The Matrix Effect of Biological Concomitant Element on the Signal Intensity of Ge, As, and Se in Inductively Coupled Plasma/Mass Spectrometry

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The non-spectroscopic interference effects that occurred in inductively coupled plasma/mass spectrometry were studied for Ge, As and Se in human urine and serum. Many biological samples contain Na, K, Cl and organic compounds, which may cause the enhancement and depression on the analyte signal. The effect of 1% concomitant elements such as N, Cl, S, P, C, Na, and K on a 100 μg/L germanium, arsenic and selenium signal has been investigated by ICP/MS. The interference effects were not in the same direction. It appeared that concomitant elements such as Cl, S, and C induce an enhancement effect, whereas N and P did not show any significant effect. And, Na and K caused a depression. We have found a link between the abundance of analytes and the ionization potential of concomitant elements (eV), except carbon and nitrogen.

Key Words : Matrix effect, Serum, Urine, ICP/MS

Introduction

Inductively coupled plasma (ICP) as an ionization source for mass spectrometry (MS) has gained general acceptance as a method to analyze the inorganic elements. The advantages of ICP/MS are well known: low limits of detection and simultaneous multi-element determination with the possibility of measuring isotopic abundance. The main limitations are the observation of isobaric interferences, mostly due to the formation of molecular compounds, in particular, oxides and non-spectroscopic interferences (matrix effect).[1,2] The accuracy of As and Se determinations is well known to be seriously affected by the occurrence of spectral interferences,[3-19] as the resolution of quadrupole mass spectrometers is not sufficient to resolve atomic and molecular species having the same nominal mass. But recently, spectral interferences has been overcome by collision cell or dynamic reaction cell.

Non-spectral interferences is usually defined as matrix-induced signal variations (both suppression and enhancement) and are therefore often referred to as matrix effects. F. Vanhaecke et al. have reported that matrix-induced signal variation is dependent on the analyte mass number.[20-22] We know from experience that the calibration of As and Se may be difficult, especially in biological and clinical matrices. These matrix effects come from the sample matrix (Na, K and organic compounds). However, there is a the number and variety of the mechanisms proposed to explain these effects.[23-26]

In the present work, we report some preliminary investigations on the matrix effect by CH_3OH, C_2H_5OH and mannitol as the organic matrix and NaOH, KOH as the alkali matrix. A study of non-spectral interferences in the determination of Ge, As and Se is described.

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Experimental Section

Instrumentation. The ICP/MS instrument in this work was a Perkin-Elmer SCIEX Elan 5000 (Norwal, Connecticut, U.S.A.) ran at normal resolution. A cross-flow nebulizer associated with a double-pass spray chamber was used. The operating parameters were power of 1.0 kW, outer gas flow rate of 15 L/min., auxiliary 0.85 L/min. and carrier gas flow rate of 0.92 L/min. Mass flow controllers were used to measure flow rates. The mass spectrometer was set to sample ion intensities (peak jumping) at the analyte masses m/z 70, 72, 73 and 74 for Ge^+, m/z 75 for As^+ and m/z 77, 78 and 82 for Se^+. A peristaltic pump was used for conventional sample introduction. Instrument sensitivity was optimized by varying on instrumental settings, using aqueous standard solutions of Pb, Rh and Mg. The instrument adjustments included the physical positioning of the plasma relative to the mass spectrometer, the ion lens voltages and the R. F. power relative to the argon plasma. Once optimized for germanium, arsenic and selenium, these variables were kept constant throughout all experiments involving the same element. The aerosol carrier gas flow was adjusted for each analyte until optimum signal intensity was reached. The ICP/MS setting is given in Table 1.

Materials and chemicals. Serum and urine samples were obtained from 30 healthy individuals living in the Seoul region. Standard solutions were prepared from 10 mg/L stock solutions of Ge, As and Se (Spex Industries Inc., Edison. New Jersey, U.S.A.). All standard solutions were made up in 1% HNO_3. High purity reagents were used and the water was produced in a Millipore Super-Q apparatus (Millipore, Milford, MA, U.S.A.).

Table 1. Instrumental and analytical parameters for ICP/MS

Descriptions	Conditions
R.F. generator	Free-running type, 40 MHz
R.F. power	1000 W
Induction coil	3-turn, 1/8 in. copper, 2.6 mm i.d.
Sampling depth	7 mm from load coil, on center
Coolant gas flow rate	15.0 L/min.
Auxiliary gas flow rate	0.85 L/min.
Nebulizer gas flow rate	0.92 L/min.
Mass flow controller	4-channel
Sample introduction	Peristaltic pump
Sample uptake flow	1.0 mL/min.
Nebulizer	Cross-flow type
Spray chamber	Double pass type (Scott type)
Torch	Demountable
Interface cones	Nickel
Mass analyzer	Quadrupole
Vacuum system	Turbo molecular pumps
Quadrupole chamber	5×10^{-7} torr
Quantitative mode	
Replicate time (ms)	300
Dwell time (ms)	100
Sweeps/Reading	3
Reading/Replicate	1
Number of Replicates	5
Points/Spectral peak	3
Ge/Mass	70, 72, 73, 74
As/Mass	75
Se/Mass	77, 78, 82
Scan mode	Peak hopping
Resolution	0.9
Total Quant Mode Mass Range	67-87

Sample preparation. 1 mL of a serum or urine samples were digested with 5 mL c-HNO_3. After digestion, the solutions were quantitatively transferred into calibrated flasks (10 mL) and made up with distilled, de-ionized water. Five replicates of each sample were prepared.

Standard solutions and calibration solutions were prepared from the stock solutions as required.

Procedure. The signal intensities obtained from the standard solutions of Ge, As and Se were measured after conventional aspiration into the ICP/MS instrument. Before introduction into ICP/MS, Ge, As and Se were each diluted by a different matrix solution. The standard solution of 100 μg/L Ge, As and Se in 1% matrices was used for the matrix effect on analyte signal. We investigated matrix effects on the signal for Ge, As and Se in the presence of increasing levels of matrices (0, 1000, 5000, 10000, 50000 μg/L).

Results and Discussion

Selection of mass for analyte. Noticeable interference was found for Ge, As and Se, showing that below m/z = 85 the background spectrum is not free of interference peaks.[27-29] Moreover, at m/z = 70-82, interference from oxides or argon dimer ion ($^{40}Ar^{40}Ar$) has been reported.[27-29] So the isotope m/z = 77 and 82 was chosen instead of m/z = 80 for Se. Because the m/z 75 ($^{40}Ar^{35}Cl$) was a possible interfering ion, it was compensated for by the m/z 77 ($^{40}Ar^{37}Cl$).[30]

Sensitivity of individual metals by concomitant elements. Acid digested urine and serum samples contain Na, K, Cl and organic compounds (Table 2, 3). These interfering matrices can be an enhancer or suppress the signal intensities of the Ge, As and Se ions in ICP/MS. The ICP/MS signal intensities of three metals dissolved in different matrixes is shown in Figure 1. The signal intensity (sensitivity) of Ge, As and Se in ICP/MS was recorded after conventional aspiration of aqueous solutions of the standard substances. The results show that concomitant elements such as Cl, S, and C, induce an enhancement effect, whereas N and P did not have any significant effect. On the other hand, Na and K caused a suppression.

The signal intensity is enhanced by 77% (^{74}Ge), 210% (^{75}As) and 156% (^{82}Se) in 1% HCl matrix, and by 26%

Table 2. The concentrations of the concomitant elements in digested serum

	wt.%					
	Na	K	P	S	C	Cl
Mean	0.0240	0.0221	0.0107	<0.1	0.14	0.057
S.D.	0.00086	0.00166	0.000833	0	0.0296	0.0233
Method	AAS	AAS	ICP/AES	Elemental Analysis	Elemental Analysis	Potentiometric Titrator

N=10

Table 3. The concentrations of the concomitant elements in digested urine

	wt.%					
	Na	K	P	S	C	Cl
Mean	0.0676	0.050	0.0073	< 0.1	0.0410	0.0229
S.D.	0.0371	0.0936	0.00462	0	0.0619	0.0528
Method	AAS	AAS	ICP/AES	Elemental Analysis	Elemental Analysis	Potentiometric Titrator

N=20

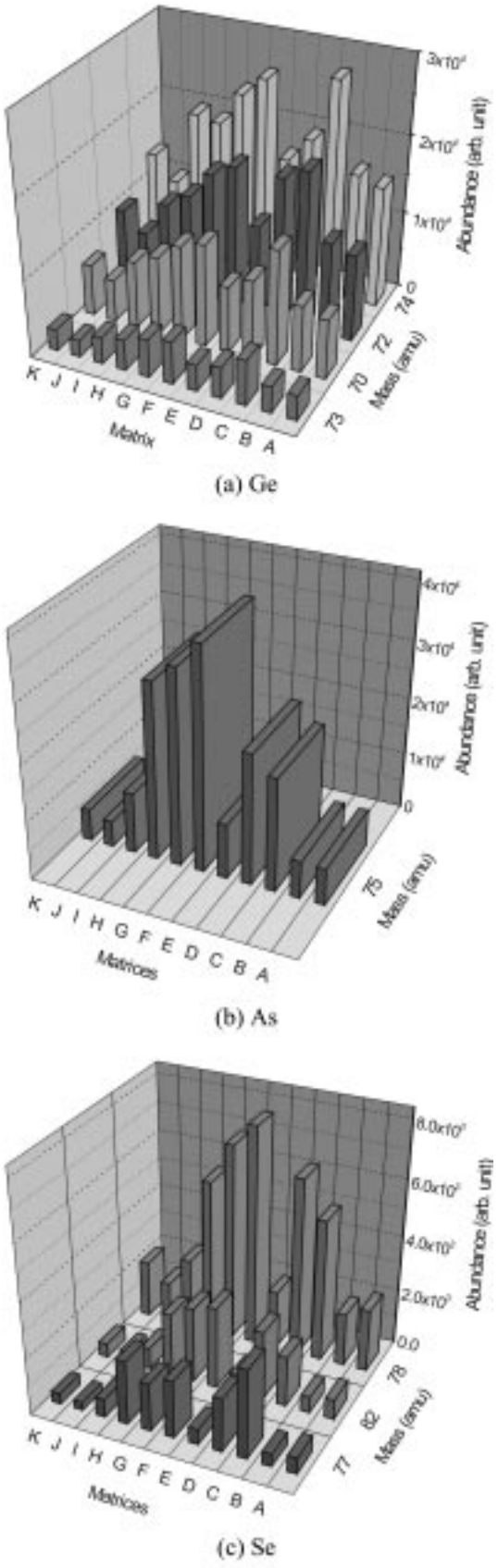

Figure 1. The signal intensity of three elements in various matrices: A: H_2O, B: HNO_3, C: HCl, D: H_2SO_4, E: H_3PO_4, F: CH_3OH, G: C_2H_5OH, H: Mannitol, I: NH_4OH, J: NaOH, K: KOH.

Table 4. The ratio of the intensity of ionic line and the intensity of atomic line for Pd in 1% matrices by ICP/AES[a]

No.	Intensity of ionic line / Intensity of atomic line		
	HNO_3	$NaNO_3$	Mannitol
Mean	0.107	0.093	0.111
S.D.	0.000805	0.00326	0.000504
Difference (%)	–	-12.9	+3.36

[a]Concentration of Pd is 10 μg/L. N=5

(^{74}Ge), 257% (^{75}As) and 251% (^{82}Se) in 1% H_2SO_4 matrix (Figure 1). In case of 1% HNO_3, the signals of these analytes showed no variation.

In the case of alkali metals (1% Na and K), the result shows the depressed signal intensity for analyte. Under these conditions the intensity of analytes was decreased by 8.8-6.7% (^{74}Ge), 7.7-6.8% (^{75}As) and 24.2-24.7% (^{82}Se) (Figure 1). And the emission intensity of ICP/AES for Pd (10 mg/L) standard solution shows a depression in 1% $NaNO_3$ of 12.9% and enhancement in 1% mannitol of 3.3% (Table 4). We projected the same effects of the matrix for Pd for Ge, As and Se in ICP/MS. From these results, we theorized that the lower sensitivity of analyte resulted from the incomplete ionization in the plasma and/or the recombination of Ge, As and Se with electrons.

The results show that the maximum metal signal enhancement is achieved when 1% organic matrices is added to the analyte solution. The signal intensities are enhanced by 24-67% (Ge), 383-501% (As) and 191-289% (Se) (Figure 1). The signal intensity of As dissolved in mannitol solution at the concentration of 1% as C increased to 383% compared with aqueous solution. This increase was similar to 1% methanol and ethanol.

The effects of matrix concentrations are summarized in Figure 2. The signal intensity of Ge, As and Se can increase 1.5%, 20% and 11%, respectively, for a CH_3OH concentration of only 0.1% as C. And the signal intensity in 0.1% $NaNO_3$ as Na decreased bt more than 10%.

Allain *et al.*, selected Eu as an internal standard.[31] The use of Eu is not adequate with most elements because the interference effects are not in the same direction (Figure 4).

Variation of signal intensity of analyte by ionization potential of matrix. We have investigated the influence of ionization energy, because the enhancement effect would be linked to the chemical or physical properties of the elements. A plot of the enhancement percentage for matrices at 1% as a function of the ionization energy for each element is given in Figure 3. Because nitrogen in the ammonium or nitrate did not show the enhancement or depression effect, their salts were used. The results show that the signal intensity of analyte is not completely dependent on the ionization potential of matrix. But there would be an effect between signal intensity and ionization potential (eV) of concomitant element. Carbon (11.20 eV) is the only noticeable exception in this range. It should be noted that nitrogen (14.53 eV) also does not exhibit an enhancement effect for sensitivity.

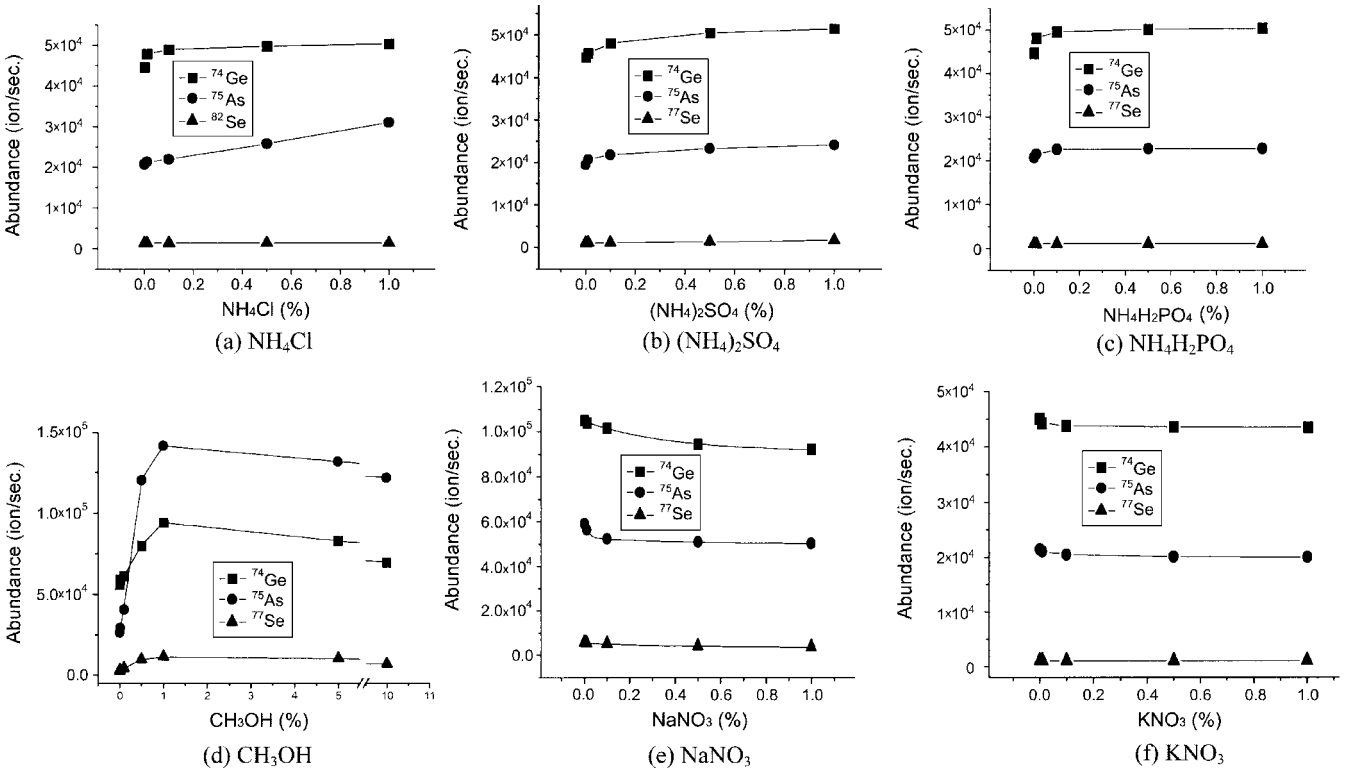

Figure 2. The effect of some matrix concentrations on the abundance of Ge, As and Se.

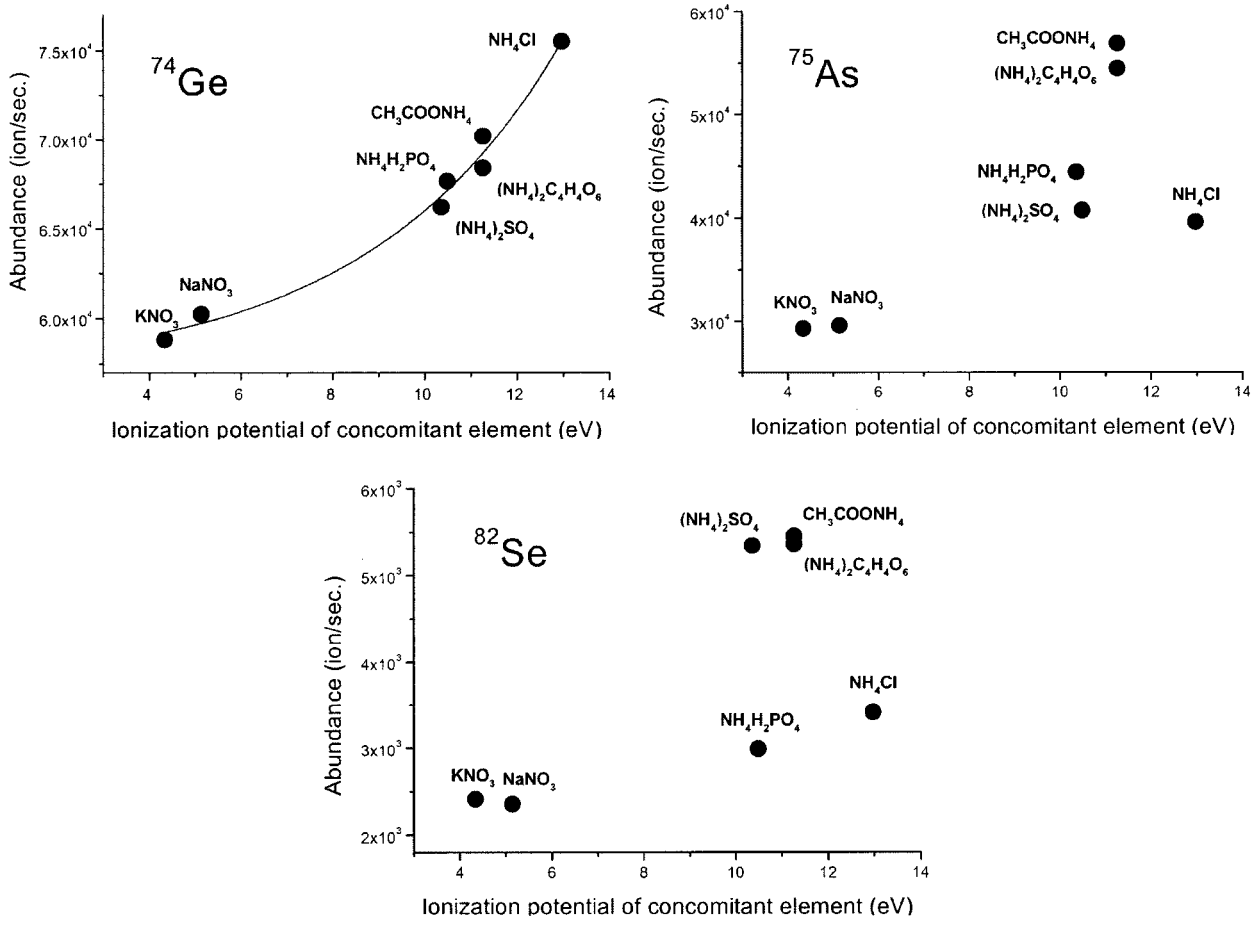

Figure 3. The effect of the concomitant elements on the abundance of Ge, As and Se.

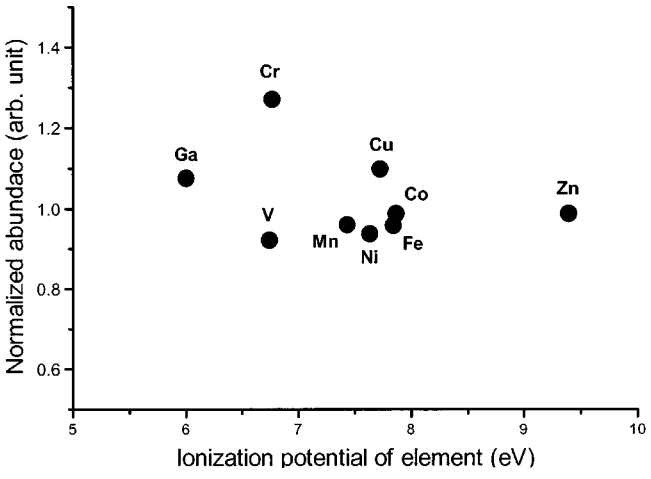

Figure 4. Normalized abundance of elements in 1% CH_3OH.

Conclusions

This work shows that interfering matrices such as Na, K and Carbon can cause signal enhancement or depression. Biological samples were digested in acid media containing concomitant elements in the range of 0.01%-0.18%. The enhancement of As can reach 20% for a CH_3OH concentration of only 0.1% as C. There is an effect between the abundance and ionization potential of the concomitant elements (eV), except carbon and nitrogen.

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