

Analytical Method Development and Validation for Trace-Level Determination of Heavy Metals in Nutraceuticals by ICP-MS

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ABSTRACT

Nutraceuticals occupy a middle ground between food and pharmaceuticals and are widely consumed for health promotion and disease prevention. Because raw materials, processing equipment and packaging can introduce elemental impurities, monitoring toxic and essential heavy metals in nutraceutical formulations is essential for consumer safety and regulatory compliance. In this study, an analytical method based on Inductively Coupled Plasma Mass Spectrometry (ICP-MS) was developed and validated for the simultaneous determination of ten elements — chromium (Cr), nickel (Ni), copper (Cu), arsenic (As), selenium (Se), cadmium (Cd), tin (Sn), antimony (Sb), lead (Pb) and mercury (Hg) — in nutraceutical products. Samples were digested by a microwave-assisted nitric acid–hydrogen peroxide procedure and analysed using rhodium (Rh) and yttrium (Y) as internal standards. The method was validated as per ICH Q2(R1) guidelines for specificity, linearity, limit of quantification (LOQ), accuracy (recovery), repeatability, intermediate precision (reproducibility) and robustness. Calibration curves for all ten analytes were linear over the tested ranges with correlation coefficients (R^2) between 0.9980 and 1.0000. Recovery at LOQ, 2×LOQ and 10×LOQ spiking levels ranged from 84.3% to 116.9%, and precision studies gave %RSD values generally below 16%, meeting the pre-defined acceptance criteria (recovery 70–120%, RSD ≤ 20%). The method was robust to small deliberate changes in digestion time, acid concentration, nebulizer gas flow and plasma power. The validated ICP-MS method is rapid, sensitive, accurate and reproducible, and is suitable for routine quality-control testing and regulatory compliance testing of heavy metals in nutraceutical formulations.

KEYWORDS

ICP-MS; Heavy metals; Nutraceuticals; Method validation; ICH Q2(R1); Elemental impurities; Trace elements.

1. INTRODUCTION

The term “nutraceutical”, coined by Dr. Stephen DeFelice in 1989, describes food-derived products that confer health benefits beyond basic nutrition, including the prevention and management of chronic diseases such as cardiovascular disorders, diabetes, arthritis and cancer. Nutraceuticals may be derived from plant, animal or microbial sources, or manufactured synthetically, and are marketed as capsules, tablets, powders, syrups and fortified foods. Because these products are often manufactured from natural raw materials grown in variable environmental conditions, and because manufacturing equipment, excipients, water and packaging can all contribute trace elemental impurities, nutraceutical

formulations are susceptible to contamination with toxic heavy metals such as arsenic, cadmium, mercury and lead, as well as elevated levels of other elements including chromium, nickel, copper, selenium, tin and antimony.

Regulatory frameworks such as ICH Q3D and the pharmacopoeial elemental-impurity chapters require risk-based control of elemental impurities in pharmaceutical and nutraceutical products, and international bodies including WHO, FAO, FDA and FSSAI have set permissible limits for toxic metals in food and dietary-supplement products. Among the analytical techniques available for elemental analysis — Atomic Absorption Spectroscopy (AAS) and Inductively Coupled Plasma–Optical Emission Spectroscopy (ICP-OES) — Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is regarded as the technique of choice because of its exceptional sensitivity (ppt–ppb detection), wide linear dynamic range, multi-element and isotopic analysis capability, and rapid throughput.

Several groups have reported ICP-MS methods for elemental analysis of dietary supplements and food matrices. Silva et al. (2024) validated a rapid ICP-MS method for essential and toxic elements in liquid dietary supplements comparing microwave digestion with direct analysis; Naz et al. (2024) surveyed heavy-metal contamination in commercial nutraceuticals and highlighted the need for validated methods and human health risk assessment; Upadhyay et al. (2024) validated an ICP-MS method for As, Cd, Hg and Pb following microwave-assisted digestion; Kwon et al. (2024) optimized microwave digestion coupled with ICP-MS for heavy-metal screening in food additives; and Si et al. (2024) reviewed ICP-MS as one of the most sensitive techniques for trace metal detection in food. ICH Q2(R2) (2023) provides the internationally harmonised framework — specificity, linearity, range, accuracy, precision, detection/quantitation limit and robustness — that is widely applied for elemental-impurity method validation.

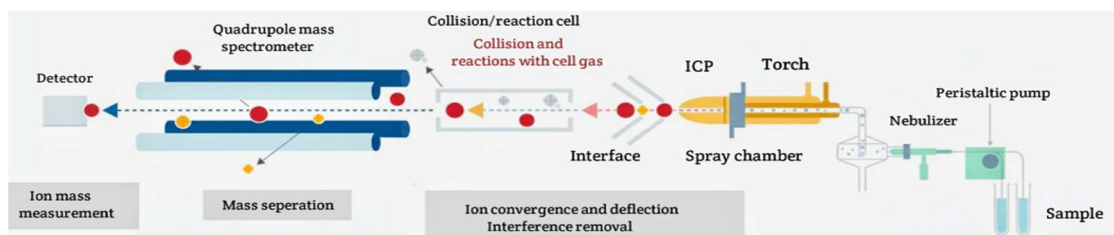
Although several ICP-MS methods have been reported for dietary supplements and food matrices, comprehensive validation specifically for nutraceutical formulations, encompassing all major validation parameters under ICH Q2(R1), remains limited. The present study therefore aimed to develop and fully validate a single ICP-MS method for the simultaneous quantification of ten elements (Cr, Ni, Cu, As, Se, Cd, Sn, Sb, Pb and Hg) in nutraceutical products, in accordance with ICH Q2(R1) guidelines, for application in routine quality control.

2. METHODOLOGY

2.1 Chemicals, reagents and reference standards

Certified single-element standard solutions (1000 mg/L) of chromium, nickel, copper, selenium, antimony, arsenic, tin, lead, cadmium and mercury were used, together with rhodium (Rh) and yttrium (Y) as internal standards (ISTD). Analytical-grade nitric acid (HNO_3) and hydrogen peroxide (H_2O_2) were used for microwave-assisted acid digestion, and deionised water was used throughout for dilution and preparation of standards and the diluent (2% v/v nitric acid in water).

2.2 Instrumentation and equipment



Analyses were performed on an Inductively Coupled Plasma Mass Spectrometer (ICP-MS) equipped with a quadrupole mass analyser, a collision/reaction cell (helium mode) and an electron-multiplier detector. Sample preparation employed a microwave digestion system, an analytical balance, a fume hood, a chiller, calibrated micropipettes (10–100 μL , 20–200 μL , 100–1000 μL , 1–5 mL), Class-A volumetric flasks (10, 25, 50 mL), polypropylene tubes (15, 50 mL) and Whatman No. 40 filter paper.

2.3 Preparation of calibration standards

From the 1000 mg/L primary stock of each metal, a 10 mg/L working stock was prepared by diluting 0.1 mL of standard to 10 mL with 2% nitric acid. A 1000 µg/L intermediate standard was prepared by diluting 2.5 mL of the 10 mg/L stock to 25 mL, and a 100 µg/L final working standard was prepared by diluting 2.5 mL of the intermediate standard to 25 mL. Serial dilution of the final working standard gave seven-point calibration curves spanning 0.5–100 µg/L for Cr, Ni, Cu, As, Se, Cd, Sn, Sb and Pb, and 0.5–25 µg/L for Hg (which was prepared as an independent stock series). A mixed Rh/Y internal-standard working solution (1 mg/L) was prepared similarly and added to all calibration standards and samples.

2.4 Sample preparation

Approximately 1.0 g of nutraceutical sample was accurately weighed into a microwave digestion vessel and treated with 5 mL concentrated HNO₃, 5 mL water and 1 mL H₂O₂, and allowed to stand briefly to minimise foaming. Digestion was carried out at 180–200°C for 45 minutes until a clear solution was obtained. After cooling, the digest was filtered through Whatman No. 40 filter paper, quantitatively transferred to a 50 mL polypropylene tube and made up to volume with distilled water. The Rh/Y internal-standard solution (10 µg/L each) was added to the digest immediately prior to ICP-MS analysis, and a reagent blank was processed identically (without sample) for background correction.

2.5 Matrix-spike (recovery) samples

To evaluate accuracy, standard solutions were spiked into the digested sample matrix at three levels — the limit of quantification (LOQ, 0.010 mg/kg), 2×LOQ (0.020 mg/kg) and 10×LOQ (0.10 mg/kg) — each in six replicates, processed and analysed identically to the unspiked test samples.

2.6 Method validation

The method was validated according to ICH Q2(R1) for the following parameters: specificity (freedom from spectral/matrix interference at the analyte m/z), linearity and range (seven-point calibration, acceptance: correlation coefficient $R \geq 0.99$ and back-calculated concentration within $\pm 20\%$ of the true value), limit of quantification (lowest spiked level giving acceptable accuracy and precision), accuracy/recovery (matrix spike recovery at LOQ, 2×LOQ and 10×LOQ; acceptance 70–120% recovery, $RSD \leq 20\%$), repeatability ($n = 6$ replicates, same day/analyst/instrument), intermediate precision/reproducibility (different day/analyst/instrument) and robustness (deliberate small variation of digestion time, acid concentration, nebuliser gas flow and plasma RF power).

3. RESULTS AND DISCUSSION

3.1 Specificity

Specificity was assessed by comparing the mean signal intensity of six reagent-matrix blanks against the lowest calibration level (LCL) for each analyte m/z. In all cases, mean blank intensities corresponded to well below the LCL, and no spectral interference was observed at the monitored isotopes for Cr, Ni, Cu, As, Se, Cd, Sn, Sb, Pb or Hg, confirming that the method is specific for the target analytes in the nutraceutical matrix (Table 1).

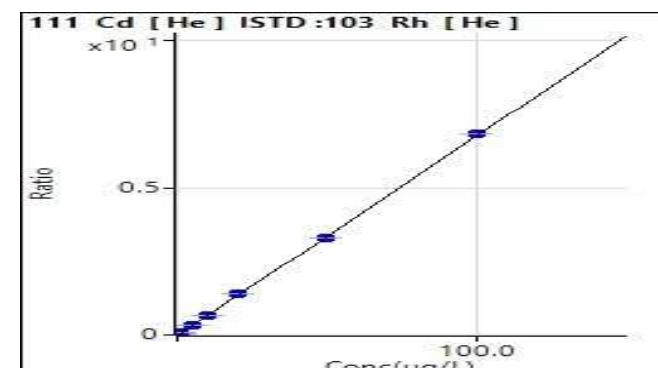
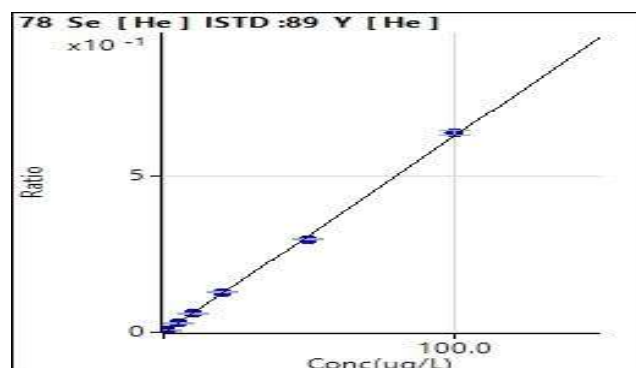
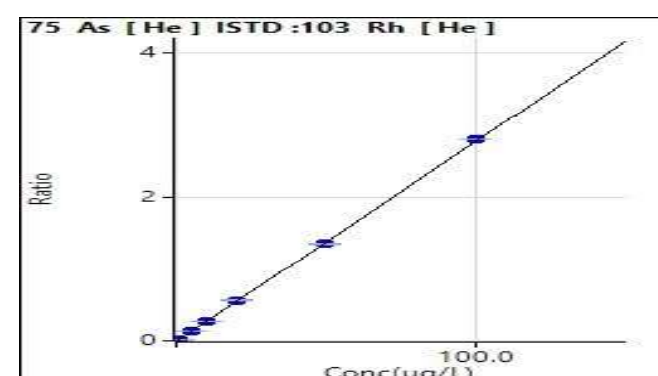
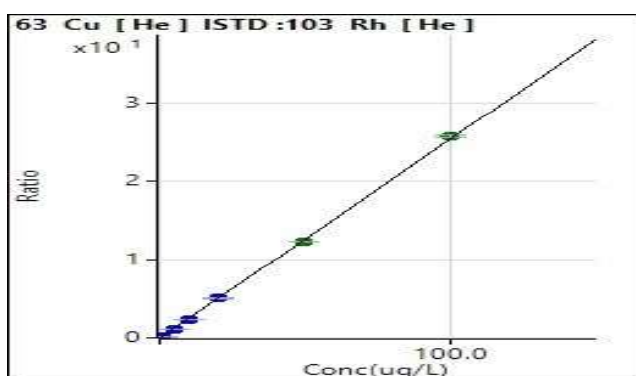
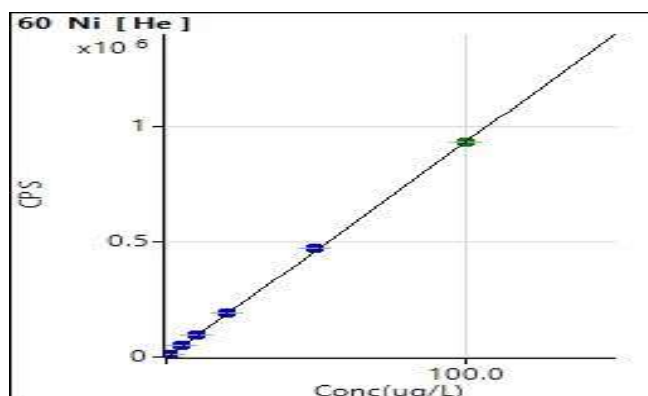
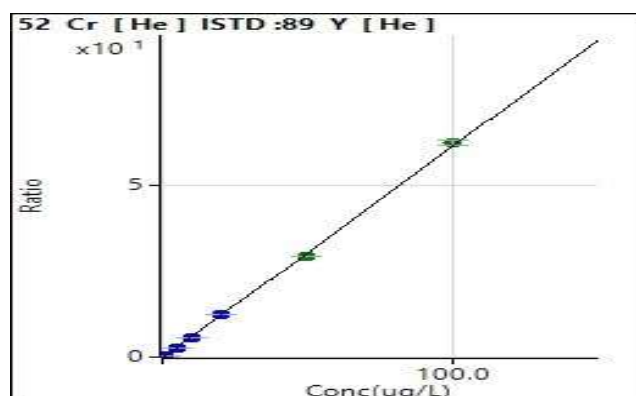
Table 1. Specificity — matrix-blank response versus lowest calibration level

Metal	Mean blank signal (cps)	Lowest cal. level signal (cps)	Blank as % of LCL	Interference
Chromium (Cr)	2681	20043	13	No interference
Nickel (Ni)	252	8304	3	No interference
Copper (Cu)	1653	28657	6	No interference
Arsenic (As)	124	2703	5	No interference

Metal	Mean blank signal (cps)	Lowest cal. level signal (cps)	Blank as % of LCL	Interference
Selenium (Se)	125	392	32	No interference
Cadmium (Cd)	74	5714	1	No interference
Tin (Sn)	4014	14182	28	No interference
Antimony (Sb)	489	16957	3	No interference
Lead (Pb)	604	5499	11	No interference
Mercury (Hg)	3383	61417	6	No interference

3.2 Linearity and range

Seven-point calibration curves (0.5–100 µg/L for Cr, Ni, Cu, As, Se, Cd, Sn, Sb, Pb; 0.5–25 µg/L for Hg) were prepared in 2% nitric acid and analysed in triplicate. Peak-area (or ISTD-normalised) response versus concentration was fitted by linear regression. Correlation coefficients (R^2) for all ten elements ranged from 0.9980 to 1.0000, exceeding the ICH acceptance criterion of $R \geq 0.99$, and back-calculated concentrations at each level deviated by less than $\pm 20\%$ from the nominal value (except at the lowest calibrator for a small number of analytes), confirming excellent linearity across the validated range (Table 2).



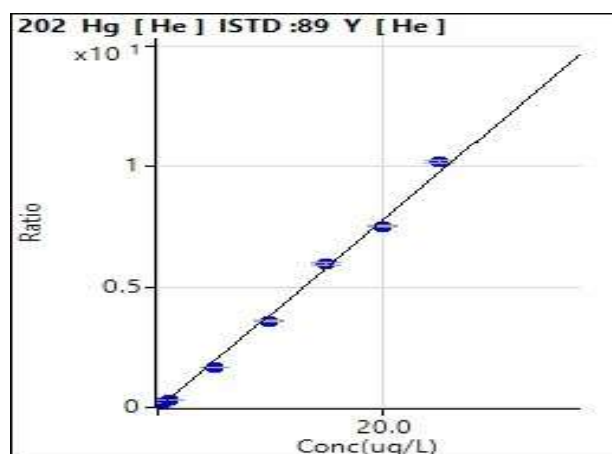
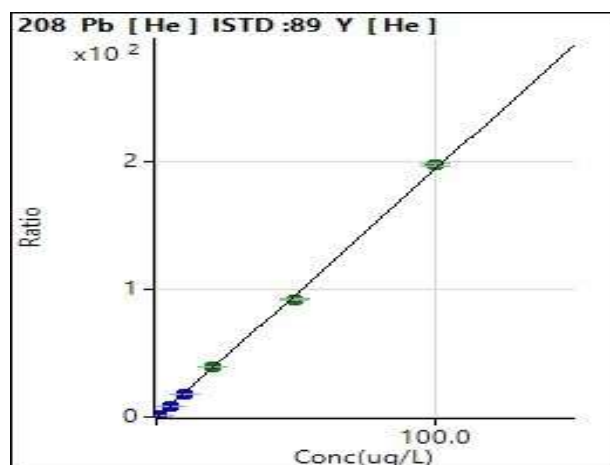
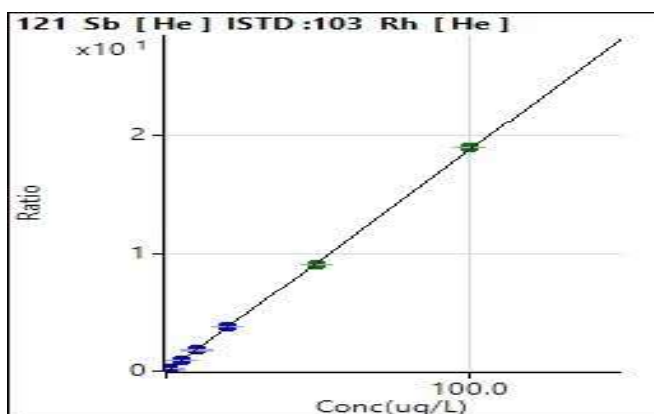
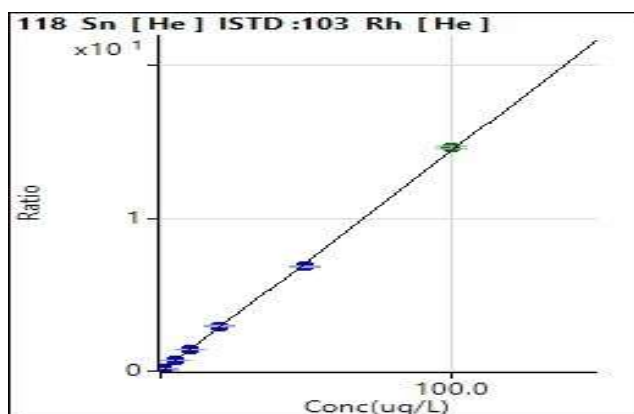


Table 2. Linearity range and correlation coefficient for each metal

Metal	Calibration range ($\mu\text{g/L}$)	Correlation coefficient (R^2)
Chromium (Cr)	0.5 – 100	0.9996
Nickel (Ni)	0.5 – 100	1.0000
Copper (Cu)	0.5 – 100	0.9997
Arsenic (As)	0.5 – 100	0.9998
Selenium (Se)	0.5 – 100	0.9995
Cadmium (Cd)	0.5 – 100	0.9998
Tin (Sn)	0.5 – 100	0.9996
Antimony (Sb)	0.5 – 100	0.9998
Lead (Pb)	0.5 – 100	0.9995
Mercury (Hg)	0.5 – 25	0.9980

3.3 Limit of quantification (LOQ)

The LOQ, established as the lowest spiked concentration (0.010 mg/kg) giving acceptable accuracy and precision, was confirmed for all analytes. Percentage RSD values ($n = 6$) were below 2.5% for nine of the ten elements; selenium showed a higher variability (%RSD 23.8%) at this low concentration, reflecting its comparatively higher background and lower sensitivity by ICP-MS, and this should be considered when reporting selenium results close to the LOQ (Table 3).

Table 3. Limit of quantification (spiked at 0.010 mg/kg)

Metal	Mean found (mg/kg)	%RSD (n = 6)
Chromium (Cr)	0.0097	1.16
Nickel (Ni)	0.0101	2.21
Copper (Cu)	0.0098	0.99
Arsenic (As)	0.0099	1.51
Selenium (Se)	0.0098	0.99
Cadmium (Cd)	0.0098	0.99
Tin (Sn)	0.0096	1.32
Antimony (Sb)	0.0096	0.63
Lead (Pb)	0.0093	0.53
Mercury (Hg)	0.0092	0.97

3.4 Accuracy (recovery)

Recovery, determined by matrix spiking at LOQ, 2×LOQ and 10×LOQ (six replicates per level), ranged from 90.8% to 102.4% at the LOQ level, 90.9% to 98.9% at the 2×LOQ level, and 94.3% to 100.9% at the 10×LOQ level, with %RSD values generally below 10% (Table 4, Section 4). All values met the pre-defined acceptance criteria (recovery 70–120%, RSD ≤ 20%), confirming the accuracy of the method across the working range and the absence of significant matrix effects.

3.5 Precision

Repeatability (intra-day precision, n = 6) gave %RSD values of 0.4–15.3% across the three spiking levels, with the highest variability again observed for selenium at the LOQ level. Intermediate precision (inter-day/analyst reproducibility) gave %RSD values of 0.5–12.1%, and recoveries of 87.0–112.8%, still within the acceptance range, though modestly higher variability was noted for several analytes (notably Se, Cu and Pb) at the lowest spiking level, which is expected given the proximity to the LOQ (Table 5 and Table 6, Section 4).

3.6 Robustness

Small, deliberate variations in digestion time, acid concentration, nebulizer gas flow rate and plasma RF power did not significantly affect method performance. Recoveries at the three spiking levels remained within 81–117%, and %RSD values were generally below 8% (with a small number of exceptions at the LOQ level), indicating that the method is robust to minor operational variation typical of routine laboratory use (Table 7, Section 4).

3.4.1 Accuracy / recovery data

Table 4. Recovery of spiked metals at LOQ, 2×LOQ and 10×LOQ levels (n = 6 per level)

Metal	LOQ level (0.010 mg/kg)			2×LOQ level (0.020 mg/kg)			10×LOQ level (0.10 mg/kg)		
	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery
Chromium	0.0098	2.01	98.43	0.0194	1.87	96.87	0.1009	0.73	100.87
Nickel	0.0102	2.27	102.35	0.0192	1.49	96.05	0.0959	1.06	95.87
Copper	0.0098	1.37	97.91	0.0189	1.20	94.42	0.0954	0.76	95.42
Arsenic	0.0099	1.53	99.37	0.0198	2.07	98.91	0.0981	0.54	98.06
Selenium	0.0092	10.13	91.64	0.0196	6.11	97.79	0.0967	5.34	96.68
Cadmium	0.0098	0.58	98.48	0.0197	0.88	98.33	0.0975	0.79	97.49

Metal	LOQ level (0.010 mg/kg)			2×LOQ level (0.020 mg/kg)			10×LOQ level (0.10 mg/kg)		
	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery
Tin	0.0096	1.08	95.88	0.0195	2.45	97.30	0.0959	0.94	95.91
Antimony	0.0096	1.14	96.49	0.0194	0.97	97.19	0.0966	0.82	96.63
Lead	0.0093	0.87	93.31	0.0188	1.28	93.83	0.0943	0.65	94.34
Mercury	0.0091	1.51	90.83	0.0182	1.47	90.94	0.0962	1.68	96.23

Table 5. Repeatability (intra-day precision) at LOQ, 2×LOQ and 10×LOQ levels (n = 6 per level)

Metal	LOQ level (0.010 mg/kg)			2×LOQ level (0.020 mg/kg)			10×LOQ level (0.10 mg/kg)		
	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery
Chromium	0.0095	3.84	95.21	0.0194	1.09	97.02	0.1002	3.76	100.19
Nickel	0.0099	4.08	99.22	0.0195	1.73	97.68	0.0958	3.40	95.83
Copper	0.0096	3.68	95.55	0.0192	0.80	95.77	0.0963	3.54	96.29
Arsenic	0.0097	3.30	97.09	0.0199	0.59	99.26	0.0903	5.45	90.27
Selenium	0.0083	15.32	82.72	0.0205	5.12	102.61	0.0914	5.31	91.36
Cadmium	0.0096	3.47	95.93	0.0195	0.92	97.48	0.0931	5.30	93.10
Tin	0.0095	5.02	94.75	0.0193	1.53	96.62	0.0907	5.53	90.70
Antimony	0.0095	2.32	95.42	0.0194	0.86	96.83	0.0899	5.68	89.87
Lead	0.0092	3.13	91.70	0.0194	0.41	96.98	0.0971	4.06	97.09
Mercury	0.0101	6.35	100.80	0.0181	1.22	90.57	0.0922	8.35	92.25

Table 6. Intermediate precision (reproducibility, inter-day/analyst) at LOQ, 2×LOQ and 10×LOQ levels (n = 6 per level)

Metal	LOQ level (0.010 mg/kg)			2×LOQ level (0.020 mg/kg)			10×LOQ level (0.10 mg/kg)		
	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery
Chromium	0.0103	7.90	102.93	0.0198	1.19	99.17	0.1024	0.55	102.45
Nickel	0.0113	5.59	112.75	0.0199	0.86	99.51	0.0969	0.54	96.93
Copper	0.0111	10.15	110.95	0.0194	1.07	97.08	0.0974	0.67	97.39
Arsenic	0.0090	7.64	90.18	0.0193	2.06	96.60	0.0966	0.52	96.59
Selenium	0.0087	9.27	86.98	0.0176	8.79	88.16	0.0909	4.94	90.94
Cadmium	0.0099	9.70	98.72	0.0193	1.15	96.32	0.0969	0.88	96.95
Tin	0.0093	8.61	93.39	0.0190	1.28	95.24	0.0951	0.55	95.08
Antimony	0.0091	7.94	90.98	0.0187	1.09	93.65	0.0951	0.73	95.07
Lead	0.0112	12.06	112.39	0.0203	0.50	101.63	0.0974	3.63	97.43
Mercury	0.0103	11.70	102.83	0.0174	2.23	86.86	0.0942	2.58	94.22

Table 7. Robustness at LOQ, 2×LOQ and 10×LOQ levels (n = 6 per level)

Metal	LOQ level (0.010 mg/kg)			2×LOQ level (0.020 mg/kg)			10×LOQ level (0.10 mg/kg)		
	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery	Conc. (mg/kg)	%RSD	%Recovery
Chromium	0.0091	2.67	90.86	0.0196	1.77	97.96	0.0977	5.98	97.67
Nickel	0.0111	3.20	110.58	0.0202	3.65	101.11	0.0975	4.64	97.50
Copper	0.0104	1.42	104.34	0.0202	3.74	100.77	0.0970	4.79	97.00
Arsenic	0.0086	0.97	86.02	0.0194	1.00	97.15	0.0961	4.79	96.13
Selenium	0.0090	15.89	90.41	0.0195	6.27	97.33	0.0933	6.10	93.28
Cadmium	0.0092	2.15	91.85	0.0196	1.74	98.21	0.0975	4.83	97.46
Tin	0.0085	2.37	85.44	0.0189	1.86	94.28	0.0949	4.53	94.87
Antimony	0.0084	1.98	84.27	0.0189	1.31	94.46	0.0953	4.80	95.30
Lead	0.0117	2.05	116.94	0.0207	11.22	103.34	0.0984	4.77	98.40
Mercury	0.0081	7.92	81.09	0.0175	6.70	87.72	0.0867	6.22	86.73

Acceptance criteria applied throughout: percentage recovery 70–120%; %RSD ≤ 20%; correlation coefficient (R) ≥ 0.99; back-calculated concentration within ±20% of the true value.

4. CONCLUSION

A microwave-assisted acid-digestion ICP-MS method, using Rh and Y as internal standards, was successfully developed and validated for the simultaneous determination of ten elements — Cr, Ni, Cu, As, Se, Cd, Sn, Sb, Pb and Hg — in nutraceutical products. The method demonstrated excellent specificity with no spectral interference, linear response ($R^2 = 0.9980$ – 1.0000) across the validated ranges, a working LOQ of 0.010 mg/kg for all analytes, and acceptable accuracy (70–120% recovery) and precision (RSD generally ≤ 20%) at LOQ, 2×LOQ and 10×LOQ spiking levels, in full compliance with ICH Q2(R1) acceptance criteria. The method was also robust to small deliberate changes in digestion time, acid strength, nebulizer gas flow and plasma power. These results support the use of this validated ICP-MS method as a rapid, sensitive, accurate and reproducible tool for routine quality-control screening of toxic and trace elemental impurities in nutraceutical formulations, in support of regulatory compliance (e.g., ICH Q3D, WHO/FAO, FDA and FSSAI requirements) and consumer safety.

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REFERENCES

1. Pham, T. H., Nguyen, T. N., Minh, T. N., Bui, M. Q., Nguyen, H. X., & Nguyen, T. Q. (2025). *Application of ICP-MS for Quantifying Trace Metals in Functional Foods*. <https://doi.org/10.20944/preprints202506.1090.v1>
2. Chebli, A. I., Reffai, M. A., Amziane, A., Shalabi, E., Khan, H. R., Djerroud, D., & Zebbiche, Y. (2023). *Development and analytical validation of a method for the determination of lead, cadmium, mercury and their isotopes in milk, honey, meat, fish and eggs by icp-ms*. <https://doi.org/10.26434/chemrxiv-2023-2ctkf>
3. Kwon, S.-Y., Kim, Y.-I., Kim, Y.-K., Lee, Y.-B., & Mok, J. H. (2024). Microwave-assisted Sample Preparation for Screening of Heavy Metal Elements in Food Additives by ICP-MS. *Lebensmittel-Wissenschaft & Technologie*, 208, 116708. <https://doi.org/10.1016/j.lwt.2024.116708>
4. Jiang, Q.-T., Zeng, L., Ma, J., Peng, L.-N., Li, W.-L., Ding, Y., & Li, J. (n.d.). *Determination Of Soluble Heavy Metals InBaiziYangxin Tablets By Inductively Coupled Plasma Mass Spectrometry With Bionic Extraction And Microwave Digestion Technology*. <https://doi.org/10.11895/j.issn.0253.3820.150927>

5. Wen, H.-M., Chen, X.-H., Dong, T.-X., Zhan, H.-Q., & Bi, K.-S. (2006). Determination of heavy metals in four traditional Chinese medicines by ICP-MS. *China Journal of Chinese Materia Medica*, 31(16), 1314–1317. <https://pubmed.ncbi.nlm.nih.gov/17061547/>
6. Rodríguez Pérez, P., Rojas, R., & de la Menta Ballesteros, M. (2016). Fine tuning and validation of an analytical method for determining heavy metals in food samples by ICP-MS technique. 5, 33. <https://www.upo.es/revistas/index.php/biosaia/article/download/1822/1489>
7. Huang, W. (2012). Contents and Dissolutions of 8 Heavy Metals in Before and After Decoctions of Traditional Chinese Medicines by ICP-MS. *Chinese Journal of Spectroscopy Laboratory*.
8. Naz, M., Ahmed, M., Aftab, F., Ali, M., Sanaullah, M., Ahmad, W., Zargar, S., Khalid, K., Wani, T. A., & Zargar, S. (2024). Contamination of trace, non-essential/heavy metals in nutraceuticals/dietary supplements: A chemometric modelling approach and evaluation of human health risk upon dietary exposure. *Food and Chemical Toxicology*, 190, 114806. <https://doi.org/10.1016/j.fct.2024.114806>
9. Nelson, J., Jones, C., Heckle, S., & Anderson, L. (n.d.). Determination of Heavy Metals in a Variety of Cannabis and Cannabis-Derived Products, First Action 2021.03. <https://doi.org/10.1093/jaoacint/qsab173>
10. YANG, X., HAN, W., LIU, H., & WAN, X. (n.d.). Determination of Heavy Metals in Fructus Akebiae and Fructus Akebiae Extracts by ICPMS with Microwave Digestion. <https://doi.org/10.3969/j.issn.1008-0805.2011.08.095>
11. HE, P., SUN, W., SUN, Y., CAO, F., & HANG, T. (n.d.). Determination of 18 Heavy Metals in Salvia Miltiorrhiza and Panax Notoginseng by ICP-MS. <https://doi.org/10.3969/j.issn.1001-1528.2011.12.024>
12. Cadar, O., Miclean, M., Tanaselia, C., & Roman, C. (2013). Method for multi-element determination of heavy metals in food samples by ultrasonic extraction followed by inductively coupled plasma mass spectrometry.
13. Gregar, F., Grepl, J., Milde, D., & Pluháček, T. (2024). Direct elemental analysis of plant oils by inductively coupled plasma mass spectrometry: Simple sample dilution combined with oxygen introduction into the plasma. *Food Chemistry*. <https://doi.org/10.1016/j.foodchem.2024.139010>
14. Yu, G. (2011). Determination of lead,arsenic,cadmium,chromium, nickel in sea products by inductively coupled plasma mass spectrometry with microwave digestion. *Science and Technology of Food Industry*. https://en.cnki.com.cn/Article_en/CJFDTotat-SPKJ201107111.htm
15. JIN, H., Lü, X., LI, L., LIU, H., & LI, T. (n.d.). Determination of 6 Heavy Metals in Meat and Meat Products by Inductively Coupled Plasma-Mass Spectrometry after Microwave Digestion. <https://doi.org/10.7506/rlyj1001-8123-201504007>
16. Liu, Z., Cao, L., Chen, H., Xiao, L., & Ma, J. (n.d.). Detection of Trace Metal Elements in Potassium Dihydrophate with ICP-MS(CCT) Method. <https://doi.org/10.13822/j.cnki.hxsj.2015.09.009>
17. Liu, Z., Cao, L., Chen, H., Xiao, L., & Ma, J. (n.d.). Detection of Trace Metal Elements in Potassium Dihydrophate with ICP-MS(CCT) Method. <https://doi.org/10.13822/j.cnki.hxsj.2015.09.009>
18. Zbinden, P., & Andrey, D. (1998). Determination of Trace Element Contaminants in Food Matrices Using a Robust, Routine Analytical Method for ICP-MS. *Atomic Spectroscopy*, 19(6), 214–219.
19. Ghuniem, M. M., Souaya, E. R., & Khorshed, M. A. (2019). Optimization and Validation of an Analytical Method for the Determination of Some Trace and Toxic Elements in Canned Fruit Juices Using Quadrupole Inductively Coupled Plasma Mass Spectrometer. *Journal of AOAC International*, 102(1), 262–270. <https://doi.org/10.5740/JAOACINT.18-0022>
20. Parimi, R., Gupta, T., Pravallika, K. E., & Ravindran, S. (2023). Analytical Method Development and Validation of Iron, Arsenic, Cadmium, Mercury and Lead Content in Sunset Yellow by Inductively Coupled Plasma Mass Spectrometry (Icp-MS). *Journal of Advanced Zoology*, 44(S6), 258–264. <https://doi.org/10.17762/jaz.v44is6.2087>
21. Gupta, P. C., Elanchezhian, A., Shukla, S. C., Sengar, A. S., Saha, A., Surendran, R., Awasthi, N. P., Prasanth, K. P., Jacob, S., & Saxena, S. K. (2019). Development, validation, and accreditation of a method for the determination of 75As, 111Cd, 201Hg, and 208Pb in Cephalopods using inductively coupled plasma mass spectrometry (ICP-MS). 1(4), 1–7. <https://doi.org/10.1007/S42452-019-0294-X>
22. Dubascoux, S., Nicolas, M., Fragniere Rime, C., Richoz Payot, J., & Poitevin, E. (2015). Simultaneous Determination of 10 Ultratrace Elements in Infant Formula, Adult Nutritionals, and Milk Products by ICP/MS After Pressure Digestion: Single-Laboratory Validation. *Journal of AOAC International*, 98(4), 953–961. <https://doi.org/10.5740/JAOACINT.14-276>
23. Tang, J., Zhang, Y., Chen, S., Li, C., Shu, F., Kong, X., & Lin, L. (2014). Method for determining traces of mercury, cadmium, lead and arsenic in food by inductively coupled plasma mass spectrometry (ICP-MS).
24. GONG, H. (n.d.). Determination of heavy metals and harmful elements in throat-clearing buccal tablets by ICP-MS. <https://doi.org/10.7539/j.issn.1672-2981.2015.11.024>
25. Shchukin, V. M., Zhigilei, E. S., Erina, A. A., Shvetsova, Yu. N., Kuz'mina, N. E., & Luttseva, A. I. (2020). Validation of an ICP-MS Method for the Determination of Mercury, Lead, Cadmium, and Arsenic in Medicinal Plants and Related Drug Preparations. *Pharmaceutical Chemistry Journal*, 54(9), 968–976. <https://doi.org/10.1007/S11094-020-02306-8>

26. Oltulu, Ç., & Daşman, M. (2023). Icp-ms ile bazı gıda takviyelerindeki toksik metallerin belirlenmesi. *Ankara Üniversitesi Eczacılık Fakültesi Dergisi*. <https://doi.org/10.33483/jfpau.1279257>
27. Lorenc, W., Hané, A., Sajnog, A., & Barakiewicz, D. (2022). Lc/icp-ms and complementary techniques in bespoke and nontargeted speciation analysis of elements in food samples. *Mass Spectrometry Reviews*, 41(1), 32–50. <https://doi.org/10.1002/MAS.21662>
28. Bu, K., Cizdziel, J. V., & Reidy, L. (2012). Analysis of herbal supplements for selected dietary minerals and trace elements by laser ablation- and solution-based ICPMS. *Analytical Abstracts*, 106(1), 244–249.
29. Foglio, L., & Davidowski, L. (2010). The Determination of Lead in Calcium-Based Antacid and Dietary Supplements Using the NexION 300 ICP-MS System to Comply With the State of California's Proposition 65 Legislation. *Atomic Spectroscopy*, 31(5), 154–158.
30. Lo Dico, G. M., Cammilleri, G., Macaluso, A., Vella, A., Giangrosso, G., Vazzana, M., & Ferrantelli, V. (2015). Simultaneous Determination of As, Cu, Cr, Se, Sn, Cd, Sb and Pb Levels in Infant Formulas by ICP-MS after Microwave-Assisted Digestion: Method Validation. *Journal of Environmental and Analytical Toxicology*, 5(6), 1–5. <https://doi.org/10.4172/2161-0525.1000328>