International Journal of Chemistry Research

Online ISSN- 0976-5689 Vol 10, Issue 1, 2026

Review Article

TRACING ELEMENTS WITH PRECISION: A REVIEW OF INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY (ICP-MS)

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Received: 12 Oct 2025 Revised and Accepted: 24 Oct 2025

ABSTRACT

Inductively Coupled Plasma–Mass Spectrometry (ICP-MS) has established itself as a preeminent technique in analytical science, providing powerful capabilities for trace element and isotope analysis due to its outstanding sensitivity, accuracy, and multi-element detection. This review offers a comprehensive overview of ICP-MS, covering its fundamental principles and instrumentation. The technique functions by ionizing samples in an argon plasma and separating ions according to their mass-to-charge ratios, achieving detection limits at the parts-per-trillion level. ICP-MS finds applications across diverse areas, including environmental monitoring, food authentication, pharmaceutical and drug testing, forensic investigations, and biomedical research on toxic elements and metal bioaccumulation. Its capacity for isotopic ratio determination and species-specific analysis provides valuable insights into contamination pathways, metabolic mechanisms, material provenance, and cellular heterogeneity. By combining high sensitivity with precision and versatility, ICP-MS continues to advance modern analytical science, enabling comprehensive, high-throughput elemental and isotopic characterization across environmental, industrial, biomedical and life science domains.

Keywords: Inductively coupled plasma mass spectrometry, Advances, Future scope, Trace element analysis, Laser ablation, Isotope ratio analysis

DOI: http://dx.doi.org/10.22159/ijcr.2026v10i1.321 Journal homepage: https://ijcr.info/index.php/journal

INTRODUCTION

Mass spectrometry (MS) is an effective technique for identifying and measuring many clinically important analytes [1]. Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is a specialized form of mass spectrometry (MS) that offers exceptional sensitivity and precision for trace element analysis, making it an effective technique for identifying and measuring many clinically important analytes [2]. While traditional methods such as atomic absorption and atomic emission spectroscopy remain in use in some laboratories, a gradual transition toward ICP-MS has occurred, especially over the past decade [3]. ICP-MS has been increasingly utilized across various biomedical disciplines for the quantification of proteins, nanoparticles, and other biomolecular substances [4]. ICP-MS has also proven indispensable in studying toxic element–related health crises such as mercury-induced neurodegeneration, organotin toxicity, and arsenic poisoning. With its exceptional sensitivity and quantification accuracy, it continues to expand in life sciences, serving as the preferred method for elemental speciation of metals, metalloids, and organometallic compounds [5]. Since the development of chromatography-coupled ICP-MS, various compounds and elements have been studied to assess species-specific factors such as toxicity, bioavailability, translocation, bioaccumulation, biomagnification, degradation, fate, and physiological impact [6]. Recent innovations in laser ablation ICP-MS (LA-ICP-MS) provide powerful tools for high spatial resolution analysis of trace elements at the cellular and tissue levels, enabling researchers to explore cellular heterogeneity and detailed patterns of elemental distribution [5, 7]. This review analyzes studies published between 1988 to 2025 sourced from Scopus, Research Gate, Google Scholar, and the Directory of Open Access Journals (DOAJ). It aims to present a thorough overview of ICP-MS analytical techniques, focusing on their applications, recent advancements, and limitations. The review also seeks to outline the core principles of these techniques and underscore their significant contributions to scientific research and various applications.

Principles and workflow of ICP-MS

ICP-MS allows sensitive elemental analysis in various samples, ranging from pure chemicals to complex digests. Maintaining low detection limits depends on minimizing contamination and spectral interferences, which requires clean work environments, appropriate reagent choice, and careful sample handling. This article presents five key strategies to control contamination and enhance detection sensitivity [8]. Fig. 1 Shows a schematic representation showing the sequential process of sample introduction, ionization in the plasma, ion extraction, mass separation, and detection for elemental analysis.

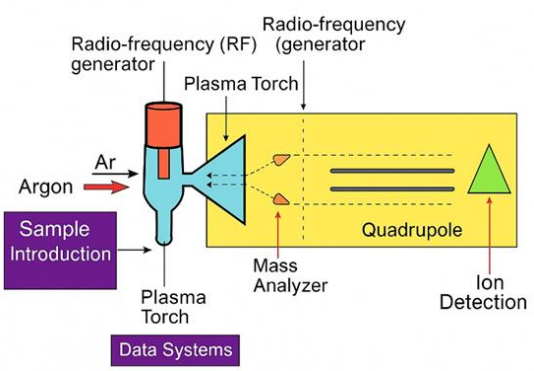

Fig. 1: Workflow of ICP-MS

Sample Introduction

Liquid samples are introduced into the nebulizer via a peristaltic pump or self-aspiration to form a fine aerosol. Nebulizer type is chosen based on sample viscosity, volume, and purity [9, 10].

Radio-frequency (RF) generator

The radio-frequency (RF) generator in ICP-MS provides continuous energy (~1.5 kW) to sustain the plasma. It delivers an RF signal through a load coil wrapped around the ICP torch. Seed electrons from a spark source, such as a Tesla coil, ionize argon atoms within the torch gas flows. These ions collide with other argon atoms, initiating a cascade of ionization that forms the plasma. The RF energy maintains this plasma, enabling the ionization of sample atoms for analysis [9].

Plasma torch

In ICP-MS, a quartz plasma torch with concentric argon gas flows generates a high-temperature plasma (≈6000–10,000 K) using an RF field. This plasma atomizes and ionizes the sample, producing ions for mass analysis [9-11].

Mass analyzer

In ICP-MS, ions pass through a high-vacuum region and are separated by a mass analyzer, typically quadrupole or magnetic sector. Quadrupoles measure sequentially and are favored for routine use due to ease of operation, while magnetic sector analyzers capable of sequential or simultaneous measurement offer higher sensitivity for specialized applications [11].

Ion detection

After mass separation, ions are detected and amplified, typically using Faraday cups or electron multipliers. Faraday cups generate a measurable current when high-velocity ions transfer charge to the cup, which is amplified for detection. They require large ion currents, making them unsuitable for single-ion detection, but offer high stability and are ideal for precise isotope ratio measurements, especially in multicollector instruments [9].

Data system

A computer and specialized software that control the ICP-MS instrument, acquire ion signal data, process the results, and perform quantitative and qualitative analysis [12].

Applications of ICP-MS across various fields

Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is a precise analytical technique used to detect and measure trace elements and isotopes in many sample types, with uses in environmental science, food safety, medicine, and materials research [10].

ICP-MS for environmental science and industrial applications

Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is a highly sensitive analytical method extensively applied for trace and ultra-trace elemental analysis in both environmental and industrial contexts. It allows accurate detection and quantification of metals and metalloids in various matrices such as water, soil, airborne particles, and industrial discharges, aiding in pollution assessment and quality assurance. Owing to its exceptional sensitivity, multi-element detection, and isotopic measurement capabilities, ICP-MS has become an essential tool for monitoring environmental pollutants and maintaining industrial standards [13].

Gramowska *et al.* [14] analyzed water samples from two lakes connected by a series of small reservoirs to compare contamination levels. Using ICP-MS, they measured eight elements and applied statistical analysis to evaluate water self-purification. Results showed significantly lower element concentrations in Malta Lake compared to Swarzedzkie Lake, highlighting the effectiveness of natural purification processes along the flow path.

W. Sun *et al.* [15] presented ICP-MS as a promising tool for environmental monitoring, detailing its capabilities in analyzing soil and water samples. The study also addressed interference factors, including isobaric, oxide, double charge, and polyatomic ions, and discussed prospects for advancing ICP-MS technology.

K. Flores *et al.* [16] reviewed how engineered nanomaterials increasingly enter the environment through consumer products and undergo transformations such as agglomeration and dissolution. They highlighted the role of ICP-MS, especially SP-ICP-MS, in studying nanoparticle behavior and toxicity in environmental and biological contexts.

Syarbaini [17] investigated artificial radionuclides in the environment, particularly fallout from historic nuclear tests. Due to their low concentrations, traditional methods are time-consuming and require large samples. ICP-MS provides a rapid, sensitive, and efficient alternative for multi-element analysis without extensive sample preparation.

Hoffmann *et al.* [18] explored laser sampling ICP-MS for trace element quantification in environmental matrices. They addressed challenges such as signal stability, sample representativity, and calibration, applying the technique to plant ash and oak tree rings.

Mansor *et al.* [19] applied single-particle ICP-MS (spICP-MS) to study the composition, size distribution, and aggregation of environmental nanoparticles and colloids. They demonstrated its use in analyzing microplastic and magnetite aggregation, arsenic mobility, and iron–carbon colloids, providing guidelines for environmental sample analysis.

Pröfrock and Prange [20] present a comprehensive review of the recent advancements and capabilities of inductively coupled plasma mass spectrometry (ICP-MS), particularly when combined with various separation techniques. The paper emphasizes how these hyphenated ICP-MS approaches have become essential for quantitative analysis in both environmental and bioanalytical contexts. Over recent years, significant technical developments such as improved sensitivity, better interference reduction, enhanced detection limits, and faster analysis have greatly expanded ICP-MS's versatility and application range. The authors highlight that these advancements have positioned ICP-MS as one of the most powerful and adaptable tools for elemental quantification.

I. Guagliardi *et al.* [21] compared X-ray fluorescence (XRF) and inductively coupled plasma mass spectrometry (ICP-MS) for detecting potentially toxic elements (PTEs) in soil, including Strontium (Sr), Nickel (Ni), Chromium (Cr), Vanadium (V), Arsenic (As), Zinc (Zn), and Lead (Pb). Results showed significant differences between methods for Sr, Ni, Cr, V, As, and Zn, with Pb showing minor variation. Correlation was strong for Ni and Cr,

but high variability for Zn and Sr limited comparability. XRF tended to underestimate V concentrations. The study highlights that method choice should consider detection limits, sample properties, and accuracy to ensure reliable contamination assessment.

M. Popp *et al.* [22] highlighted the growing use of inductively coupled plasma mass spectrometry (ICP-MS) for elemental speciation in environmental analysis, owing to its extremely low detection limits, wide linear range, multi-element capability, and compatibility with isotope dilution mass spectrometry (IDMS). The two primary approaches involve coupling ICP-MS with high-performance liquid chromatography (HPLC) or gas chromatography (GC). Traditionally applied to metals and metalloids such as tin (Sn), mercury (Hg), and arsenic (As), ICP-MS speciation now also includes elements like phosphorus (P), sulfur (S), bromine (Br), and iodine (I). Advances such as isotope dilution analysis and isotopically labeled species-specific standards have further enhanced ICP-MS applications, enabling more precise and comprehensive environmental studies.

B. Pranaityte *et al.* [23] developed a sector field high-resolution inductively coupled plasma mass spectrometry (ICP-MS) method to measure trace metals cadmium (Cd), chromium (Cr), copper (Cu), nickel (Ni), and lead (Pb) in textiles following microwave-assisted acidic digestion at 300 °C for 28 min. Spectral interferences were identified and eliminated, achieving detection limits from 0.5×10^{-11} g/g (Pb-208) to 8.5×10^{-11} g/g (Cd-110). The method, validated with certified reference materials, demonstrated high accuracy when applied to textile samples using standard addition calibration.

M. Horn, [24] stated that contamination in the semiconductor industry poses a significant challenge in integrated circuit production. With ongoing miniaturization, even trace amounts of metal contamination can adversely affect circuits. Due to its exceptional detection limits, ICP-MS is extensively used in this industry. Its primary applications include analyzing metals and semi-metals in deionized water, process chemicals, and wafer surfaces. Key challenges involve achieving the required detection limits, which are often constrained by contamination during sample preparation and instrument background interference.

ICP-MS for food science applications

Food fraud poses serious threats to both public health and the economy, driven by growing food demand and practices like substitution and mislabeling for profit. To address this, a multidisciplinary field has emerged to verify food authenticity and trace its origin. Among various analytical tools, Inductively Coupled Plasma Mass Spectrometry (ICP-MS) stands out for its high precision and sensitivity in determining the elemental composition and geographical origin of food products [25].

K. Loeschner *et al.* [26] highlighted that nanomaterials (NMs), valued for their unique nanoscale properties, are increasingly used in foods, additives, and packaging. However, gaps in understanding their behavior, bioaccumulation, and toxicity call for more extensive research. Conventional analytical methods offer limited data due to low throughput and restricted measurement ranges, making complementary techniques essential. Single particle inductively coupled plasma mass spectrometry (spICP-MS) has emerged as a powerful, high-throughput tool for analyzing nanoparticle size, concentration, and transformation in food-related studies.

M. Chudzinska and D. Baralkiewicz [27] analyzed 140 Polish honey samples honeydew, buckwheat, and rapecollected from 16 regions to determine 15 elemental concentrations using ICP-MS. Chemometric methods, including Linear Discriminant Analysis (LDA) and Classification and Regression Trees (CandRT), were applied to classify samples by type and origin. The analysis achieved complete separation by honey type with 100% accuracy using LDA, while classification by geographical origin showed more variability among the different honey types.

H. M. Crews *et al.* [28] investigated the accurate measurement of low-level lead in foods, such as dried milk and wine, using ICP-MS combined with standard additions and isotope dilution analysis (IDA). IDA, which measures isotopes separately and calculates concentrations from fortified isotopes, proved precise for determining lead at around 10 ng/g despite matrix effects that limit traditional atomic absorption methods. Comparison of scanning versus peak-hopping modes showed scanning provided better precision, though peak-hopping was faster. The study demonstrated that ICP-MS with IDA allows reliable quantification of lead for nutritional, metabolic, and geographical origin studies, with results validated against standard addition methods.

F. Ferraris *et al.* [29] developed an ICP-MS method to determine total titanium in foods and supplements following microwave-assisted acid digestion. The study optimized factors affecting accuracy, including acid composition and spectral interferences, resolved via ICP-MS/MS. Method validation demonstrated reliable detection, while single-particle ICP-MS (spICP-MS) was used to identify TiO_2 particles. Together, these approaches provide an effective strategy for screening and confirming the absence of E 171 (titania) in food products.

T. I Todorov and P. J. Gray [30] presented an ICP-MS method for measuring iodine in diverse food samples and reference materials using alkaline extraction. They determined that at least 3% 2-propanol was required to stabilize the iodine-to-internal-standard ratio. The method achieved a limit of quantification (LOQ) of 36 ng/g in solid foods. Validation with seven standard reference materials and 21 fortified foods demonstrated good precision (2–7% RSD) and recoveries of 81–119%, with SRM accuracies ranging from 85–105%, including samples fortified at 50% of the LOQ.

E. P. Nardi *et al.* [31] presented a straightforward inductively coupled plasma mass spectrometry (ICP-MS) method for quantifying sixteen elements in various food samples. Between 100–250 mg of powdered food was digested in a Teflon vessel with 4 ml of 20% nitric acid (HNO_3) and 2 ml of hydrogen peroxide (H_2O_2) using microwave-assisted decomposition. The method's accuracy and precision were validated using five National Institute of Standards and Technology (NIST) standard reference materials, including egg powder, rice flour, wheat flour, typical diet, and bovine muscle. Further validation was performed on 18 different food types, with results compared to atomic absorption spectroscopy (AAS), confirming the method's reliability for diverse matrices.

F. Laborda *et al.* [32] presented single particle inductively coupled plasma mass spectrometry (SP-ICPMS) as an advanced method for nanoparticle (NP) analysis, allowing particle-by-particle detection, sizing, and quantification. Initially applied to aerosols and microparticle suspensions, SP-ICPMS is now widely used for engineered nanomaterials, providing data on elemental composition, particle size, number concentration, and distinguishing dissolved from particulate forms. The technique relies on time-resolved ion signals from individual NPs in the plasma, offering high sensitivity and rapid analysis for environmental, biological, and consumer product samples. Coupling SP-ICPMS with separation or imaging methods enhances size determination and multielement analysis, making it a versatile tool for nanomaterial research and regulatory monitoring.

Q. Han *et al.* [33] analyzed 35 black, oolong, and green tea samples from China using inductively coupled plasma mass spectrometry (ICP-MS) after developing an optimized digestion method based on response surface methodology. Linear discriminant analysis was applied to classify the teas according to type and origin, achieving complete separation with 100% discrimination efficiency. The study also examined variations in selected elemental concentrations among the tea samples based on their type and geographic origin.

N. Birse *et al.* [34] reported that organic fruits and vegetables are increasingly preferred due to lower contaminant exposure. Detecting fraud is challenging because chemical residues degrade or can be washed off. Combining Direct Analysis in Real Time–Mass Spectrometry (DART-MS) with a single quadrupole mass spectrometer allowed differentiation of organic and conventional leeks with 93.8–100% accuracy, while Inductively

Coupled Plasma–Mass Spectrometry (ICP-MS) achieved 92.5–98.1% accuracy. The study supports vegetable certification as organic and highlights the need for data libraries to expand these methods.

ICP-MS as a tool for accurate pharmaceutical and drug characterization

Medical science affects everyone, but pharmaceutical, biomedical, and life sciences demand particularly precise analyses. Accurate measurement of inorganic elements and organic compounds, such as nucleotides and sulfur-or phosphorus-containing peptides and proteins, is essential for drug development. Since the 1980s, inductively coupled plasma mass spectrometry (ICP-MS) has become a powerful tool for elemental and isotopic analysis, enabling qualitative, quantitative, and semi-quantitative measurements, as well as isotopic ratio determination. Today, ICP-MS is widely recognized as the leading technique for quantifying inorganic impurities in pharmaceutical and biomedical applications [35].

M. Mittal *et al.* [36] review the application of inductively coupled plasma-mass spectrometry (ICP-MS) as a crucial analytical tool for pharmaceutical quality control. The technique is particularly valuable for detecting and quantifying elemental impurities that may arise during drug development, manufacturing, storage, or transport. By accurately measuring both toxic and essential elements in pharmaceutical formulations, ICP-MS ensures product safety and compliance with regulatory standards, making it an indispensable method for safeguarding patient health.

N. Lewen *et al.* [37] established a reliable inductively coupled plasma-mass spectrometry (ICP-MS) method to replace traditional wet chemical tests for heavy metals in pharmaceuticals, as outlined in the United States, British, Japanese, and European Pharmacopoeias. The method enables precise detection and quantification of elements including arsenic (As), selenium (Se), cadmium (Cd), indium (In), tin (Sn), antimony (Sb), lead (Pb), bismuth (Bi), silver (Ag), palladium (Pd), platinum (Pt), mercury (Hg), molybdenum (Mo), and ruthenium (Ru), removing the subjectivity inherent in visual semi-quantitative assays. It has been validated across diverse sample matrices, achieving average element recoveries between 89% and 102%, highlighting its accuracy and broad applicability.

N. Sugiyama and Y. Shikamori [38] highlight that triple quadrupole ICP-MS (ICP-QQQ) enables highly sensitive detection of heteroatoms like sulfur (S), phosphorus (P), and chlorine (Cl), making it ideal for analyzing molecular compounds in life sciences and drug development. Its tandem MS/MS setup, with quadrupoles before and after the reaction cell, provides superior control over ion-molecule reactions compared to conventional single quadrupole ICP-MS. This enhanced interference management was demonstrated on samples including drug active pharmaceutical ingredients (APIs) and peptides containing S, P, or Cl.

B. Gam Melgaard *et al.* [39] examined ICP-MS as a detection method in drug metabolism studies, highlighting its high sensitivity, element specificity, and independence from molecular structure. The review focused on approaches combining ICP-MS with online separation. The technique is effective for drugs containing halogens, sulfur, metals, or metalloids, though interference from endogenous compounds can limit quantitative analysis of non-metal drugs. ICP-MS also allows simultaneous monitoring of metals in drugs and intrinsic elements in biomolecules, making it invaluable for studying metallo-drug interactions, but less applicable to traditional drugs.

Ihsan *et al.* [40] describe inductively coupled plasma–mass spectrometry (ICP-MS) as a powerful technique for elemental and isotope analysis. In its simplest form, an argon plasma (5,500–6,500 K) ionizes analytes from a nebulized sample, and a mass spectrometer separates ions by mass-to-charge (m/z) ratio for detection. Modern ICP-MS instruments include time-of-flight and magnetic sector systems capable of high-precision isotope ratio measurements. Since its introduction in 1980, ICP-MS has become the gold standard for quantifying inorganic impurities in pharmaceuticals and analyzing a wide range of elements in biological and chemical samples, including sulfur-and phosphorus-containing molecules.

R. N. Rao and M. V. Talluri [41] reviewed the use of inductively coupled plasma–mass spectrometry (ICP-MS) for detecting trace inorganic impurities in drugs and pharmaceuticals. The study highlighted the application of ICP-MS combined with liquid chromatography (LC), gas chromatography (GC), and capillary electrophoresis (CE) for heavy metal speciation.

W. Chen *et al.* [42] reviewed the application of inductively coupled plasma–mass spectrometry (ICP-MS) for analyzing minerals and heavy metals in medicinal materials from plants, animals, minerals, Chinese patent medicines, and biological samples. Among 234 studies, ICP-MS was most commonly applied to plant-derived materials, with copper (Cu) measured most frequently. The technique was also used for animal-and mineral-derived materials and Chinese patent medicines, though studies on biological samples were limited. ICP-MS, alone or combined with other methods, enabled elemental quantification, speciation, and isotope analysis, helping establish characteristic inorganic profiles and supporting quality control as well as evaluation of active and toxic components in traditional medicines.

A. Udristioiu *et al.* [43] used inductively coupled plasma–mass spectrometry (ICP-MS) to measure trace and major mineral elements in human hair, evaluating both potential toxic exposures Aluminum [Al], Lead [Pb], Mercury [Hg]and essential minerals Calcium [Ca], Magnesium [Mg], Copper [Cu], Zinc [Zn]) in 75 healthy adult women. Hair samples (3 cm, 100 mg) were collected from the scalp. Results showed that 16% of participants had high intracellular magnesium and calcium but low calcium/magnesium ratios, while 8% had low magnesium and calcium with high calcium/magnesium ratios. No participants showed signs of acute heavy metal intoxication, and trace element levels reflected environmental and lifestyle exposures.

G. Yenduria and S. Navuluri[44] utilized inductively coupled plasma–mass spectrometry (ICP-MS) with microwave acid digestion to analyze 14 elemental impurities, including lithium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, arsenic, molybdenum, cadmium, antimony, mercury, and lead—in parenteral ofloxacin. Validated according to the United States Pharmacopeia, the method demonstrated excellent accuracy, precision, linearity, and robustness. Analysis of six batches showed all impurities were below detection limits, highlighting ICP-MS as a reliable approach for monitoring elemental impurities in pharmaceuticals.

Al-Hakkani [45] provided a practical guideline for inductively coupled plasma–mass spectrometry (ICP–MS) users, covering fundamental theory, instrument composition, quality control and assurance requirements, reagent preparation, detection limit calculations, and method validation parameters, offering a comprehensive reference for ICP–MS analysis.

A. J. Vyas *et al.* [46] developed a microwave-assisted sample preparation method using diluted nitric acid for analyzing elemental impurities in Fenofibric Acid Tablets, following United States Pharmacopeia (USP)<232>, USP<233>, and International Council for Harmonisation (ICH) Q3D guidelines. The method enables simultaneous determination of Class 1 (arsenic [As], cadmium [Cd], mercury [Hg], lead [Pb]) and Class 2A (cobalt [Co], vanadium [V], nickel [Ni]) elements through spike-and-recovery experiments, addressing low recovery challenges. The procedure was validated for specificity, sensitivity, linearity, precision, accuracy, and system suitability, providing a reliable approach for regulatory-compliant elemental impurity assessment in pharmaceuticals

F. Gregar *et al.* [47] highlighted the importance of assessing trace metals in plant oils as a quality and safety measure, influencing health risks, flavor, and oxidative stability. They developed and validated a simple inductively coupled plasma mass spectrometry (ICP-MS) method using an argon–oxygen plasma, enabling direct analysis of oil samples with minimal preparation and low contamination risk. Complete solubilization of the oil

allowed total metal determination from a single test tube with a fivefold dilution. The optimized plasma conditions produced a robust and accurate method with sub-nanogram per g ($ng \cdot g^{-1}$) detection limits, enabling measurement of barium (Ba), cadmium (Cd), copper (Cu), iron (Fe), manganese (Mn), lead (Pb), tin (Sn), vanadium (V), and zinc (Zn) in olive, sunflower, and rapeseed oils.

E. Köse *et al.* [48] investigated elemental impurities in allergy and cancer tablets, highlighting their importance for drug safety and public health. Using microwave digestion for sample preparation and inductively coupled plasma-mass spectrometry (ICP-MS) for analysis, they developed and validated a method in line with ICH Q3D(R1) guidelines. The method demonstrated high precision and accuracy, with detection limits of 0.001–1.756 µg/l, correlation coefficients between 0.9993 and 1.000, and satisfactory recoveries, confirming its suitability for routine drug analysis.

ICP-MS techniques and their forensic applications

Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is a powerful analytical method for quantifying elements in samples, with sensitivity reaching parts per million (ppm) and even parts per billion (ppb). It can analyze both liquid and solid samples, with laser ablation ICP-MS (LA-ICP-MS) allowing precise measurements on very small areas, typically 25–100 μm^2. This chapter reviews the technique's principles and its forensic applications, including the analysis of glass, soil, bullets, and biological tissues [49].

X. Li *et al.* [50] developed an inductively coupled plasma mass spectrometry (ICP-MS) method to detect gunshot residues (GSRs) obscured by bloodstains, a limitation of conventional SEM analysis. The method successfully identified tin (Sn), antimony (Sb), barium (Ba), and lead (Pb) in GSRs, showing that blood does not interfere with detection. With low detection limits, high sensitivity, and adaptable sample preparation, this approach offers valuable support for forensic investigations and expert testimony.

J. Ogana *et al.* [51] reported that ICP-MS is a highly precise and sensitive method for detecting metals and non-metals, even at part-per-trillion levels. The technique is widely used in nuclear forensics to identify uranium isotope ratios, trace elements, and rare earth elements, helping to track the source of nuclear materials and prevent smuggling. Four uranium ore samples from northern Nigeria were analyzed, revealing lead, thorium, and uranium concentrations from 3.2 to 4300 cps/ppb, and trace elements from 2.08 to 7472 ppb. These results confirmed ICP-MS as a reliable and effective tool for nuclear material characterization.

D. Clases *et al.* [52] highlighted ICP-MS as a leading technique for analyzing elements in complex biological systems. Its high sensitivity, isotopic selectivity, and wide dynamic range make it ideal for biomonitoring major, trace, and toxic elements, as well as for studying disrupted metabolic pathways. Coupling ICP-MS with laser ablation or chromatography expands its capabilities for quantitative speciation and bioimaging, while isotopic analysis enables tracer studies and metabolic investigations. Advances in instrumentation and methodologies, including immunochemical approaches, have extended its applications to single-cell analysis, nanomedicine, biomolecules, and novel bioassays. ICP-MS is now recognized as a versatile tool in medical sciences, with clinical trials exploring its potential.

S. Montero *et al.* [53] applied ICP-MS to analyze glass fragments from a case involving 15 vehicle break-ins. Alongside traditional assessments of color, density, and refractive index, 17 known samples and 42 questioned fragments were examined. Elemental analysis of 16 elements enabled clear differentiation of all known samples and linked several questioned fragments to their sources, demonstrating the effectiveness of combining ICP-MS with conventional forensic glass methods.

Aboul-enein *et al.* [54] emphasized the importance of forensic document examination, which includes handwriting, ink, typescript, and the physical and chemical characterization of paper. This study investigated the use of ICP-MS to differentiate paper samples based on their elemental composition. Common office papers from various sources were digested using a nitric acid–hydrogen peroxide microwave method, and trace element concentrations were measured with ICP-MS, demonstrating its applicability in forensic analysis.

A. M. Pryor [55] highlighted that chemical analysis of bullet and shotgun pellet lead (CABL) can provide critical information when traditional projectile identification methods are not feasible. The study developed a laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) technique to establish the provenance of lead projectiles. CABL principles were explored through detailed manufacturing and ammunition studies, and the method was successfully applied in shooting trials, demonstrating a reliable approach for tracing bullet lead in forensic investigations.

C. C. Chang *et al.* [56] developed and validated an ICP-MS method to quantify lithium in postmortem whole blood, addressing the challenge that serum is often unavailable in forensic cases. The method required only 40 µl** of blood, with a 100-fold acid dilution, optimized nebulizer gas flow (1.15 l/min), and germanium as the internal standard. It demonstrated linearity between 0.10–1.5 mmol/l, high precision (≤2.3% CV), and accuracy (105–108%), and was successfully applied to 103 autopsy cases, showing robust and consistent performance.

A. M. Ghazi and J. Millette [57] used laser ablation sector ICP-MS to determine lead (Pb) concentrations and isotope ratios in a layered paint chip for environmental forensic analysis. Four of the six layers (C–F) contained significant Pb, and isotopes 204Pb, 206Pb, 207Pb, and 208Pb were measured, with mercury isotopes (202Hg, 204Hg) used to correct for interference. Isotope ratio analysis showed distinct signatures: layer F matched Mississippi Valley-type Pb-Zn mines (eastern Missouri), layer E resembled Pb-Zn-Ag mines in the Sierra Madre (Mexico), and layer D had a non-radiogenic signature. The study demonstrates the reliability of ICP-MS for rapid source fingerprinting of lead in samples.

C. Latkoczy *et al.* [58] conducted a forensic interlaboratory study on glass samples within the NITE-CRIME European Network using various laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) systems. Initial tests with reference glasses (NIST SRM 610 and 612) showed up to 60% variation in trace element concentrations across labs. After discussions and the creation of new glass standards (FGS 1 and FGS 2), an improved protocol was applied to a well-characterized float glass sample (FG 10-1), reducing deviations to less than 10%. The study demonstrates that LA-ICP-MS can provide accurate quantitative measurements of major, minor, and trace elements in glass for forensic applications.

J. P. Goullé *et al.* [59] developed and validated ICP-MS methods for simultaneous quantification of 27–32 metals and metalloids in human whole blood, plasma, urine, and hair. Samples were prepared via simple dilution or acid mineralization, with rhodium as an internal standard, achieving high linearity ($r>0.99$) and precision (intra-assay CV<5%, inter-assay CV<10%). Limits of quantification varied by element and matrix, and reference values were established from healthy volunteers, demonstrating ICP-MS as a reliable tool for clinical and forensic toxicological analysis.

B. Michalke [60] highlighted the importance of elemental analysis in clinical and biological samples for diagnostics, drug development, and monitoring. The review discussed advanced sample introduction techniques coupled with inductively coupled plasma-mass spectrometry (ICP-MS), enabling insights into element binding, redox states, and spatial distribution in tissues and single cells. Applications include spatial mapping of elements, use of natural or artificial tags for drug monitoring, iron redox speciation in oxidative stress and ferroptosis, copper speciation in Wilson's disease, and single-cell ICP-MS for studying cellular uptake, accumulation, and release of metal-containing compounds.

A. A. Ammann [61] described inductively coupled plasma mass spectrometry (ICP-MS) as a versatile and highly sensitive tool widely used in environmental, life, forensic, and industrial sciences. Its high-temperature plasma efficiently atomizes and ionizes diverse samples, enabling ppt–

ppq level detection with high accuracy, salt tolerance, and compound-independent response. When coupled with species-specific separation techniques, ICP-MS allows molecular-level identification, complementing traditional molecular ion source MS. This tutorial highlights the principles, advantages, and recent applications of ICP-MS for trace element analysis.

Z. Abrego *et al.* [62] introduced a laser ablation–inductively coupled plasma mass spectrometry (LA-ICP-MS) method for identifying gunshot residue (GSR) on skin using tape lifts. Key metals (antimony [Sb], barium [Ba], lead [Pb]) and other isotopes were monitored to classify particles as characteristic or consistent with GSR. The method, validated with different firearms and ammunition, offers a faster alternative to scanning electron microscopy–energy dispersive spectroscopy (SEM-EDS), completing analyses in under 66 min.

C. Jantzi [63] optimized laser ablation–inductively coupled plasma mass spectrometry (LA-ICP-MS) and laser-induced breakdown spectroscopy (LIBS) for forensic soil analysis, introducing the first use of a 266 nm laser for LIBS. Sample preparation for bulk soils, sediment-laden filters, and tape-mounted evidence achieved consistent performance. Inter-laboratory tests with LA-ICP-MS, LIBS, and micro X-ray fluorescence (μXRF) showed low detection limits and high precision, with LA-ICP-MS being most sensitive. Principal components analysis (PCA) and linear discriminant analysis (LDA) discriminated soils from different sites (≥94.5% accuracy), even with similar mineralogy or color, confirming these methods' effectiveness for forensic soil provenance.

P. Becker *et al.* [64] developed a single-pulse laser ablation–inductively coupled plasma time-of-flight mass spectrometry (Single-Pulse LA-ICP-TOFMS) method for forensic float glass analysis. Unlike traditional LA-ICP-MS methods, this technique can analyze much smaller fragments using multiple laser pulses per fragment. Eighteen elements were quantified per pulse, and a modified 5-sigma criterion successfully matched fragments from the same source while distinguishing different sources, enabling analysis of smaller forensic glass fragments than previously possible.

C. Liu *et al.* [65] performed the first ICP-MS profiling of cocaine in China, analyzing 26 inorganic elements using ultrasonic-assisted sample preparation. Analysis of 183 seized samples (2011–2015) established element concentration ranges. Using 131 linked/unlinked samples, various pre-treatment and correlation methods were tested for discrimination, with normalization+standardization+logarithm/Cosine correlation performing best. Hierarchical cluster analysis identified 21 linked sample groups, aiding case connections and mapping distribution networks.

A. Ulrich *et al.* [66] emphasized the importance of meticulous evidence tracing at crime scenes for suspect conviction. While fingerprints and ballistic control samples are key, traditional bullet comparisons based on weight, dimensions, shape, or distinctive markings may be insufficient due to deformation or mechanical strain. In cases where only particles remain, trace-element composition and lead-isotope ratios can be compared to control samples. The study applied this method to two cases, comparing elemental fingerprints of particles and deformed bullets with potential bullet types from suspects, and discussed data interpretation along with method limitations.

R. N. Udey *et al.* [67] analyzed porcine tissue samples shot with jacketed and non-jacketed bullets to detect gunshot residue (GSR) using inductively coupled plasma mass spectrometry (ICP-MS). Microwave-digested tissues were tested for elements including antimony (Sb), barium (Ba), lead (Pb), iron (Fe), and copper (Cu). Sb, Ba, Pb, Cu, and Fe differentiated shot from gunshot tissue and distinguished bullet types. In fresh tissues, Cu, Sb, and Pb differentiated bullets at the 95% confidence level, while Cu and Pb remained discriminatory through moderate decomposition at 99% confidence.

Advantages and limitations of ICP-MS in various fields

Table 1 indicates Key Advantages and Limitations of ICP-MS Across Applications

Table 1: Key advantages and limitations of ICP-MS across applications

Name of the field	Advantages	Limitations	References
ICPMS in Environmental Science and Industry	High sensitivity, multi-element detection, trace metal monitoring, regulatory compliance	Expensive, sample preparation required, matrix interferences	[57, 61]
ICPMS in Food Science	Precise quantification of nutrients/contaminants, low detection limits, multi-element analysis	High cost, spectral interferences, skilled operation required	[52, 57]
ICPMS in Pharmaceuticals	Accurate trace element and impurity analysis, high precision, simultaneous multi-element detection	Complex sample prep, high cost, matrix effects	[48, 63]
ICPMS in Forensic Science	Trace evidence analysis (glass, soil, GSR, biological samples), high discriminating power, sensitive	Contamination risk, requires validation, expert interpretation	[19, 53, 67]

Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is a highly sensitive, multi-element analytical technique widely used across disciplines. In environmental science and industry, it enables trace metal monitoring and regulatory compliance, though high costs, sample preparation, and matrix interferences can be limiting [57, 61]. In food science, ICP-MS allows precise quantification of nutrients and contaminants at low detection limits but requires skilled operation and can face spectral interferences [52, 57]. In pharmaceuticals, it ensures accurate analysis of trace elements and impurities with high precision, despite complex sample preparation and matrix effects [48, 63]. In forensic science, ICP-MS is employed for sensitive analysis of trace evidence such as glass, soil, and biological samples, requiring strict contamination control and expert interpretation [19, 53, 67].

Advancements and future directions in ICP-MS

Inductively Coupled Plasma–Mass Spectrometry (ICP-MS) has become one of the most advanced and versatile analytical tools for multi-elemental and isotopic analysis, recognized for its outstanding sensitivity, accuracy, and broad dynamic range. Over the years, a series of instrumental breakthroughs—such as high-resolution (magnetic sector) ICP-MS, multicollector ICP-MS for highly precise isotope ratio determination, and triple-quadrupole ICP-MS for superior interference control—have significantly enhanced analytical capability and reliability. The integration of ICP-MS with complementary technologies like laser ablation (LA-ICP-MS) and laser-induced breakdown spectroscopy (LIBS-ICP-MS) has further extended its application to spatially resolved and microscale investigations. Additionally, time-of-flight (TOF) ICP-MS has increased analytical throughput through rapid, simultaneous multi-element detection, fostering advances in environmental, geological, and biomedical research [68].

In the coming years, the role of artificial intelligence (AI) and machine learning (ML) in ICP-MS is expected to expand rapidly, transforming both data interpretation and instrument operation. AI-based algorithms are being utilized to enhance spectral interpretation, correct matrix effects, predict instrument performance, and automate calibration, thereby improving reproducibility and reducing operator dependence. These intelligent systems are also proving invaluable for analyzing complex, multidimensional datasets generated from imaging and single-cell ICP-MS studies. When combined with miniaturization, automation, and hybrid analytical platforms, AI-driven ICP-MS is paving the way toward "smart" analytical instrumentation capable of adaptive analysis and autonomous quality assurance. Such advancements will continue to position ICP-MS at the forefront of analytical science, driving innovation in environmental monitoring, nanomaterial characterization, and clinical diagnostics [52, 69].

CONCLUSION

Inductively Coupled Plasma–Mass Spectrometry (ICP-MS) continues to be a pivotal tool in contemporary analytical science, celebrated for its exceptional sensitivity, accuracy, and ability to perform comprehensive multi-element and isotopic analyses. Its versatility makes it indispensable across a wide array of fields, including environmental monitoring, food safety and authentication, pharmaceutical quality control, and forensic investigations. Ongoing technological innovations, such as triple-quadrupole systems for improved interference suppression and laser ablation for high-resolution spatial mapping, have further enhanced its analytical capabilities. The emerging integration of artificial intelligence and machine learning promises to revolutionize ICP-MS workflows by streamlining data analysis, improving predictive accuracy, and enabling self-optimizing instrumentation with unprecedented reproducibility.

Several critical limitations persist that must be addressed to maximize the technique's potential. Standardized protocols and universal reference materials remain insufficient, particularly for advanced applications like nanoparticle analysis in complex matrices and single-cell ICP-MS, impeding reliable cross-laboratory comparisons. Sample matrix complexity continues to cause spectral interferences, necessitating elaborate mitigation techniques and often cumbersome sample preparation. The high cost of instruments and the requirement for specialized technical expertise restrict widespread adoption, especially in smaller laboratories. Additional challenges include translating high-end ICP-MS research into routine clinical or industrial practice, particularly for elemental speciation and diagnostic applications. Furthermore, emerging demands such as real-time, in situ analysis, seamless integration with complementary analytical techniques, and strategies for accurate detection of ultra-trace elements in complex biological and environmental matrices highlight important areas for future development. Overcoming these challenges will be essential to fully leverage ICP-MS for next-generation analytical solutions and to ensure its continued relevance across diverse scientific domains.

ACKNOWLEDGMENT

We thank the researchers whose work is referenced for their contributions to the field. All fig. and tables presented are the original work of the authors.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

Written by Fakeha Shaikh under the guidance of Ashish Uzgare.

CONFLICT OF INTERESTS

Authors declare no competing or conflict of interest

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