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Innovations in inductively coupled plasma-mass spectrometry: bridging scientific fields

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ABSTRACT

Inductively coupled plasma mass spectrometry ICP-MS is a versatile analytical tool with several research uses and regular applications in many domains, including biological materials, environmental analysis, and geochemistry. This technique detects trace components in water, soil and clay, blood, urine, pharmaceutical products, and medicinal cases. Although other methods, such as atomic absorption and atomic emission, are still used by researchers, there has been a noticeable shift toward ICP-MS, notably over the last decade. Developing accurate and precise methods for measuring components at low concentrations is crucial for detecting abnormalities in the human body and detecting trace amounts of metal in many other species. ICP-MS is a viable approach for the elemental determination of biological fluids, water, clay, and pharmaceuticals because it allows for reliable analysis at trace and ultra-trace levels while maintaining a wide dynamic range. Many breakthroughs have been made in ICP-MS analytical capabilities over the last few years. This review discusses the most recent works that use trace element analysis by ICP-MS in several fields.

Introduction

Measuring trace elements in biological and other samples has numerous clinical applications. The rise in xenobiotics in the environment directly results from technological advancement. Biomonitoring is an essential tool for estimating human exposure to pollutants, and their concentrations in the blood are commonly utilised as biomarkers [1]. This highlights the need for faster and more sensitive procedures requiring less sample handling. Thus, traditional techniques like atomic absorption or electrochemical approaches are gradually replaced by multi-element techniques with suitable sensitivity, such as ICP-MS [2]. These methods may be able to detect components at trace quantities with the necessary sensitivity, but they lack speed and usability. Because of the high sensitivity and low detection limits of ICP-MS, toxicologists can accurately assess ambient metal exposure and toxic levels, making it a valuable tool for various clinical applications [3]. Additionally, this approach opens up new opportunities in several disciplines, including environmental exposure, workplace testing, clinical toxicology, and forensic toxicology. It is also suitable for epidemiological investigations and detecting many elements in urine, pharmaceuticals, water, and clay samples [4–8].

Mass spectrometry's sensitivity and selectivity make it ideal for monitoring tiny concentrations of components in biological materials [9]. These low-abundance substances often play essential roles in their corresponding chemical or biological systems [10]. This review aims to present the most recent research and some noteworthy older works, applying trace element analysis by ICP-MS in several fields to understand clinical and environmental conditions better.

ICP-MS Instrument

A single quadrupole ICP-MS comprises six basic compartments: the sample introduction system, inductively coupled plasma (ICP), interface, ion optics, mass analyser and detector [11]. Ions with varying mass-to-charge ratios are separated in MS using the basic characteristics of electric, magnetic, and radio frequency fields. In the case of ICP-MS, the inductively coupled high-frequency plasma serves as the ion source, where the ions to be separated are produced. A sample introduction system that transforms the sample into a physical condition most suited to the ion source's operation. Pneumatic nebulisation of a liquid sample is the most common method used for sample introduction in ICP-MS. The plasma ion source uses external energy from a high-frequency electromagnetic field coupled inductively to create ions from atoms. The aerosol is dried, broken down, dissociated, atomised, stimulated, and positively ionised in the plasma source. The interface system removes the ions from the plasma and comprises a vacuum fore pump, a sample cone, and a skimming cone. This apparatus is also required to lower the ion source's pressure to the necessary vacuum in the mass analyser area. The ions are focused into the mass analyser using a lens mechanism. The ions are separated based on their mass-to-charge ratio in the mass analyser (quadrupole [ICP-QMS], magnetic sector field [ICP-SF-MS], and time of flight analyser [ICP-TOFMS]).

A device known as a Faraday cup or secondary electron multiplier is also used to detect the ions. Lastly, the computer that manages every aspect of the mass spectrometer gathers information and outputs the mass spectrum, showing the ions' mass-to-charge ratios and their measured intensities. ICP-MS is a method commonly used for liquid analysis. To generate an aerosol from a solid or particle sample, it must be transformed into a solution using a pneumatic nebuliser. Aerosol is continually carried to the plasma ion source, which operates at atmospheric pressure, via a transport gas (often Argon) and tubing [12,13]. **Figure 1** is a schematic of an ICP-MS machine [14]. The advancements in ICP-MS technology have enabled the detection of challenging analytes at trace and ultra-trace levels in many samples. For example, comparing the technique with atomic absorption techniques shows that ICP-MS has incredible speed, precision, and sensitivity. The limitations of the technique include the equipment's relatively high cost and a group of elements that cannot be detected [15].

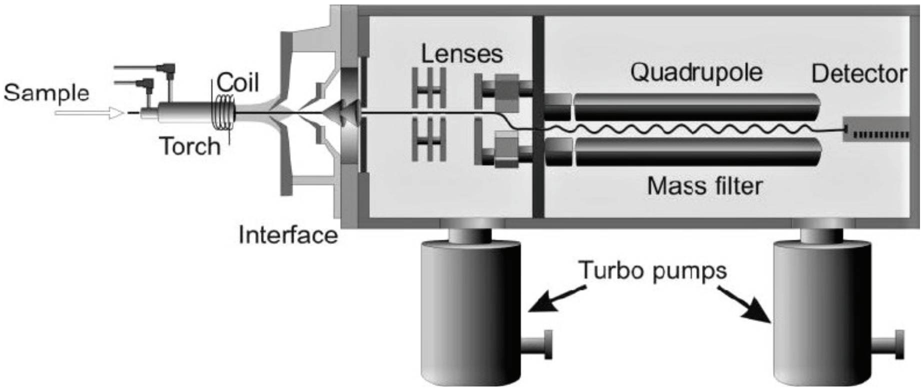

Figure 1. Cross-section schematic of an ICP-MS (ref. 14).

Determination of elements in blood samples

The focus on trace element content in biological fluids has led to the development of analytical techniques specifically for this purpose. The low quantities of specific components in human fluids, combined with the complexity of the matrix, challenge analytical methods [14].

The various biological functions that trace elements play in human health indicate their significance in clinical research, diagnosis of deficiency disorder, or prevention of unintended exposure to toxic metals. It is crucial to examine the trace element profile and functional elemental biomarkers in biological fluids to learn more about an individual's nutritional status, the diagnosis and treatment of diseases, and the relationship between these conditions and other contributing factors [16,17]. Based on their chemical characteristics and binding affinities, trace elements in blood are dispersed between the extracellular compartment (blood plasma) and the intracellular compartment (mostly in erythrocytes) [18]. ICP-MS was the most effective and frequently used analytical technique for measuring numerous trace elements in biological fluids such as blood and plasma [19].

ICP-MS was used in microsampling, which became more popular in recent decades, and it is used for standard analyses such as trace element quantification. Researchers compared dried blood spots and microtubes to assess their capacity for analysing 12 trace components in human whole blood [20]. The technique detected trace elements (K, Zn, Se, Cu, Mn, Fe, Mg) in serum and whole blood. The suggested methodology was validated by analysing certified human serum and whole blood with known amounts of all elements. The method is suitable for routine usage in biomonitoring investigations [21]. An enhanced micro-sampling ICP-MS technique was developed in another study to measure the concentrations of Ca, Mg, Cu, Zn, Fe, Mn, Se, and Pb in uremic patients receiving long-term hemodialysis [22].

On the other hand, the technique was used to investigate baseline blood levels of 12 toxic and/or essential metals and metalloids in Wuhan, central China, including As, Cd, Pb, Hg, Cr, Tl, Mn, Cu, Zn, Ca, Fe, and Mg [23]. Researchers developed a method to measure the content and size of silver nanoparticles in blood for use in in vivo toxicological assessments. The approach can be applied to characterise AgNPs in toxicity research [24]. Cu content in human red blood cells was studied using time-resolved ICP-MS. Human red blood cells (1.5 × 105 /mL) were transformed into fine aerosols using a modified nebuliser and spray chamber for efficient single-cell insertion into the ICP [25]. A new high-precision and high-throughput technique for directly identifying major and trace elements in whole blood samples was developed, and it was based on the laser ablation ICP-MS equipment. This technique significantly increased precision by using a specially made cryogenic ablation cell to prevent droplet splashes during the ablation procedure by solidifying liquid whole blood samples [26]. The effects of storage temperature and stability of various clinical trace elements in human blood and plasma were investigated over an extended storage period. It was found that human blood and plasma specimens could be stored for up to six months at low temperatures (4 °C and -20 °C) without experiencing significant changes in elemental content [27].

Urine Elemental Analysis

Urine is a mixture of waste metabolites that are soluble in water and is produced when the kidneys filter blood at a consistent rate. Urine analysis is well-established and has been used to analyse exposure to harmful elements or chemicals, find irregularities in absorption, or study diseases to determine causes and enhance prognosis [28,29]. Urine analyses are less complicated than blood or faeces because sample pre-treatment is made easier by the comparatively low concentrations of organic and inorganic solutes. Additionally, collecting urine samples is a simple and non-invasive procedure that may be completed without the help of qualified medical professionals [30].

Numerous studies have shown that ICP-MS is the most effective method for identifying elements in urine. An analysis method for the detection of six arsenic compounds, trivalent arsenic, pentavalent arsenic, methyl arsenic, dimethyl arsenic, arsenical choline and arsenical betaine in urine was established by high-performance liquid chromatography combined with ICP-MS to provide a theoretical basis for health assessment of arsenic poisoning patients [31]. ICP-MS was used to assay elements in the urine alternation and correlation of Mg, Ca, Cu, Zn, Fe, Cr, and Se among diabetic peripheral neuropathy patients and healthy people using multivariate statistical analysis [32]. Chelation therapy was tried for a patient whose symptoms were thought to be consistent with Chronic Fatigue Syndrome, suggesting that the patient may have been intoxicated with metals. Simultaneously, the elemental excretion profile in urine was established. Most toxic elements showed an excretion peak in 12–24 hours after EDTA treatment [33]. An investigation was carried out to examine the impact of physical exercise on the concentrations of Cu in both intracellular (erythrocytes and platelets) and extracellular (serum, plasma, and urine) using ICP-MS [34]. A 14-day excretion study with 20 volunteers involved daily applications of 1 mg of CoCl2 or 1 mg of cyanocobalamin. The samples were obtained from 7 days before treatment to 7 days after. Total Co concentrations found by ICP-MS indicated considerably increased values exclusively after inorganic cobalt consumption [35]. Fifteen metals and metalloids (As, Be, Bi, Cd, Co, Cr, In, Mn, Mo, Ni, Pb, Sn, Tl, V, and Zn) were determined using ICP-MS spectrometry. All elements were detected in urine samples above the limit of quantification in ng/L ranges, except indium [36]. An experiment was done using ICP-MS to see if acid-washed containers were required for the 24-hour urine copper analysis. Assay diluent and unidentified urine samples were spiked with the copper calibrator to produce copper solutions at concentrations relevant to clinical decision limits. It was found that measuring the amount of copper in 24-hour urine does not require acid-washed containers [37].

Medicinal applications

In living organisms, numerous metal ions have structural and catalytic activities in proteins and enzymes, and they contribute to several physiological processes, such as antioxidation, metabolism, signalling, and gene expression [38]. Approximately ten elements are required for life: Na, K, Mg, Ca, Mn, Fe, Co, Zn, Ni, Cu, and Mo. Biologically necessary metals are classified into two types: non-transition elements (Na, K, Mg, and Ca) and transition elements (Fe, Co, and Cu) [39]. Ions like divalent Ca2+, which are found in relatively high concentrations, are among the necessary metal ions: Ca2+ is a required component of bones and teeth and accounts for 1% to 2% of the human body weight [40]. Mg2+ is also an essential element in rather substantial amounts in the human body and constitutes about 0.05% of body weight [41]. Metal ions frequently act as cofactors for enzymes and are required for their proper function, permitting catalytic activity. Metal ions are also responsible for the structural stability of proteins and for controlling various biological events. A metal binding site's shape may be distorted by the binding of a non-specific metal ion or an ion lacking a specific binding capacity, which could reduce the activity of the corresponding metalloprotein [42]. Because of their increased quantities as a direct result of human activity, the requirement to identify the species (oxidation state/chemical form) of elements present in the environment and biological matrices has excellent importance [43]. It was found that the search for a superior proteomics quantification method has essentially been resolved with the aid of ICP-MS [44].

ICP-MS analysis of a single cell has significant promise for evaluating components within cells [45]. In cells, trace elements are essential. It was found that ICP-MS is crucial for examining trace elements and their species in cells and that it can help with both clinical and biological research [46]. The technique was used to map elements in mouse brain tissue [47]. Results of a study on the impact of oral deferiprone treatment on Cd accumulation and the homeostasis of vital components in the brains of mice exposed to Cd were presented. The results showed that, in comparison to untreated controls, mice exposed to Cd for 14 days had considerably higher Cd concentrations and significantly lower brain levels of Mg, P, and Zn [48]. A sensitive and specific assay has been developed to detect platinum in biofluids. This technique allowed for the characterisation of patients' long-term platinum exposure after receiving oxaliplatin treatment [49]. Sector-field ICP-MS is a versatile tool for quantifying target elements, such as iron and sulfur, in bio-nano systems. When combined with ultrafiltration, it creates an adaptable screening platform for assessing the pharmacological properties of engineered iron oxide nanoparticles [50].

Elemental analysis of pharmaceutical products

Substances in pharmaceuticals, excipients, and drug formulations are known as elemental impurities. They can originate from any raw components used in the drug product [51]. Controlling pharmaceutical products is vital to maintaining the high quality of pharmaceutical manufacturing. Official pharmacopoeias and authorised supervising bodies have called for more thorough and accurate quantitative screening of specific elemental impurities in medications since some may be seriously harmful to human health [52].

ICP-MS was utilised to identify plant-derived therapeutic compounds, with Cu being the most prevalent [53]. The technique was used to determine the factors influencing titanium dioxide nanoparticle size in cosmetic samples [54]. A study shows how effective high-resolution ICP-MS is for qualifying nanoparticles. It showed that crucial requirements for biomedical applications, like resistance to the action of the human serum milieu or reactivity toward serum biomolecules, can be accurately evaluated by recording the signals of gold or sulfur isotopes using novel gold nanoparticles stabilised by N-heterocyclic carbenes as test nanoparticles [55]. To investigate the toxicity levels of 22 nasal spray saline samples, Al, Sb, As, B, Cd, Cr, Co, Cu, Fe, Mn, Ni, Si, and Zn were analysed using ICP-MS [56]. It was also used to assess the concentration of metals (Ag, Ba, Bi, Cd, Pb, Sr, Tl) in 94 eye shadow samples from the Polish market [57]. It was also used to distinguish between ultra-trace quantities of transition metals (Co, Cr, Cu, Fe, and Ni) that interact with therapeutic proteins and free metal in solution in the drug formulation [58]. It was also used to determine Ag and Zn in microcapsules, as they are mighty antibacterial metals [59], and to assess 18 plasticiser residues (phthalates, adipates, sebacates, and others) in sixteen drugs that are sold in Tunisian pharmaceutical markets [60]. ICP-MS, with other techniques, was used to analyse a poison vial found in the remains of a soldier who died in 1944 in Normandy, France [61].

Assessing elements in water

Pure drinking water is crucial to survival and essential for optimal nutrition. Different natural and artificial processes pollute many water sources worldwide, causing various health issues for humans [62]. Water quality is deteriorating due to the ongoing addition of harmful chemicals and bacteria and the constant addition of domestic and industrial sewage sludge, garbage, and other hazardous waste that is damaging to humans and the environment [63]. Spectroscopic methods such as ICP-MS enabled the determination of the total metals and metalloid content in the water at low concentration levels [64].

Single particle ICP-MS was used to examine the presence of Ti- and Pb-based particle nanomaterials in the aquatic environment in 63 locations in the Melbourne area of Australia [65]. It was also used to evaluate a variety of elements in water, such as Ra-226 [66], Cr(III) [67], and F, by measuring BaF+ ions [68]. A technique for determining the total concentrations of the rare earth elements La, Ce, Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, and Lu in mineral water was developed and validated [69]. Another ICP-MS study examined the environmental geochemical properties of rare-earth elements in surface waters in the Anhui Province, China's Huainan mining area [70]. ICP-MS was used to compare water lead measurements made by two field analysers using anodic stripping voltammetry and fluorescence spectroscopy to reference laboratory measurements [70]. The technique was employed in a study on exposure to the high fluoride concentration in spring water in the Bazman volcanic Area in southeast Iran [72]. A cathodic stripping voltammetry electroanalytical technique on a miniature platinum working electrode was used to develop a new set of miniature sensors for Mn determination [73]. Combined with cobalt ions, the method enhanced photochemical vapour production and highly sensitive analysis of trace antimony in water samples [74].

Clays and soil analysis

Since human activity and industrial development are expanding at alarming rates, scientists are focusing on the issue of detecting these pollutants in the environment. ICP-MS has proven sufficient for this area's analysis [75]. On the other hand, the technique is widely used for analysing several elements in geological samples for trace element levels [76]. The study of the provenance of archaeological pottery has extensively used elemental chemical analysis in archaeometry. The method involves determining the highest number of major, minor, and trace elements in ceramics and comparing them to known or assumed origins [77].

ICP-MS was used to determine sediment samples from the Itapicuru-Mirim River in Jacobina, Bahia, Brazil, for As, Cd, Cr, Cu, Fe, Hg, Mn, Ni, Pb, and Zn concentrations [78]. Three Lemnian and three Silesian medicinal earths from the University of Basel's Pharmacy Museum were examined for antibacterial activity using [79]. The technique was used to study the *in vitro* release of aluminium from the geophagic clay Chacco in the Peruvian highlands [80]. In a study comparing the multi-element composition of forest trees to soil chemical and physical properties, 46 elements were measured [81]. A study examined the distribution of Li during the evaporation of brine ponds that produce halite and gathered the first data on the amount of Li in the salt plugs in southern Iran [82]. Another study examined metal(loid) presence and size-dependent variations in concentration in recent marine sediments from coastal and open-sea habitats in the eastern Adriatic [83]. Single particle-ICP-MS was used to analyse the size distribution of copper oxide nanoparticles in aqueous test soil extracts [84]. ICP-MS and other techniques were used to identify the mineral compositions of 28 soil samples collected from various places in the Disi area (South East Jordan) [85]. The technique was combined with Laser ablation to study the clay fraction of archaeological pottery [86]. The particle size distribution of colloids containing Cr(III) and Cr(III) species in mobile colloids was determined using the technique [87].

Conclusions

Even while researchers continue to use other methods, including atomic absorption and atomic emission, to detect metals in various species, there has been a discernible movement toward ICP-MS, particularly over the last decade. Because it enables dependable analysis at trace and ultra-trace levels while preserving a broad dynamic range, ICP-MS has proven to be a practical method for elemental measurement of biological fluids, water, soil, and clay, as well as pharmaceuticals. In this review, we demonstrated that the capabilities of the ICP-MS analytical technique have witnessed various developments.

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Conflict of interest statement
The authors declare no conflict of interest.

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