

X Series ICP-MS Clinical Applications Note 1: Rapid and accurate measurement of As and Cr in urine

Key Words

- Arsenic
- Chromium
- Clinical analysis
- Urine

Introduction

In comparison to blood, urine is a relatively simple biological liquid. It is composed of 95% water, 2.5% urea and 2.5% other substances, including major and trace elements, such as Na and Cr, which are filtered from the blood. With respect to the minor components, the composition of urine changes day to day and throughout the day, as a result of the individual's diet and state of health. For this reason, measuring the composition of urine aids medical practitioners in their diagnosis of certain conditions and also enables occupational exposure of workers in high-risk industries to be monitored and assessed. Of particular concern is occupational exposure to Cr (as Cr^{VI}) and exposure to As species through consumption of contaminated foodstuffs. Cr^{VI}, which has been identified as a carcinogen when inhaled, is used as a pigment in paints, inks and plastics, as an anti-corrosion agent and as a major component in chrome plating materials. The toxic effects of As are also well-known, as is the fact that its toxicity depends on the species which is present. It is a known carcinogen², used in wood treatment (to protect it from rot and fungal attack), gun shot and some glass materials.

The salt content of urine is around 0.1% (m/v) so in principle it could be aspirated directly into an ICP-MS, but most users dilute it 1:10 prior to analysis, to reduce the analyte signal suppression problems that such a matrix induces. The detection limits achievable with ICP-MS for the elements of biological interest are considerably below the levels found in urine, so dilution in this way does not compromise the analytical performance. Historically, flame and graphite furnace AAS have been the techniques of choice for this application, but in recent years ICP-MS has been growing in popularity, mainly due to its fast, multi-element capability and its ease of operation and method development. With the advent of collision cell technology, the well-known Ar-based interference problems that previously limited the detection limit capability of the technique for elements such as Se (Ar₂⁺ interference), As (ArCl⁺) and Cr (ArC⁺) have been overcome. In addition, new developments in sample introduction technology have made it possible to efficiently aspirate clinical samples for long periods without causing nebuliser or torch injector blockage, leading to improved data quality. This application note describes the performance of the X Series ICP-MS for measurement of the key elements As and Cr in urine.

Sample preparation

All samples and standards were diluted 1:10 with a custom diluent containing the following reagents:

- 3% butan-1-ol, to match the carbon content of standards and samples, with the aim of ensuring that the ionisation efficiency of elements such as Se and As is the same in all solutions.
- 0.1% TAMA super cleaner (a high purity surfactant), to maintain a stable emulsion with the diluted sample.
- 0.05% HNO₃, to ensure that trace elements are maintained in solution and to aid washout of these elements between samples. The acid concentration must be kept to a minimum, otherwise cellular components in blood samples in particular will precipitate or aggregate, thereby removing some analytes from solution.
- Ga, Rh and Re as low, mid and high mass internal standards respectively (only Ga was required for the application described here).

This customised diluent is also used for preparation of serum and blood samples, enabling a standard method to be used for all liquid clinical sample analyses.

Calibration solution preparation

External calibration solutions containing As (blank to 40 ng mL⁻¹) and Cr (blank to 8 ng mL⁻¹) were prepared by serial dilution of parent 1000 µg mL⁻¹ stock solutions, using the same diluent used to dilute the samples.

Instrument configuration

The instrument was operated in collision cell mode, using 8% (v/v) H₂ in He as the collision gas. This mode is the optimum method for obtaining the most accurate data for As and Cr in a chloride rich solution such as urine. The instrument was configured as a standard X7 system with CCT, (i.e. with a Peltier cooled impact bead spray chamber, single piece quartz torch (1.5mm i.d. injector) and PlasmaScreen *Plus* operated in the hot screen mode for enhanced sensitivity) with the optional Xi interface for enhanced matrix tolerance. A Burgener Miramist high solids parallel path nebuliser was used (see Figure 1) as this device does not block during aspiration of clinical samples and can be run at lower sample uptake rates (down to 0.4 mL min⁻¹) than conventional Burgener nebulisers.

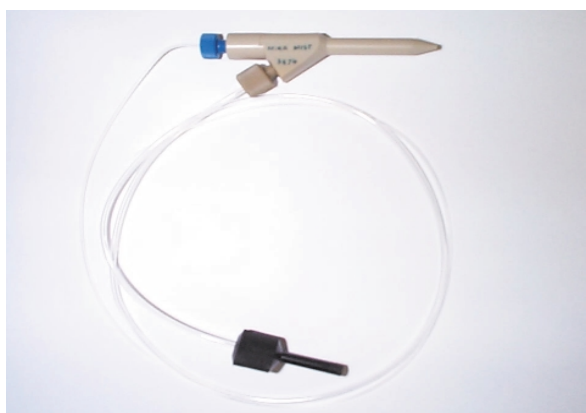


Figure 1. Burgener Miramist high solids parallel path nebuliser

Instrument parameters

The instrument was operated using the following parameters:

RF power:	1340 W
Nebuliser gas flow:	0.78 L min ⁻¹
Auxiliary gas flow:	0.80 L min ⁻¹
Cool gas flow:	13.0 L min ⁻¹
CCT gas flow (8% H ₂ /He):	3 mL min ⁻¹
Isotopes measured:	⁵² Cr, ⁷¹ Ga (internal standard), ⁷⁵ As
Dwell time per isotope:	20 ms
Sample uptake and wash time:	40 s
Sample acquisition time:	60 s per repeat (3 repeats per sample, 5 for the blank)

Results and discussion

Prior to measuring the samples, the short (10 minutes) and long (8 hours) term stability of the instrument (in standard mode) during aspiration of the 1:10 diluted urine matrix was evaluated. The results are presented in Table 1.

ANALYTE	SHORT TERM STABILITY, RSD (%)	LONG TERM STABILITY, RSD (%)
Be	1.1	3.0
Co	1.2	2.3
In	1.0	2.4
Ce	1.0	2.3
Bi	1.7	2.3
U	2.2	2.4

Table 1. Instrument stability during aspiration of 1:10 diluted urine.

Table 1 shows that excellent short and long term instrument stability (equivalent to the performance expected while aspirating clean matrix solutions) was achieved across the mass range while aspirating the diluted urine matrix.

Three well-characterised reference urine samples were supplied for analysis. The CCT mode calibrations obtained for the target analytes (Cr and As) are shown in Figures 2 and 3 below.

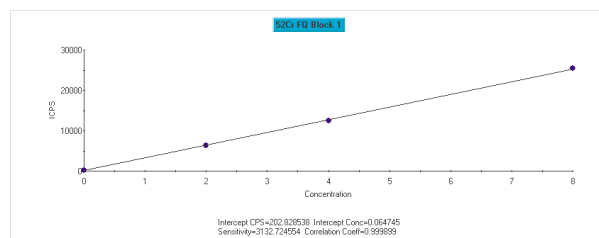


Figure 2. ⁵²Cr calibration (CCT mode), blank to 8 ng mL⁻¹.

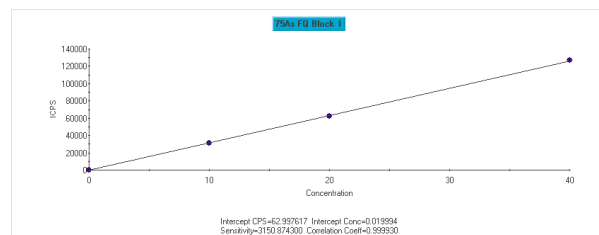


Figure 3. ⁷⁵As calibration (CCT mode), blank to 40 ng mL⁻¹.

The figures of merit for the ⁵²Cr and ⁷⁵As calibrations are given below (Table 2).

PARAMETER	⁵² Cr	⁷⁵ As
Sensitivity (cps/ ng mL ⁻¹)	3133	3151
Blank equivalent concentration (BEC) / ng mL ⁻¹	0.065	0.020
3 sigma detection limit (ng mL ⁻¹)	0.009	0.005

Table 2. Figures of merit for the ⁵²Cr and ⁷⁵As calibrations.

The calibrations and the corresponding figures of merit show the excellent linearity, sensitivity and detection limit capability of the X Series ICP-MS when operated in CCT mode. Since the sample diluent matrix contains butanol, a large ⁴⁰Ar¹²C⁺ interference on ⁵²Cr is observed in standard instrument operation. The above results demonstrate how this interference is efficiently eliminated with the use of the CCT option.

The analysis results together with the reference values are presented below (Table 3).

Analyte	URINE 1		URINE 2		URINE 3	
	As	Cr	As	Cr	As	Cr
Measured	135 ± 2	3.97 ± 0.03	22.9 ± 0.2	1.21 ± 0.05	17.5 ± 0.2	53.2 ± 0.4
Reference	132	n/s	24	n/s	n/s	46
Relative accuracy (%)	102	n/s	96	n/s	n/s	115
Reported range	107 - 164	n/s	4 - 44	n/s	n/s	43 - 53

n/s – not specified

The measured results for both analytes in all three samples were found to be in good agreement with the reference values and with the expected concentration range (based on measurements of these samples performed in other laboratories). All the measured values were significantly above the detection limit achievable with the X Series ICP-MS, even with the 10-fold dilution.

The high precision of the measurements enables small differences in a patients urine to be identified with confidence, and the accuracy of the measurements allows confirmation of toxic / healthy / deficient levels to be established, thereby prompting the necessary medical treatment. The excellent relative accuracy results (i.e. relative to the reference values) for As also clearly illustrate the effective attenuation of the $^{40}\text{Ar}^{35}\text{Cl}^+$ interference on ^{75}As achieved using the advanced collision cell technology of the X Series ICP-MS.

Conclusions

The X Series ICP-MS is an ideal tool for trace element determination in clinical samples. It is a robust, easy to use instrument, capable of measuring hundreds of samples per day, should the need arise. Measurement of trace elements of medical interest in urine and other clinical samples can be accurately and precisely achieved, with only minimal sample preparation – a simple dilution step applicable for all liquid clinical samples is all that is required. Through the powerful combination of PlasmaScreen *Plus*, CCT technology and the Xi interface, complemented by improved sample introduction systems, high sensitivity, interference-free clinical sample analysis using ICP-MS can now be performed.

References

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- ² Arsenic and Arsenic Compounds, IARC Monographs, Supp.7, International Agency for Research on Cancer, WHO, Lyon, France, 1987, pp. 100 - 106

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