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Inductively Coupled Plasma Mass Spectrometry ICPMS-2050 LF

Application News

Determination of More Than 25 Nutritional, Essential and Toxic Elements in Whole Blood by ICP-MS Using Alkaline Dilution

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User Benefits

- Offering gas switching times <5 sec and ProActive Rinsing function, short sample cycle times can be achieved
- Using whole blood calibrators and control samples in research labs simplifies working routines
- Alkaline media drastically improves washout capabilities for mercury and ensures proper sample stabilization compared to acidic media

■ Introduction

Inductively coupled plasma mass spectrometry (ICP-MS) like Shimadzu ICPMS-2050 (Fig. 1) offers ultra-low detection limits and fast multi-element capability required for reliable high throughput measurement of nutritional, essential, and toxic elements in various complex biological samples.

While urine has been widely used to monitor elemental excretion, blood serum represents the protein-free fraction of circulating blood. Whole blood, however, contains both cellular and extracellular components, enabling a more integrated assessment of an individual's nutritional status and exposure to potentially toxic metals than either urine or serum alone. Accordingly, whole-blood ICP-MS analysis is well suited for research applications such as nutritional assessment, toxicology, and biomonitoring studies.

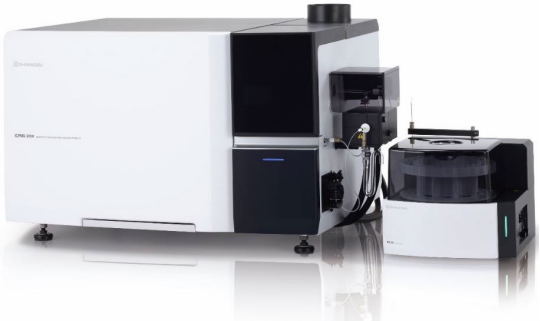

Fig. 1 ICPMS-2050 LF with AS-20 Autosampler

■ Sample Preparation and Calibration

Whole blood for trace element analysis can be easily contaminated during sampling and storage. Thus, special attention needs to be paid to all collection devices, including needles, stoppers, lubricants and separator systems, as even µg/L-levels can bias results[1)].

Usually, samples are immediately transferred into pre-cleaned, trace-metal–certified polypropylene or PMP tubes to minimize contact with glass and stainless-steel surfaces that can leach chromium, nickel, antimony or other elements. To prevent clotting, laboratories employ anticoagulants added in precisely defined blood-to-additive ratios[1)]. It should be well noted, which kind of anticoagulant has been used. Depending on anticoagulant, an extraordinary portion of e.g. potassium, sodium, lithium or other components is added to the blood, which might affect the analysis.

Instead of laborious and time-consuming sample preparation, e.g., by microwave-assisted acid digestion, this approach is simple dilution.

Because protein-rich matrices can be unstable or cause clogging when acidified, an alkaline dilution strategy (Table 1) provides the robustness and element stability needed for accurate whole-blood analysis while offering improved mercury washout capabilities. The same alkaline dilution strategy was successfully applied in recent ICP-MS Application News to urine [1.] and serum [2.].

Table 1 Components of Alkaline Diluent prepared in Water*1

Reagent	Description	Purpose
Ammonia	25% (v/v), Suprapur®, Merck, Germany	adjusts alkaline pH
Tergitol™ 15-S-9	extra pure, Carl Roth, Germany	Homogenizes sample, supports lyse of cells
EDTA (Na-free)	>99.999% Sigma-Aldrich, USA	stabilizes ions in solution
Isopropanol	≥99.999%, Sigma-Aldrich, USA	compensates carbon enhancement effect*2

*1 All solutions are prepared using ASTM Type 1 ultrapure water (18.2 MΩ resistivity, Arium® Pro VF, Sartorius AG).
*2 Carbon present in sample will otherwise increase response of less ionized elements (e.g. As, Se), resulting in false positives.

For matrix matched calibration, Whole Blood Calibrator (ClinCal® 9943, Recipe) was injected in different dilution levels (cf. Table 2). For quality control like proving stability and sensitivity characteristics of the method, Whole Blood Controls Level I, II, III (ClinCheck® 8840-8843, Recipe) were measured frequently throughout the batch.

Controls as well as samples are simply 20-fold diluted by alkaline diluent and well homogenized (vortex mixing) prior to analysis.

Table 2 Recipe® Calibrator in alkaline diluent, µg/L

Element, unit		Cal 1 Blank Diluent	Cal 2 12.5%	Cal 3 25%	Cal 4 50%	Cal 5 100%*
Ag	µg/L	0	1.04	2.60	5.20	10.4
Al	µg/L	0	2.96	7.40	14.8	29.6
As	µg/L	0	1.46	3.65	7.30	14.6
Ba	µg/L	0	3.93	8.83	19.7	39.3
Ca	mg/L	0	4.80	12.0	24.0	48.0
Cd	µg/L	0	1.38	3.45	6.9	13.8
Co	µg/L	0	1.49	3.725	7.45	14.9
Cu	mg/L	0	0.171	0.42750	0.855	1.71
Fe	mg/L	0	38.2	95.5	191	382
Hg	µg/L	0	3.59	8.98	18.0	35.9
I	µg/L	0	9.49	23.7	47.5	94.9
K	mg/L	0	236	590	1180	2360
Mg	mg/L	0	4.36	10.9	21.8	43.6
Mn	µg/L	0	2.59	6.48	13.0	25.9
Mo	µg/L	0	1.04	2.60	5.20	10.4
Na	mg/L	0	206	515	1030	2060
P	mg/L	0	37.0	92.5	185	370
Pb	µg/L	0	34.7	86.8	174	347
Pd	µg/L	0	0.659	1.65	3.30	6.59
Pt	µg/L	0	0.673	1.68	3.37	6.73
Sb	µg/L	0	1.68	4.20	8.40	16.8
Se	µg/L	0	30.8	77.0	154	308
Sn	µg/L	0	1.07	2.68	5.35	10.7
Sr	µg/L	0	6.78	17.0	33.9	67.8
Tl	µg/L	0	1.06	2.65	5.30	10.6
Zn	mg/L	0	0.828	2.07	4.14	8.28

* 100% corresponds to 0.5 mL in 10 mL (considering a 20-fold dilution)

■ Configuration and Measurement Conditions

System configuration of ICPMS-2050 LF was selected according to Table 3. All components have been selected with care to fulfill body fluid analysis requirements.

Table 3 ICPMS-2050 LF Configuration and Basic Method Settings

Autosampler	:	AS-20 (Covered Round Table / Dual Rinse / Spacer for low dead volume)
Extended Cover	:	ENC-280 (in case dust is an issue)
Sample Probe	:	Inert Guardian™ Probe with inline filter
Spray Chamber	:	Cyclonic Twister (reduces carry-over)
Chamber Temperature	:	5 °C
Nebulizer	:	Coaxial DC 04 (~0.4 mL/min)
Peristaltic Pump	:	4 Channels, 12-roller @ 20 rpm
Internal Standard Tubing	:	PVC, flared-end, orange-blue
Sample Tubing	:	PVC, flared-end, black-black
Drain	:	Automatic overflow type
Torch	:	Shimadzu Minitorch
Cone Material	:	Ni
Sampling Depth	:	9.0 mm
RF-Power	:	1.20 kW
Plasma Gas	:	Ar 9.0 L/min
Auxiliary Gas	:	Ar 1.10 L/min
Carrier Gas	:	Ar 0.47 L/min
Dilution Gas	:	Ar 0.38 L/min
Cell Gas	:	He 6.0 mL/min H_2 7.0 mL/min
Cell Voltage	:	-21.0 V
Energy Filter	:	7.0 V

More than 25 elements have been selected for quantification (Table 4) whereat some of the selected isotopes are partwise affected by polyatomic interferences. To eliminate interferences, ICPMS-2050 LF highly efficient He-collision mode, H_2-reaction mode as well as high-resolution mode was applied.

Table 4 Elements and Isotopes

Element	Isotope	Integration time [s]	Cell Gas	Internal Standard
Ag	107	0.4	He	^{103}Rh
Al	27	5.0	H_2	^{45}Sc
As	75	1.0	He	^{89}Y
Ba	137	0.4	He	^{103}Rh
Ca	44	0.1	He	^{45}Sc
Cd	111	2.0	He	^{103}Rh
Co	59	0.5	He	^{45}Sc
Cu	63	0.1	He	^{89}Y
Fe	57	0.1	He	^{45}Sc
Hg	202	0.3	He	^{193}Ir
I	127	0.2	He	^{103}Rh
K	39	0.1	He	^{45}Sc
Mg	25	0.1	He	^{45}Sc
Mn	55H*	1.0	He	^{45}Sc
Mo	95	0.5	He	^{89}Y
Na	23	0.1	He	^{45}Sc
P	31	0.1	NoGas	^{45}Sc
Pb	206+207+208	0.3	He	^{193}Ir
Pd	105	0.5	He	^{89}Y
Pt	195	0.3	He	^{193}Ir
Sb	121	0.5	He	^{103}Rh
Se	78	0.3	H_2	^{89}Y
Sn	118	0.5	He	^{103}Rh
Sr	88	0.3	He	^{89}Y
Tl	205	0.2	He	^{193}Ir
Zn	66	0.1	He	^{89}Y

*measured in high resolution mode

Alkaline diluent was measured as blank sample. All calibration curves (Fig. 2) are weighted inversely (1/I) to improve the precision in the low-end trace region.

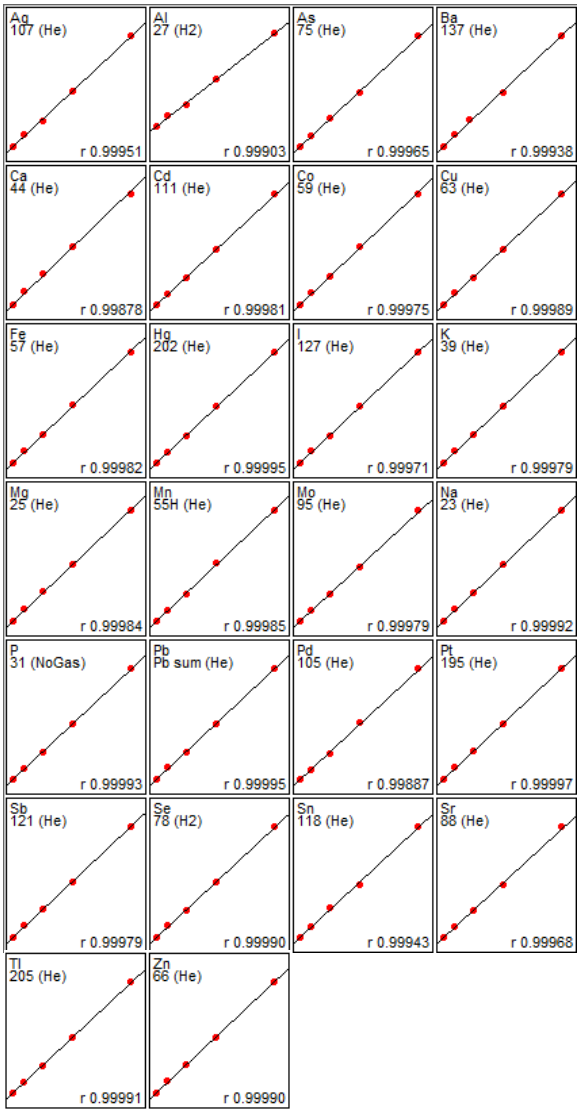

Fig. 2 Calibration Curves

■ Results and Discussion

Method Stability

The method was stable over the full 100 samples runtime indicated by internal standard recovery, standardized to the lowest calibration curve blank level (Fig. 3). At the same time, whole blood control LI-LIII were frequently measured and have been satisfactorily traced back to given values within specified reference ranges.

The reference values may be entered to the LabSolutions™ ICPMS method directly, allowing for quick assessment of the quality of the results obtained from each run, as outliers will be highlighted automatically. The software also allows to easily monitor internal standard stability.

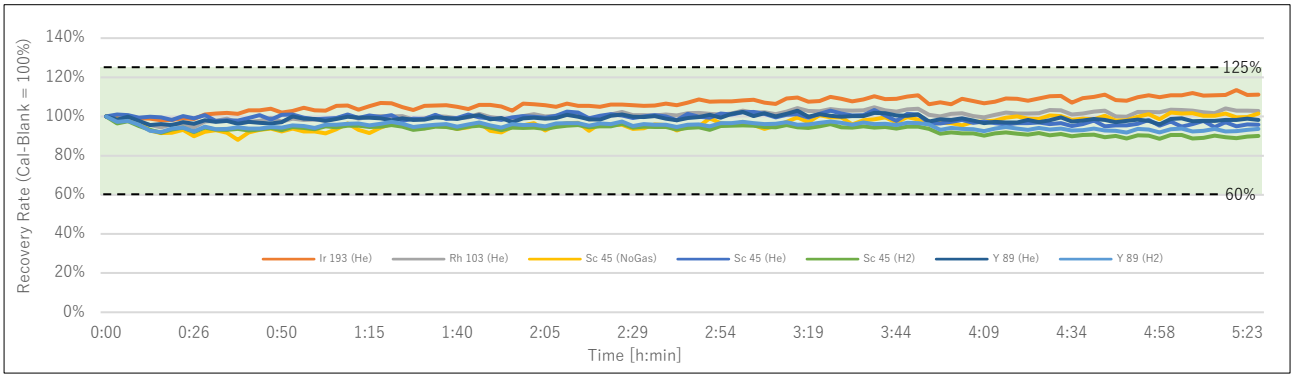

Fig. 3 Internal Standard Stability Plot

Method Sensitivity

In general, the method is developed to be stable while allowing to analyze the usual reference ranges (Table 5). The sensitivity is determined by standard deviation of the calibration curve blank sample. Because samples and reference samples are treated in the same way, the dilution factor can be disregarded, allowing to use the given limit of quantification (LOQ) as approximation for the method quantification limit (MQL).

Table 5 ICPMS-2050 LF Method Sensitivity [µg/L]

Element, unit		LOD (3s) ≈ MDL	LOQ (10s) ≈ MQL	Common Reference Range[3)]	Recipe Control Range (LI – LIII)	ICPMS-2050 LF suitable?
Ag	µg/L	0.02	0.05	< 0.6	1.55-7.55	●
Al	µg/L	0.95	3.18	< 20.5	12.0-26.9	●
As	µg/L	0.05	0.15	< 3.4	3.1-10.8	●
Ba	µg/L	0.48	1.61	< 2.9	8.71-25.3	●
Ca	mg/L	0.46	1.52	44.9-63.4	45.3-46.3	●
Cd	µg/L	0.05	0.17	< 1.0	1.59-6.98	●
Co	µg/L	0.04	0.13	< 0.9	1.45-12.7	●
Cu	mg/L	0.0002	0.0006	0.65-1.31	0.758-1.51	●
Fe	mg/L	0.18	0.61	378-600	376-385	●
Hg	µg/L	0.09	0.31	< 2.0	2.31-18.5	●
I	µg/L	0.53	1.75	-	25.7-59.8	
K	mg/L	0.30	0.99	1485-1955	1260-2050	●
Mg	mg/L	0.02	0.08	15-26 (serum)	26.8-38.2	●
Mn	µg/L	0.29	0.96	5.0-13.5	8.68-6.51	●
Mo	µg/L	0.09	0.29	0.2-1.3	2.00-8.17	●
Na	mg/L	0.46	1.54	1563-1954	1960-1980	●
P	mg/L	0.68	2.27	314-443	345-353	●
Pb	µg/L	0.08	0.27	< 30	35.0-264	●
Pd	µg/L	0.03	0.10	< 0.2	1.2-4.98	●
Pt	µg/L	0.02	0.05	< 0.2 (serum)	1.67-5.06	●
Sb	µg/L	0.02	0.08	< 0.2	2.10-8.39	●
Se	µg/L	0.06	0.20	73-165	88.2-204	●
Sn	µg/L	0.18	0.59	< 2.0	2.59-8.05	●
Sr	µg/L	0.19	0.63	9.0-41.0	15.3-48.6	●
Tl	µg/L	0.07	0.23	< 0.6	0.868-8.68	●
Zn	mg/L	0.001	0.005	4.0-7.8	4.83-7.77	●

● means the method sensitivity is in line with common reference ranges.

To further increase sensitivity and accuracy for individual elements, a simple approach can be to increase its integration times, which is recommended for Molybdenum, Palladium and Tin.

Eliminate Possible Interferences

A usual troublesome element is Selenium: "From a clinical biochemistry point of view, perhaps the most significant example is the interference of gadolinium with selenium. […] Gadolinium isn't normally present in biological samples; however, it is present in some intravenous contrast agents used for magnetic resonance imaging (MRI) […]. The presence of gadolinium in a clinical sample can cause an artefactually elevated selenium result"[2)], as double charged ^{156}Gd interferes ^{78}Se. As it was shown within the related application note [2.], Gd-interferences can be sufficiently removed by applying H2-reaction mode (Table 6).

Table 6 Eliminated effect of ^{156}Gd to ^{78}Se in H_2-mode

	Solution A	Solution B	Solution C	Solution D
Gd-level	0 ppm	10 ppm	20 ppm	50 ppm
Se-level	20 ppb	20 ppb	20 ppb	20 ppb
Se-Result H_2-mode	9.9 ppb	19.7 ppb	19.7 ppb	19.8 ppb

Another issue to be addressed in whole blood is the accurate recovery of trace Manganese levels (^{55}Mn, ~10-20ppb), being partially influenced by the neighboring dominant iron signal (^{56}Fe, ~400ppm). This is not an issue in case the iron-content is stable and matrix matched calibration is applied. But in case the Fe-level varies in sample or was not considered in creating the curve, special attention needs to be paid to avoid false positive or false negative Mn-results, resp.

To be independent from variations in iron levels, ^{55}Mn was selected to be measured in high resolution mode while applying Inter Element Correction (IEC), which ensures any remaining interfering levels are determined and corrected with each sample individually, allowing to achieve most accurate Mn-results. In Table 7 it is shown that even 500ppm iron does no further result in false-positives.

Table 7 Eliminated effect of ^{56}Fe to ^{55}Mn

	Calibration	Solution A	Solution B	Solution C
Fe-level	0 ppm	500 ppm	500 ppm	500 ppm
Mn-level	0-50 ppb	0 ppb	10 ppb	50 ppb
Mn-result	-	<0.3 ppb	9.4 ppb	48.4 ppb

■ Conclusion

The ICPMS-2050 LF was specifically configured for robust small volume analysis while reducing carry over, sample cycle times and environmental contamination impacts while being capable of successfully addressing several kind of possibly interference providing most accurate and reliable results.

The collision- and reaction cell performs efficiently with flowrates of helium and hydrogen in low levels of 6-7mL/min. At the same time, the method uses the well established Minitorch plasma system, allowing lowest argon consumption while reducing power consumption, which makes it exceptionally cost-effective without compromising performance characteristics.

LabSolutions ICPMS software allows to easily control the device, consumable lifetime, QC-recoveries and internal standard stability. Furthermore, features like ProActive Rinsing and Extended Rinsing speed up the method while reducing carry-over risks.

<References>

1) Blood collection device components: issues, innovations, and recommendations for clinical laboratories and manufacturers – a narrative review, Journal of Laboratory and Precision Medicine, Vol 10 (2025) https://jlpm.amegroups.org/article/view/10316/html
2) Inductively Coupled Plasma Mass Spectrometry: Introduction to Analytical Aspects, Clin Biochem Rev 40 (3) 2019, p. 126.
3) Medical laboratory Bremen, https://www.mlhb.de/analysen (accessed 24.04.2026)

<Related Applications>

1. Determination of 23 Nutritional, Essential and Toxic Elements in Urine by ICP-MS Using Alkaline Dilution, Application News 05-SCA-116-013-EN
2. Determination of 20 Nutritional, Essential and Toxic Elements in Blood Serum by ICP-MS using Alkaline Dilution, Application News 05-SCA-116-010-EN
3. ICP-MS Analysis of 25 Essential, Trace and Nutritional Elements in Blood Serum Using Recipe ClinMass® Complete Kit, Application News 05-SCA-116-012-EN

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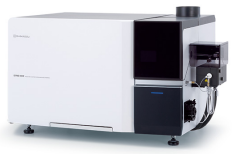

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