Easy and Fast Determination of Trace Elements in Clinical Samples using Quadrupole ICP-MS

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■ Overview and Objective

The analysis of trace elements in clinical samples is a frequent required objective nowadays and oftentimes connected to the use of ICPMS techniques.

The first question then is, which technique exactly can meet the user requirements as different measurement principle are available within commercial quadrupole ICPMS devices to overcome interferences and achieving correct results. In addition to standard measurement mode these commonly are kinetic energy discrimination (KED) using Helium as collision gas or special reaction modes with gases like Hydrogen or Ammonia.

Whereat the kinetic energy discrimination mode is very easy to handle, as it affects the resulting mass spectra in basically the same way and no account has to be taken to specific behaviours to specific isotopes, the reaction modes with each different gas always needs to be improved for different isotopes individually in order to reduce interferences.

For each mode mentioned above, the ICPMS collision/reaction cell needs to be stabilized. Thus, as more and more different modes are applied, the measurement times are drastically extended.

Within this poster the ease of uses of matrix matching is shown with the goal to use as less measurement modes as possible in order to save analysis time.

Figure 1: Inductively Coupled Plasma Mass Spectrometer ICPMS-2030 (Shimadzu)

■ Clinical Samples and Typical Interferences

For the determination of trace elements in urine, serum and whole blood, different measures must be considered to achieve correct results.
While it is quite easy to determine trace elements in urine after dilution using acid media (x10), the same is getting more challenging for serum or whole blood matrix, due to the higher amount of carbon and subsequent appearing interferences for example for the determination of selenium.

In general for quantification of trace elements the most abundant isotope is selected. Taking Selenium into consideration, this would be ^{80}Se (49.61%). But at the same time, one of the most frequent polyatomic interferences affect m/z 80, in this case it is the polyatomic ion of $^{40}Ar^{40}Ar$ from the Argon used as plasma gas. That is why the 2nd most abundant isotope, ^{78}Se is most commonly selected (23.78 %). Here polyatomic ions of Argon interfere as well ($^{38}Ar^{40}Ar$). But as the ^{38}Ar is much less abundant than the ^{40}Ar, the level of interference to 78 m/z is appr. factor 1500 less than to 80 m/z. As a result, the signal to noise ratio of ^{78}Se is several times better leading to higher sensitivities compared to ^{80}Se, even ^{78}Se is less sensitive.

[1] Nelms, Simon M., Inductively Coupled Plasma Mass Spectrometry Handbook, CRC Press LLC, 2005

But still as Argon is one of the major element present within the mass spectrometer, the Argon-Argon polyatomic interference needs to be considered, especially when the major components of the sample is changing. In this case for urine, serum and whole blood, the changing amount of Carbon gives some further difficulties. The reason is, that carbon forms polyatomic ions with Argon as well. So as more carbon is present, as more Carbon-Argon-Ions are formed, thus it influences the equilibrium of the formation of Argon-Argon-Ions and affects the determination of ^{78}Se.

At the same time with the increasing amount of Carbon, other elements like ^{52}Cr are interfered by $^{40}Ar^{12}C$, which gives the idea that easy matrix matching by adding a carbon source to the internal standard could solve these troubles without the need for applying reaction gases which would save additional measurement time.

■ General Method Parameters

The ICPMS-2030 has been used in basic Minitorch setup, enabling drastically lower flow rates of Argon. Even for high matrix samples the total consumption is below 10 l/min. At the same time the Argon purity requirements for the ICPMS-2030 are on a very low level (min. Argon 3.5 = 99.95 %). The basic method parameters are summarized in table 1.

Tab. 1:
ICPMS-2030 Configuration and Method Parameters

Parameter	Setting
RF generator power	1.2 kW
Plasma gas	8 l/min
Auxilliary gas	1,1 l/min
Carrier gas	0.7 l/min
Nebulizer	coaxial
Sampling depth	6 mm
Spray Chamber temperature	5 °C
Collision Cell Gas flow (Helium)	6 ml/min
Cone material	Copper
Internal Standard	Automatic Addition (T-piece)
Sample tube	Black-black, PVC
Internal Standard tube	Orange-blue, PVC
Optional Fast Rinse Unit	ASXPress Plus (Catac Teledyne)

■ Sample Measurement - Urine

For Urine, the preparation of samples is very easy. All samples have been diluted by a factor of 10 using acidified purified water (1 Vol-% HNO_3). As the internal standard solution is added automatically, the sampler just have to be placed to the sampler. Urine typical consist of 95% water. After applying factor 10 dilution the amount of TDS cannot exceed 0,5%. Thus, the determination of trace elements using ICPMS technique is not most challenging.

For evaluation of the method and instrument capabilities, certified reference material has been analysed (Table 2). The result mentioned is an average of 2 single measurements, whereat both single results meet the certified range.

■ Sample Measurement – Serum and Whole blood

For the measurement of these two types of sample it now starts that the influence of Carbon is increasing. The samples are more and more different compared to the reference calibration solutions, which do not containing any carbon. For example Serum contains appr. 91% water and about 7 % proteins (albumin and globulins).

Tab. 2: Urine quantification results (all in µg/l)

Isotope	Mode	Internal Std. Element	Recipe Level I			Recipe Level II		
			Certified		Result	Certified		Result
			Min	Max	Average	Min	Max	Average
^{52}Cr	KED	Ge	3.26	4.89	**4.17**	15.9	23.8	**19.9**
^{65}Cu	KED	Ge	29.4	44.1	**38.7**	73.5	110	**91.3**
^{55}Mn	KED	Ge	3.13	4.69	**3.93**	15.5	23.2	**19.5**
^{60}Ni	standard	Ge	4.73	7.10	**5.91**	34.4	51.7	**41.6**
^{75}As	standard	Ge	34.4	51.6	**42.7**	66.6	99.9	**79.8**
^{111}Cd	standard	Te	1.97	2.95	**2.46**	11.5	17.2	**14.5**
^{206}Pb	KED	Ho	19.2	28.8	**20.2**	52.0	78.0	**54.9**
^{203}Tl	KED	Tb	5.79	8.69	**6.40**	15.2	22.8	**17.3**
^{78}Se	KED	Rh	24.0	35.9	**28.7**	66.6	99.9	**87.4**
^{27}Al	standard	Be	26.4	39.6	**31.6**	68.7	103	**84.9**
^{59}Co	standard	Ge	1.63	2.44	**1.94**	27.8	41.7	**32.2**
^{68}Zn	KED	Y	163	245	**192**	428	642	**515**
^{127}I	KED	Y	89.9	150	**136**	373	622	**528**
^{57}Fe	KED	Ge	30.8	46.3	**42.5**	179	268	**232**

Tab. 3: Serum quantification results (all in µg/l)

Isotope	Mode	Internal Std. Element	Recipe Level I			Recipe Level II		
			Certified		Result	Certified		Result
			Min	Max	Average	Min	Max	Average
^{63}Cu	KED	Ge	681	921	821	1140	1540	1410
^{195}Pt	KED	Lu	7.11	10.7	10.1	68.8	103	917
^{78}Se	KED	Rh	52.9	79.3	67.9	84	126	109
^{64}Zn	KED	Y	1120	1520	1400	1730	2350	2280

Tab. 4: Whole Blood quantific. results ([A]µg/l [B]mg/l)

Isotope	Mode	Internal Std. Element	Recipe Level I			Recipe Level III		
			Certified		Result	Certified		Result
			Min	Max	Average	Min	Max	Average
^{52}Cr [A]	KED	Ge	0.94	1.57	1.55	8.74	13.1	10.9
^{63}Cu [B]	KED	Ge	0.54	0.82	0.61	1.34	2.00	1.39
^{56}Fe [B]	KED	Sc	303	454	322	302	452	317
^{55}Mn [A]	KED	Ge	6.41	9.61	6.72	17.1	25.7	17.4
^{78}Se [A]	KED	Rh	61.4	92.1	81.5	135	203	170
^{66}Zn [B]	KED	Y	3.75	5.62	5.41	6.57	9.85	8.95

A similar concentration of water (90%) is the main component of whole blood. Anyway – in accordance to diagnostic sensitivity requirements, different dilution factors have been applied. The serum was diluted similar to urine by a factor of 10 and the whole blood by a factor of 20. For both dilutions again the applied media was 1 Vol-% nitric acid.

To cover additional interferences caused by carbon, the internal standard solution contains a certain level of Ethanol and Triton X-100 in order to have a final concentration of 3 vol.-% Ethanol and 0,3 weight-% Triton X-100 present after mixing by T-piece.

■ Summary

As indicated by table 2-4 all results meet the certified range of the reference material by just using standard and/or the very common KED mode. Any additional reaction gases have not been necessary. So the ICPMS-2030 is easy to use for the measurement of clinical samples by e.g. adding a carbon source to the internal standard solution.

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