9. Sugiyama, N. The accurate measurement of selenium in twelve diverse reference materials using on-line isotope dilution with the 8800 Triple Quadrupole ICP-MS in MS/MS mode; Application note, Agilent Technologies, Inc. Publication number 5991-0259EN, **2012**.

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