

Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES): Exploring Versatile Applications in Industrial and Analytical Fields

Melinda Kakuk^{1,4}, Dóra Farkas¹, Barnabás Kállai-Szabó², Krisztina Pencz²,
Lilla Alexandra Mészáros³, Péter Gábor Tonka-Nagy⁴, Nikolett Kállai-Szabó¹, István Antal^{1*}

¹ Department of Pharmaceutics, Faculty of Pharmacy, Semmelweis University, Högyes Endre str. 7., H-1092 Budapest, Hungary

² Cornexi Ltd., Repkény str. 1., H-8000 Székesfehérvár, Hungary

³ Department of Organic Chemistry and Technology, Faculty of Chemical Technology and Biotechnology, Budapest University of Technology and Economics, Műegyetem rkp. 3., H-1111 Budapest, Hungary

⁴ Egis Pharmaceuticals PLC, Bökényföldi str. 118–120., H-1165 Budapest, Hungary

* Corresponding author, e-mail: antal.istvan@semmelweis.hu

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Abstract

The first inductively coupled plasma optical emission spectroscopy (ICP-OES) instrument became commercially available more than 50 years ago, in 1974. Over recent decades, it has emerged as a key spectroscopic technique for analyzing numerous elements, offering a powerful tool for elemental analysis at milliparticle (ppm) and parts-per-billion (ppb) levels. This comprehensive review highlights the applications of ICP-OES across various scientific disciplines, with a particular focus on pharmaceutical technology, illustrated through a practical solution.

Keywords

dissolution, ICP-OES, ICP-based technologies, coupled technologies, dosage forms

1 Introduction

In today's world, one of the most significant challenges is ensuring the quality of medicines. Because of this, many analytical methods have been reviewed or updated due to the requirements for the maximum tolerable limit of drugs [1]. In order to increase the safety of drug therapy, it is important that the concentration of impurities is constantly monitored and kept at a low level [2, 3].

Various regulatory authorities, such as the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), the United States Food and Drug Administration (US FDA), and the Canadian Drug and Health Agency have established comprehensive guidelines to address the control of impurities in pharmaceutical substances [4]. These guidelines are applicable to both new drug substances and products [5], as well as residual solvents [6] that may remain after the manufacturing process. To ensure the safety and efficacy of pharmaceutical formulations, the permissible limit values for impurities present in either the active pharmaceutical ingredients (APIs) or the final drug products are gradually being adopted into

standard references, like the British Pharmacopoeia (BP) and the United States Pharmacopoeia (USP) [7]. These incorporation efforts aim to harmonize global standards and ensure consistency in drug quality. Furthermore, experts such as Ahuja [8] and Görög [9] have compiled a wealth of knowledge in their books, where they summarize the governmental regulations and provide detailed guidelines concerning the identification, quantification, and control of impurities in pharmaceuticals.

The composition of elements in (mostly water-dissolved) samples can be determined using inductively coupled plasma – optical/atomic emission spectrometry (ICP-OES/ICP-AES). The origins of plasma-based spectroscopy can be traced back to 1956, when Eugen Bădărău first attempted to utilize plasma emissions as a source for spectroscopic analysis. However, it wasn't until nearly two decades later, in 1974, that the first commercially available instrument was introduced by an analytical instrument sales engineering company (Kontron) [10]. This technique has gained widespread application across various industries, primarily because of its

ability to effectively handle diverse sample types. In addition to analyzing liquid samples, it is equally effective for gas and solid samples, making it an invaluable tool in fields such as pharmaceuticals, environmental analysis, metallurgy, and materials science. This adaptability allows it to address diverse analytical challenges, further solidifying its role as a cornerstone method in modern spectroscopic analysis [11]. The unique photophysical signals of the individual elements are utilized for the successful detection by the technique, during which the type and relative amount of the individual elements within a complex sample can be determined [12].

Elemental contamination in pharmaceuticals refers to the presence of impurities that can originate at various stages of the drug development and manufacturing process. These contaminants may arise from several sources, including catalyst residues left over from chemical synthesis, inadvertent introduction of particles during production, and degradation or wear of storage and production equipment over time. Addressing such contamination is critical, as it can impact the safety, efficacy, and the overall quality of the pharmaceutical products [13–16]. These pharmaceutical impurities are unwanted chemical substances and these traces of impurities can create significant problems in a preparation [7, 8, 17]. They can reduce their stability at the same time they can change their shelf life. They can catalyze the degradation of the APIs and they can also cause toxicity, which can be dangerous to human health [7, 18]. In the literature many researchers have utilized ICP-OES to measure metal content in various substances, including APIs [19], antibiotic tablets and various dosage forms [20–23]. Nowadays, modern separation methods play a crucial role in research, as they can efficiently separate and quantify individual impurities simultaneously [1]. Currently, ICP-OES is used as the most powerful tool in pharmaceutical analysis due to its high accuracy and sensitivity [24]. ICP-OES is a sensitive technique for elemental analysis. For this reason, ICP-OES can detect elements at levels as low as ppb or ppt, depending on the specific element and instrument configuration. The Limit of Detection (LOD) and Limit of Quantification (LOQ) values depend on the type of element, composition of the matrix and the instrument configuration. Smichowski et al. [25] measured the LOD values of different elements in solution (As 4.3 ng/mL, Cd 0.6 µg/mL, Cr, 9.8 ng/mL, Cu 1.8 ng/mL, Pb 3.0 ng/mL) by ICP-OES. In other literatures it was observed that slightly different values were obtained using different parameters and material of different compositions. For example, LOD values was 0.034 mg/kg and LOQ is 0.043 mg/kg of Cd [26], but in other experiment LOD values were the following: As 0.00712 µg/kg,

Cd 0.00896 µg/kg, Cr 0.00847 µg/mL, Cu 0.00845 µg/kg, Pb 0.00939 µg/mL and the LOQ values of As 0.02136 µg/kg, Cd 0.00896 µg/kg, Cr 0.02567, Cu 0.02535 µg/kg, Pb 0.02847 µg/kg [27].

This article highlights the applications of ICP-OES across various scientific disciplines, with a particular focus on pharmaceutical technology. Notably, many of the elements that can be determined by ICP-OES are crucial for the salt formation of the active ingredients. For instance, in pharmaceutical formulations containing ibuprofen, the sodium salt form is commonly found. In our manuscript, we aimed to demonstrate that for pharmaceutical dosage forms containing the sodium salt of ibuprofen, in addition to determining ibuprofen, the release of sodium can also be detected. This makes the ICP-OES technique potentially suitable for *in vitro* dissolution studies.

2 Fundamental principles of ICP-OES

The ICP-OES/ICP-AES employs an ICP source for sample atomization and thermal excitation. The argon [28], or nitrogen gas [29] used in the ICP plasma generates a high electron density and temperature (5726.85 °C–9726.85 °C) [30] which is ideal for analyzing gas, liquid, or finely powdered solid samples. This capability has led to the development of various sample introduction systems over the years to accommodate different types of samples [12].

For sample introduction of liquids or suspensions, nebulizers are the most commonly used for liquids or suspensions, with various types available [31], such as concentric, V-groove, ultrasonic nebulizer. For powdered solid samples, graphite tube furnaces and laser are typically employed [32]. Since only very small droplets of the aerosol can be injected into the plasma, a spray chamber is placed between the nebulizer and the torch to ensure the proper droplet size. Gases can be introduced directly into the plasma by mixing them with argon [12, 33, 34].

The draining system (which can include a loop, trap, U-tube, etc.) is responsible for carrying excess samples from the spray chamber to a waste container. This system plays a critical role in maintaining the performance of the ICP instrument by removing the excess sample and ensuring proper back pressure. If the drainage system does not flow smoothly or allows bubbles to pass through, it can disrupt the injection of the sample into the plasma, leading to unstable and noisy emission signals [12].

Corrosion-resistant ceramic injectors are commonly used for sample introduction, while narrow-bore injectors are preferred for analyses involving organic solvents. On the other hand, wide-bore injectors are more suitable for introducing

samples with a high dissolved solid content, as they can accommodate larger particles without clogging [12].

Emission from thermally excited sample components, which travel upward through the central channel of the vertically oriented plasma torch, is typically observed from the side, known as radial observation. The emitted radiation is typically collected using focusing optics, such as a convex lens or a concave mirror, which direct the light to the detector for analysis [35] after separating the light into its component wavelengths. The detected radiation is then measured by a variety of detectors, typically a photomultiplier tube (PMT), array detectors, charge-injection device (CID), or more recently, a charge-coupled device (CCD), which captures the signals for further analysis [36]. Currently, in ICP-OES CID and CCD devices are used widespread to detect the light emitted by the plasma. These detectors have mainly replaced traditional PMTs. Although both CIDs and CCDs use a two-dimensional pixel array to convert light into electrical signals, they differ in how the data is extracted. CCDs are favored for their excellent sensitivity and minimal signal noise, whereas CIDs provide enhanced control over the detection process and allow for non-destructive signal readout. In some instruments, the emitted light is observed axially [37], or by using a dual observation approach [38]. However, these methods are less common due to technical challenges, such as the need to protect the photon analyzer from the upward-moving, high-temperature gases in the plasma. The operational wavelength range typically falls between 180–800 nm, although in more advanced instruments, this range can extend from 130–800 nm. To achieve wavelengths below approximately 180 nm, vacuum or argon-purged monochromators/polychromators are required [37].

The ICP-OES/ICP-AES method is a quantitative elemental analysis technique that can accurately determine the total concentration of an element in a sample. Due to the high temperature of the plasma, all compounds are thoroughly atomized, which makes the chemical form of the element in the sample irrelevant. This allows for the precise measurement of the elemental content, regardless of the sample's initial chemical composition. Another advantageous effect of the high plasma temperature is the highly efficient thermal excitation of atoms, which results in significant excitation and ionization of many elements. As a result, the emission spectrum peaks from the ICP plasma are very intense, enabling low detection limits. However, the spectrum is complex, containing both atomic and ionic lines. In fact, a spectrum from a complex sample can include up to 800,000 peaks, making the analysis of such spectra challenging but highly informative [20].

During detection, the electrical current measured at the PMT anode is converted into a usable signal for the computer. Nowadays, PMT has been partially or completely replaced by more modern detector systems, for example CID or CCD detectors. The first step is to transform the anode current (which represents the emission intensity) into a voltage signal. This voltage signal is then processed using digital signal processing techniques. Next, the voltage is converted into digital data by an analog-to-digital or A/D converter. The resulting digital information is subsequently used by the computer for further analysis, ultimately providing the final processed data to the user [12].

3 ICP-based measurement techniques

Numerous articles have reported the development of elemental analysis methods based on ICP [39, 40]. For ICP-OES, the detection limit typically reaches micrograms per liter, while for inductively coupled plasma mass spectrometry (ICP-MS), it can reach nanograms per liter. This high sensitivity makes ICP-based methods ideal for detecting trace elements in complex samples [41, 42]. The use of ICP-MS instruments for trace element analysis and isotope analysis became widespread in laboratories starting in the 1980s [43]. ICP-MS is also widely used to maintain pharmaceutical safety by detecting trace elements and impurities in drug formulations [44]. It is primarily used as a measuring instrument for solution samples [45, 46] and a standalone ICP-OES or ICP-MS is generally suitable only for determining the total concentration of the elements. These techniques are effective for measuring the overall elemental content in a sample, but they may not provide detailed information about the chemical form or speciation of the elements present. Therefore, ICP techniques, especially ICP-MS, are often coupled with a separation technique to obtain detailed information on the concentration of individual species within a mixture. Chemical vapor generation (CVG), or collision/reaction cell with gas is another alternative for introduction analytes into ICP-based instruments, effectively allowing the separation of analytes from the matrix. This often leads to reduced interferences and improved the LODs. For example, the application of CVG-ICP-MS systems has been successfully used for the determination of mercury by Muller et al. [47] and Antes et al. [45] in the pharmaceutical industry. Furthermore, microwave-assisted (MIC-ICP-MS) measurements have been performed for various pharmaceutical products, such as acetylsalicylic acid tablets [48], Abidol [49], Carbamazepine [50], Enalapril, Ramipril tablets [51] and Levodopa [47]. This technique enhances the sample digestion process, allowing

for more efficient and thorough analysis of trace elements and impurities in complex pharmaceutical formulations. In addition to these, other techniques, such as electrothermal vaporization (ETV-ICP-OES) [52], electrothermal vaporization dynamic reaction cell (ETV-DRC-ICP-MS [53], DRC-ICP-MS [45, 47, 53], flow injection (FI-ICP-MS) and double focusing (electric and magnetic), also called sector field (FI-ICP/SF-MS) [54, 55] are also highly useful.

4 Application of ICP-OES in various disciplines

ICP-OES is a versatile analytical technique used across various industries due to its ability to detect and quantify trace elements in different types of samples [56, 57]. Recent reviews have demonstrated that this technique has already been applied in a wide range of settings, including food analysis, agricultural testing, geological testing, drug/metabolism analysis and environmental science (Fig. 1) [58, 59]. These applications are summarized in Table 1 [58–93].

4.1 Geology, environment

The definition and measurement of rare earth elements (REE) in geological materials are critical for geochemical research, requiring precise concentration analysis [56].

Trace element profiling is essential for understanding the formation and evolution of rocks and minerals. The ICP-OES is commonly used to analyze soil, rock and sediment samples to locate and assess ore deposits,

including precious metals (gold, silver) base metals (copper, lead, zinc), and REE [57]. It is also employed to evaluate soil contamination by measuring concentrations of heavy metals, providing valuable data for environmental remediation. Additionally, ICP-OES is used to analyze groundwater and surface water samples for trace metals, supporting water quality monitoring and management, particularly in mining regions and other geological environments. By measuring isotopic ratios and elemental concentrations, ICP-OES offers insights into the age and history of rocks and minerals [58].

By analyzing the elemental composition of igneous, metamorphic and sedimentary rocks, ICP-OES plays a key role in understanding the processes involved in their formation and transformation. It helps in identifying and characterizing minerals based on their elemental makeup, supporting mineralogical studies and classifications.

In this field, ICP-OES is used to analyze the composition of volcanic lava and ash, providing valuable information on volcanic activity, magma evolution and potential hazards. It can be also applied to study volcanic gas emissions by analyzing trace metals and other elements, contributing to a deeper understanding of volcanic processes and their environmental impact [59].

To determine the heavy metal content and concentration in water, an interesting study [60] observed the diversity of plankton, as plankton play a crucial role in the transport of heavy metals in aquatic environments. Plankton has a significant ability to accumulate heavy metals, making them an important factor in understanding the distribution and movement of contaminants in water systems. This study highlights the potential of plankton as bioindicators for monitoring water quality and heavy metal pollution [57].

A journal has reported on the determination of cadmium, mercury, nickel and lead content in fish, crustaceans, sediments and living waters by ICP-OES [94]. Another study examined the accumulation of copper, zinc, manganese, iron, magnesium, nickel, chromium, cobalt and boron in a variety of bream and mullet [95]. These studies help to understand the bioaccumulation of heavy metals in aquatic organisms and the potential environmental and health risks associated with contaminated water bodies. These studies often utilize microwave digestion for efficient sample preparation, but in this industry acid digestion is frequently required for solid samples, such as soil and sediments. Strong acids (e.g., nitric acid, hydrochloric acid) are used to break down the matrix and release the elements into solutions. This method is also employed for the extraction of elements from water, soil,

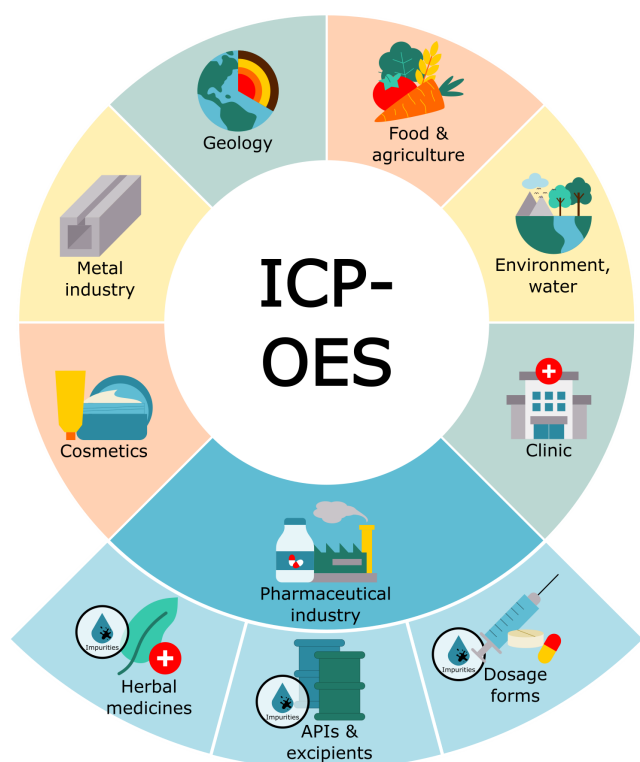


Fig. 1 Applications of ICP-OES in different scientific fields, industries

Table 1 The most common domains of applications for ICP-OES and ICP-based techniques

Application	Samples	Elements	Coupled techniques	Ref.
Metal industry and geology	Textile materials toxic, coal, slags	Sb, Cu, As, Cd, Cr, Co, Pd, Hg, Ni, Zn	ICP-OES, LIBS	[61–63]
	Low alloy steels	As, B, Bi, Ce, La, P, Sn, Ta		
	Vulcano ashes, rocks, soils, sediments, related materials	Metals		
	Ore grade material	U	ICP-OES, ICP-MS	[59, 60, 64–66]
	River sediments	Several metals		
Environment and waters	Plankton	Several metals		
	Sewage sludge, domestic or industrial refuse, coal, coal fly ash, dust, other airborne particulates, nuclear waste	Fe, Cd, Cu, Mo, Ni, V, Zn		
	Seawater	P	ICP-OES, ICP-MS	[67–72]
	Municipal wastewater	Heavy metals		
Agriculture and foods	Inner-city dust			
	Soils, fertilizers, plant materials, feedstuffs, foods, animal tissues, body fluids, vegetables seeds, milk	Ca, Cu, Fe, Mg, Mn, P, K, Na, Zn, Pb, Li	ICP-OES, ICP-MS	[58, 73–78]
	Beer, wine	Metals		
Biology and clinic	Hen egg	Al, As, Pb, Cd, Hg, Sb		
	Urine, blood, brain tissue, liver, breast milk, bone, oyster/tuna tissue, bacteria	Cr, Ni, Cu		
	Blood	Al		
	Brain tissue	Cu	ICP-OES, ICP-MS, AAS	[79–86]
	Liver	Se		
	Breast milk	Ni		
	Bone	B, P, S		
	Oyster, tuna	Trace elements	ICP-MS	[87–89]
Organics	DNA, proteins			
	Petroleum products, lubricating oils, gasoline	Trace metals		
	Cooking oils	Cu, Fe, Ni, P, Si, V	ICP-MS, ICP-OES	[90–93]
	Antifreeze	Major and trace elements		

and air particles, ensuring accurate elemental analysis by ICP-OES. It is common for water samples to be filtered or diluted when dealing with high concentrations of analytes. ICP-OES is widely used for water quality monitoring, as the levels of lead, mercury, arsenic, and cadmium are critical indicators of water safety and environmental health. This technique is also valuable for determining the concentration of heavy metals and nutrients in soils and sediments, which is essential for agricultural management and ensuring the health of ecosystems. By accurately measuring these elements, ICP-OES helps in managing contamination risks and improving soil and water quality. ICP-OES can be used not only to determine water and soil pollution, but also to measure air quality by quantifying pollutants in the air. Suzuki [96] analyzed airborne particles and trace metals deposited on tree bark using ICP-OES. In this experiment, the accumulated particles were prepared by

microwave-assisted HNO_3 digestion. Additionally, other researchers have used a natural herb (*Struthanthus flexicaulis*) to detect air pollution. Their experiment proved successful, as higher levels of lead and copper were detected in polluted areas, demonstrating that this herb can be used as a biomonitor for air pollution [97].

4.2 Agriculture and food industry

Metal contamination in groundwater and air is a serious concern for public health, environmental management and food safety. Therefore, metal analysis in plants and animals is essential for ecotoxicological studies [98], as it helps to assess the impact of heavy metals on ecosystems and the potential risks to human health through the food chain. ICP-OES plays an important role in agriculture, particularly in the analysis of fertilizers, plant tissue, pesticides, herbicides, irrigation water or even food.

In this industry, ICP-OES is used to determine soil concentrations of essential nutrients, such as nitrogen, phosphorus, potassium and trace elements. This analysis helps to assess soil fertility and plan appropriate fertilization strategies. As part of quality control, manufacturers use ICP-OES to ensure that fertilizers contain nutrients in the correct ratio as indicated on the label, ensuring their effectiveness and safety. This process also guarantees the effectiveness and safety of fertilizers used by farmers, and that they meet agricultural standards. Furthermore, ICP-OES provides detailed information on the elemental composition of fertilizers, aiding in the development of more effective and balanced fertilizer formulations [99].

It is also important in plant tissues analysis. In this case, the plant nutrient uptake can be determined in order to optimize fertilization strategies. Nutrient uptake determined by analyzing plant tissues is crucial for adjusting fertilization practices to optimize crop growth and yield. ICP-OES helps to understand how well plants absorb nutrients from the soil [58]. In addition, it helps diagnose nutrient deficiencies or toxicity in plants allowing timely intervention to these problems and prevent yield loss. It can detect potentially harmful elements in soil, such as heavy metals (lead, cadmium, mercury) that can affect crop health and food safety [100]. This technique detects and quantifies residues of pesticides, herbicides and other chemicals in agricultural products, ensuring that they remain within safe consumption limits [78]. In addition, it analyzes the trace element content of crops and food products, which is important for nutritional labeling and food quality control. It is not only suitable for the analysis of fertilizers, plants and food but also for the analysis of irrigation water. ICP-OES is used to monitor irrigation water quality by detecting elements that can affect soil and crop health, such as sodium, chloride, calcium, magnesium and potentially toxic metals. It helps measure water salinity and hardness, which are critical factors in maintaining soil health and crop yield. It can help in investigating the interactions between soil properties and plant nutrient uptake, providing insights for sustainable agricultural practices [73].

4.3 Applications in the biological, medical and pharmaceutical fields

ICP-OES is an essential tool in biological sciences, facilitating a wide range of studies from clinical diagnostics to environmental biology. Today, humans are exposed to most of the toxic and heavy metals that come from many sources, namely the burning of coal, natural gas, and petroleum, as

well as the burning of waste worldwide. ICP-OES is used to measure essential minerals and trace elements, such as calcium, magnesium, iron, zinc and copper in tissues and organs. However, it also detects toxic metals, such as lead, mercury, cadmium and arsenic in biological tissues, aiding environmental exposure and toxicity studies. Therefore, the accurate and precise determination of these elements in bodily fluids and tissues is extremely important [101–103]. Several diagnostic and therapeutic studies on health issues necessitate quantifying the accumulation of trace metals in biological tissues. In these issues ICP-OES was used for the identification and quantification of elemental biomarkers associated with various diseases, such as reduced immune efficiency, heart diseases, fetal abnormalities, gastrointestinal cancer, redox reactions, cellular energy processes and abnormal neurological activity patterns [104, 105]. It is used to monitor metal-based drug treatments, such as platinum-based chemotherapy agents, by measuring their levels in tissues and body fluids [40].

By analyzing blood, urine and other biological samples, ICP-OES can determine the effect of diet on the body's mineral status. This is crucial for studying nutritional deficiencies or excesses. It helps to understand how different elements are metabolized and utilized in the body, providing insight into metabolic pathways and disorders [80].

Determination of the accumulation of metals in various organisms is an essential information for assessing ecological risks and impact of contaminations. The technique can analyze the elemental composition of cells and subcellular components, providing insights into cellular functions and elemental homeostasis. Also can be used to measure metalloproteins and the role of metal ions in enzymatic activities and structural functions within cells [106]. The detection and quantification of elemental impurities in pharmaceuticals is critical to patient safety. Regulatory guidelines, such as ICH Q3D and USP <232> [107] and <233> [108] set strict limits for allowable levels of elemental contaminants, such as arsenic, lead, cadmium and mercury. ICP-OES is widely used to ensure that pharmaceutical products meet these regulatory specifications, helping to minimize the risk of toxicity and ensuring the safety and quality of the medications.

The ICP-OES provides greater sensitivity, lower detection limits, it causes less chemical interference and is less time consuming compared to other spectrometric techniques. ICP provides continuous wavelength coverage and gives more accurate results. Robust plasma in ICP-OES provides reliable and reproducible results even for the

most complex matrix. Simultaneous multielement analysis increases performance and productivity [109].

4.3.1 Raw materials

ICP-OES is used to determine the presence of beneficial or required elements in raw materials. For instance, certain APIs or excipients might require specific mineral content for their stability or efficacy. ICP-OES helps verify that these elements are within the desired range. APIs must have a precise elemental composition to ensure their pharmacological activity and stability.

This technique provides detailed information on the elemental profile of APIs, helping in the characterization and quality control of these critical components. During the synthesis of APIs, impurities from reagents, catalysts or reaction vessels can be introduced [13, 14]. These are times when impurities are introduced directly into the product, e.g., in the form of a catalyst during the production process. In some cases, these elements cannot be completely removed after synthesis. In many articles, atomic spectrometric methods are used to detect and quantify catalysts (osmium, palladium, platinum, rhodium, ruthenium and tungsten) [45–47, 53, 110, 111]. Other contaminations are associated with materials during the process in equipment and on any surface (usually metal) in direct contact with the API or commercial product. Corrosion,

extraction/leaching or delamination may occur if inappropriate materials were used [14, 16]. This could be the case for contamination by aluminum from glass [112], zinc from plastic [113] and rubber materials [114], and aluminum, arsenic and tungsten from glass syringe container closure systems [115]. Another source of elemental contamination is associated with the use of inadequate water purification systems. It is used in many processes, from synthesis to manufacturing, so the product may contain some degree of contamination that is sometimes difficult to detect. Impurities must be kept below the detection limit ensuring that the APIs meet the purity standards [2, 3].

In addition to all this, it should also be taken into account that pharmaceutical companies purchase raw materials from various suppliers. This technique is also used to evaluate and qualify suppliers by analyzing the elemental composition of their materials. This ensures consistency and quality between different lots and suppliers.

In the pharmaceutical industry, starting samples typically refer to raw materials such as excipients and APIs (Table 2) [13, 50, 113, 114, 116–123]. These components must meet strict purity standards to ensure that the final drug products are safe. Contaminants or impurities in starting samples can lead to adverse health effects, reduced drug efficacy, and regulatory non-compliance [1].

Table 2 ICP-based techniques used in pharmaceutical industry*

Sample	Elements	Coupled technique	Ref.
Choline citrate, betaine and racemethionine			
Dipyron monohydrate	Ag, As, Au, Ba, Cd, Co, Cr, Cu, Hg, Ir, Li, Mo, Ni, Pb, Pd, Pt, Rh, Ru, Sb, Se, Sn, Tl, V	ICP-OES	[116]
Dexchlorpheniramine maleate			
Paracetamol			
Amitriptyline hydrochloride	As, Cd, Hg, Pb	ICP-OES	[50]
Carbamazepine			
Imipramine hydrochloride			
Levothyroxine sodium			
Gestodene and ethinylestradiol			
APIs			
Sodium dipyron	As, Cd, Hg, Pb	ICP-OES, ICP-MS	[117]
Orphenadrine citrate			
Monohydrated dipyron			
Caffeine anhydrous			
Diclofenac sodium			
Paracetamol			
Carisoprodol			
Metformin hydrochloride	Cd, Pb, Hg, As, Co, V, Ni	ICP-OES	[118]
Losartan potassium			
Ibuprofen (gel, tablet, suspension)			

* See the resolution of method acronyms in the Nomenclature

Table 2 ICP-based techniques used in pharmaceutical industry (continued)*

Sample		Elements	Coupled technique	Ref.
Intravenous solutions		Zn, Cu, Se	AES	[114]
Enantiomeric impurities	Levofloxacin	S-isomeric form		
	Ofloxacin	R-isomeric form		
	Esomeprazole	S-omeprazole		
	Levalbuterol	R-albuterol		
Organic impurities		Oxidative degradation		
		Decarboxylation		
		Hydrolysis		
Inorganic impurities		Reagents, ligands, catalysis	NMR, Raman, LC-MS, LC-NMR,	
		Heavy metals	LC-NMRMS,	[13, 113]
		Filter aids, charcoal	GC-MS, LC-MS, ICP-OES	
		Crystallization related impurities		
		Stereochemistry related impurities		
In-process production impurities		Solvents remain after processing		
		Synthetic intermediates and by-products		
		Impurities from storage		
		Metal impurities		
		Leachables/extractables (plastic tubing process)		
Excipients	Modified cellulose			
	Calcium carbonate	Cl	ICP-OES, ICP-MS	[117, 119]
	Maltodextrin			
Herbal medicines	Hypericum perforatum leaves and flowers, their teas, tinctures and tablets	Cd, Co, Pb Al, Cr, Fe, V	ETAAS ICP-OES-USN	[120]
	Shampoo, shampoo and conditioner, sunscreen, anti-wrinkle day cream, day cream, facial serum, night cream, toothpaste, lip balm	Ti, Al, Zn, Fe, Si, Ca, K, P	ICP-MS, ICP-OES, SP-ICP-MS,	[121]
Cosmetics	Lipstick	Al, Cd, Cr, Co, Cu, Ni, Pb, Fe, Sb, Mn, Zn	ICP-OES	[122]
	Soaps	Al, As, Bi, Cd, Co, Cr, Cs, Hg, Li, Mo, Sb, Se, Se, V, B, Cu, Ni, Pb, Sr, Ba, Na, Ti, Fe, Ca, Mg, Mn, K, P	ICP-OES	[123]

* See the resolution of method acronyms in the Nomenclature

4.3.2 Dosage forms

Solid dosage forms

Solid samples in the pharmaceutical industry include a variety of forms, such as powders, dry powder inhalers, tablets, capsules and granules, pellets, nanofibers, films. These samples must be thoroughly analyzed to detect and quantify elemental impurities and ensure compliance with regulatory standards. Contaminants in solid samples can affect the quality and performance of the final product, potentially leading to adverse health effects and regulatory noncompliance. One of the key steps in analyzing solid samples is proper sample preparation. Any sample must be converted into a form that can be introduced into the plasma. Solid samples typically require extraction

or digestion before injection [124]. Different digestion processes are used, such as tube dry ashing, wet ashing, microwave assisted digestion (MAD), high pressure asher (HPA) digestion. Samples are prepared in a closed vessel, as this shortens the digestion time and releases less caustic material than in an open vessel [125–127]. During dry ashing the sample is heated to a high temperature to convert it into ash, which can result in the decomposition of organic components of the sample. This can sometimes lead to the loss of volatile elements (Hg, As, Se, Cd, etc.) which can cause inaccurate results [128, 129]. In addition, using this method there is a potential for contamination from crucible or furnace, environment, tubes or during transfer [128]. This can affect the accuracy of trace metal

analysis, especially when dealing with very low levels of contamination in pharmaceutical samples. Furthermore, this method can be time-consuming because of the heating [129] and this can be disadvantage in pharmaceutical industry where rapid testing is crucial. Because of these reasons the use of dry ashing method in the pharmaceutical industry is limited and therefore this method is less commonly used. Many APIs or sensitive products are very hard to digest even under extreme temperature and pressure conditions. It is important to consider the vessels capacity, since in closed vessels the sample mass is generally limited to approximately 500 mg, in contrast to open vessels which can hold even 1 g or more [130]. Treatment of the substances with oxidizing reagents by conventional heating or microwave radiation is the most common way to digest the matrix. This approach is known as wet digestion and has been applied to almost all matrices. Wet digestion of organic matrices is mainly done with oxidizing acids. Nitric acid is the most commonly used, because of its adequate oxidizing capacity. A mixture of HNO_3 with HCl , HF , HClO_4 , H_3PO_4 and H_2SO_3 are also used depending on the matrix, analytes and/or digestion system [130].

In 1975, Abu-Samra et al. described the use of microwave energy to rapidly complete acid-assisted wet digestion [131]. Since then, microwave heating has become a well-established technique for sample digestion [132]. Microwave digestion is an advanced sample preparation technique used to rapidly and efficiently break down complex samples, especially for the determination of trace elements by analytical methods such as ICP-OES and ICP-MS. This method uses microwave energy to heat and digest samples in an open/closed vessel system, often using concentrated acids at high pressure and temperature. The process is widely used in industries such as pharmaceuticals [63], environmental analysis [133], food testing [134] and biotechnology [135]. The principle behind this method is based on the interaction of microwave energy with polar molecules, primarily water and acid solutions in the samples. The polar molecules absorb microwave energy, causing them to vibrate which generates heat. The heat is then transferred to the sample, leading to the decomposition of organic matter and the breakdown of chemical bonds. Although open-vessel microwave wet digestion is popular, they have several disadvantages like dry ashing. In particular, the digestion temperature is restricted to the boiling point of the acids used, which can limit the effectiveness of the process [136, 137]. In contrast, the higher temperatures achievable in closed-vessel systems enhance the oxidative

strength of mineral acids, enabling more effective breakdown of matrix components [132]. This method is capable of complete digestion of complex matrices with minimal contamination and low analyte loss. In closed-vessel microwave digestion a small amount of sample is placed in a high-pressure vessel (also known as a "bomb" or autoclave) with concentrated acids (typically nitric acid, sometimes mixed with hydrochloric acid, hydrofluoric acid or perchloric acid) which are then heated with microwave energy. The pressure and temperature can reach 100 bar (1450 psi) and 200–300 °C, allowing the digestion of very tough organic compounds, pharmaceuticals and plant/animal tissues. The vessels are made of teflon (PTFE), perfluoro- and polyfluoroalkyl (PFA) or quartz, housed in a strong outer casing (usually stainless steel or ceramic) [132, 138], which can withstand the elevated temperatures and pressures during the digestion process. After the digestion the vessels are rapidly cooled to bring the temperature and pressure back to safe levels, preventing samples loss or contamination. The closed system prevents the loss of volatile element (As, Hg, Se etc.) unlike the previously mentioned dry ashing. All in addition it has a lower risk of contamination because of the closed vessel. It is a quick method (20–60 min) and it is safer and more environmentally friendly due to low acid requirement [139]. Widely accepted by pharmacopoeias (e.g., USP <233> [108], ICH Q3D [140]) for elemental impurity analysis [141].

The fusion technique can be used for inorganic solid forms, and a molten mixture can be formed by heating. Once cooled, the solidified melt is dissolved in dilute acid to produce a solution suitable for ICP-OES analysis. Although less common, some ICP-OES instruments are equipped with accessories for direct solid sampling, which can analyze the solid material without the need for complete dissolution. However, this method may be limited by sensitivity and matrix effects [142].

Semisolid dosage forms

Semisolid formulations, like ointments and creams are an essential class of pharmaceutical products, providing targeted delivery of medications for a variety of therapeutic purposes. Various analytical techniques are employed in the pharmaceutical industry to assess the quality and safety of semisolid formulations. One important technique is ICP-OES, which is used to detect and quantify elemental impurities in this type of material. Other techniques, such as chromatography, spectroscopy, and rheology testing, are also used to assess the chemical composition, stability, and

physical properties. ICP-OES is also a powerful method for detecting trace elements in these dosage forms. Since these products can be more challenging to analyze than liquids, sample preparation techniques, like microwave digestion or acid digestion are often required to break down the sample matrix to release the elements into solution. Musazzi et al. [143] investigated the effect on skin penetration of a semisolid preparation containing iron oxide nanoparticles. Samples collected from a Franz diffusion cell were analyzed and quantified for nanoparticles using ICP-OES. A similar Vertical Franz diffusion cell was used by Berenguer et al. to investigate the semisolid dosage form of meglumine antimoniate, where the toxic effect of the preparation on cell line was investigated by ICP-OES [144].

Liquid formulations

Liquid dosage forms are commonly used due to their ease of administration and rapid absorption. As the presence of elemental impurities can affect their safety and effectiveness, rigorous testing of these forms is crucial to prevent adverse health effects and to ensure regulatory compliance. Raw materials used in liquid formulations, including solvents and excipients, must be of high purity. ICP-OES is used to analyze these materials to ensure they do not introduce harmful elemental impurities into the final product. Jancevska et al. [118] used microwave-assisted digestion (tablets, gel) of Ibuprofen and analyzed with ICP-OES.

For liquid dosage forms the most common sample preparation procedure is the dilution, which helps to adjust the appropriate concentration level, thus minimizing matrix effects. It is important to use high-purity deionized water or other appropriate solvents to dilute the sample. If the sample has very high concentrations of certain elements, serial dilution can also be performed. It can be

important to use acids (usually nitric acid or hydrochloric acid) to stabilize the elements in the solution and improve the atomization process.

Since most APIs are organic substances, combustion methods can be very convenient for digesting samples, considering that they practically allow for the complete destruction of the matrix, reducing carbon effects in ICP-based analyses. The reaction mainly produces CO₂ and H₂O, along with the inorganic residue (ash), which is typically solubilized with diluted reagents before analysis. Moreover, since oxygen is usually the only necessary oxidizing reagent, the interferences associated with the use of concentrated acids are significantly reduced [145]. This method is very simple and used for the preparation of high sample mass (max. 10 g) of organic samples, and it does not require vessels [146].

Another option is to dissolve the samples directly in a solvent before injecting them. By using this approach, treatment time can be reduced, which reduces the chance of cross-contamination. The samples are usually dissolved in an aqueous medium with dilute acid solution (HCl or HNO₃ solutions). To minimize the interference, the sample mass is limited to a few milligrams (10–100 mg). This limit gives better LOD but reduces the input organic matter content the plasma [54, 55]. However, many APIs are insoluble in water, so this method cannot be used, but the dissolution in organic solvents can be considered a complementary approach. Before the sample is injected, a syringe filter or membrane filter with the appropriate pore size can be useful to remove particles that could clog the nebulizer or interfere with the analysis. Table 3 shows the applications of ICP-based techniques for different dosage form [20, 116, 118, 147–163].

Table 3 ICP-based techniques used in pharmaceutical industry*

Formulation	Ingredient/analyte	ICP technique	Reason	Ref.
Titan based dental implants	Titan	ICP-OES, ICP-MS	Titanium found in peri-implant tissues has been shown to be located alongside elements regarded as impurities in biomedical alloys.	[147]
Ibuprofen 200 mg/5mL oral suspension	Ibuprofen	ICP-OES	Quantitative analysis of multi-element solutions in different pharmaceutical dosage forms of ibuprofen	[118]
Ibuprofen 400 mg film coated tablets	Ibuprofen			
Ibuprofen 50 mg/g gel	Ibuprofen			
Parenteral drugs	Metamizole magnesium	DES-based DLLME-ICP OES	Eco-friendly, sensitive method meeting the green analytical principle	[148]
	Diclofenac sodium			
	Dexketoprofen			
Children's cough syrup		MIP OES	SDA-MIP OES is an efficient alternative tool for the accurate analysis of pharmaceuticals.	[149]

* See the resolution of method acronyms in the Nomenclature

Table 3 ICP-based techniques used in pharmaceutical industry (continued)*

Formulation	Ingredient/analyte	ICP technique	Reason	Ref.
Selenium Sulfide Topical Suspension	Selenium sulfide	MIP OES	This method can be applied to numerous matrices for a finished dosage of selenium sulfide formulations.	[150]
Moisturizing creams	Silver	SP-ICP-MS	ICP-MS instrumentation has allowed the determination of Ag NPs of small size (lower than 40 nm) in complex samples	[151]
Natural cough syrup for infants	Plant extracts	ICP-OES	Both products and medicinal herbs are currently prescribed by pediatricians	[152]
Natural cough elixir for infants	Plant extracts			
Natural flu drops for infants	Plant extracts			
Escitalopram Oxalate drug	Escitalopram oxalate	ICP-OES	Method was developed and validated for the estimation of Co, Mg and Zn in escitalopram oxalate drug and in other drug substance	[153]
Multivitamin tablets (Supradyn, Pharma-ton)	Fe, Cu, Mn and Zn	ICP-OES	Compare them with the reference values given in their prospectus	[154]
Liquid pharmaceutical samples	Choline citrate, betaine and racemethionine	ICP-OES	The dilute-and-shoot method is a straightforward, cost-effective, and faster alternative to traditional sample preparation techniques, such as microwave-assisted digestion. This approach can be readily applied in pharmaceutical laboratories for monitoring elemental impurities in liquid medications.	[116]
	Dipyrrone monohydrate			
	Dexchlorpheniramine maleate			
	Paracetamol			
Cleaning validation swabs	Lithium	ICP-AES	Certain analytes can be more efficiently monitored using atomic spectroscopy. The lithium concentration on equipment can be quickly, easily and accurately measured using ICP-AES, with filter flags as an alternative to cotton swabs.	[155]
Bulk drug substance and intermediates	Tungsten	ICP-MS, ICP-AES	Determination of tungsten in bulk drug substance and intermediates, precisely, accurately and rapidly	[156]
Antibiotics (solution for injection)	Clarithromycin	ICP-AES	No sample pretreatment is needed, thus the method is convenient for routine and quantitative analysis of antibiotics in powder forms.	[20]
	Cefadroxil			
	Cefaclor			
	Amoxicillin			
Pharmaceutical Neusilin-based tablets		LA-ICP-MS and LA-ICP-AES	The relative standard deviation is better with ratios signals and with continuous scanning	[157]
Drug samples in tablet form	Miscellaneous	ICP-OES, ICP-MS	Compare the analyte concentration by different digestion procedure by ICP-OES and ICP-MS	[158]
Captopril-HCT 25/12.5 mg tablets	Captopril and hydrochloro-thiazide	ICP-MS, ICP-OES, GFAAS, CVAAS, HGAAS	They check that the impurities present in the products on the market meet the requirements	[159]
Captopril 50 mg tablet				
Benazepril-HCT 20/25 mg tablet	Benazepril HCl and hydrochloro- thiazide			
Quinapril 20 mg tablet	Quinapril HCl			
Silver-based nanomedicines	Silver	ICP-MS	Little is known about the stability of nanoparticles in relation to particle surface charge.	[160]
Suppositories	Hydroalcoholic extract-based Lawsonia inermis L. (henna) leaves	ICP-OES	Henna leaf extract suppositories may be proposed as a superior alternative to various conventional antimicrobial vaginal products currently available on the market.	[161]
Green nanoemulsions	Erythromycin	ICP-OES	Effluent released into an aquatic system negatively impacts the health of both the flora and fauna in the ecosystem, as well as human health.	[162]
AF-NP composite gel	Auranofin	ICP-OES	Topical treatment offers potential benefits	[163]

* See the resolution of method acronyms in the Nomenclature

5 Case study

Our aim was to use the applicability of ICP-OES in *in vitro* drug release studies where sodium acts as the salt form of

the active substance in the dosage form (pellets or medicated straw). Unfortunately, there was no opportunity to utilize the best feature of ICP-OES, namely that it can

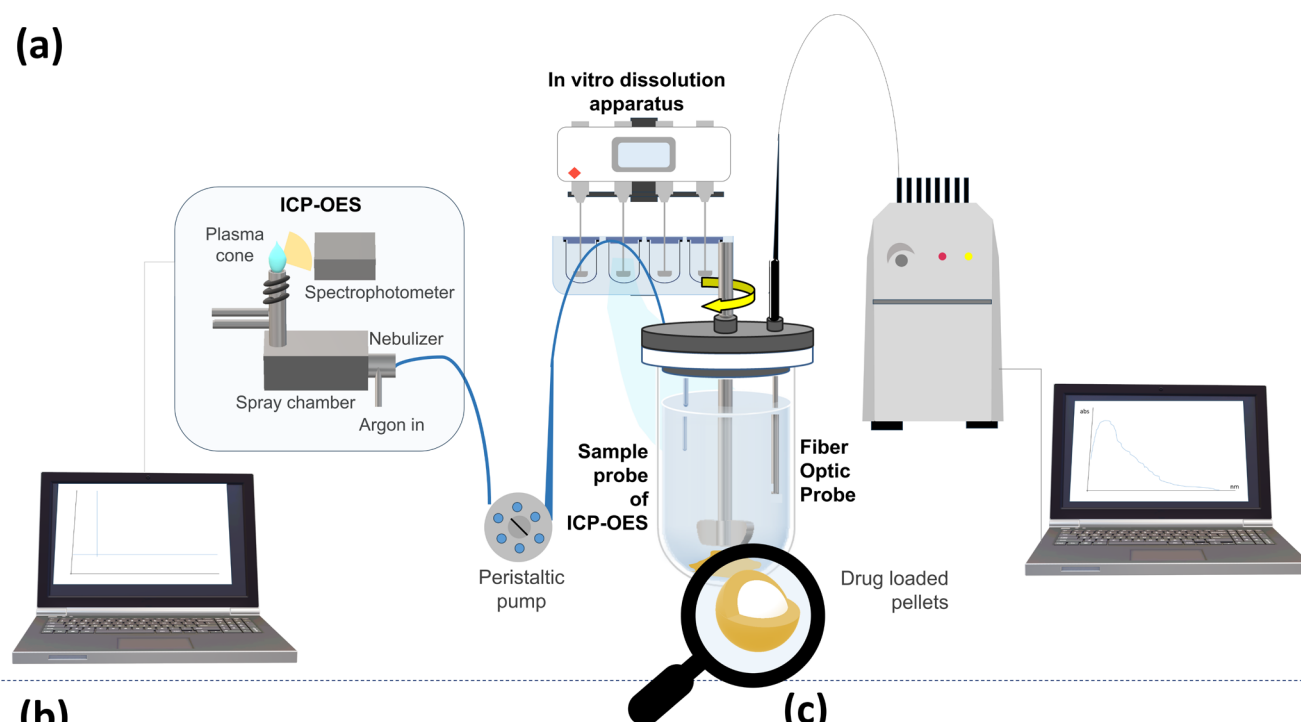
measure multiple components simultaneously, instead ibuprofen sodium was selected as a model compound. For this purpose, ibuprofen sodium (Sigma Aldrich, Bangalore, India) was coated onto inert pellet cores (Hanns G. Werner GmbH+Co.KG, Tornesch, Germany) through a fluidization process with 2% hypromellose as the binder.

The release profile of the ibuprofen sodium-containing pellets was investigated in a Hanson Vision Elite 8 apparatus (Hanson Research, Chatsworth, CA, USA) using the basket method. A dissolution medium of 900 mL purified water at 37 °C was used. Pion Rainbow, a fiber optic spectrophotometer (Pion Inc., Billerica, MA, USA), was used to determine the concentration of the dissolved drug *in situ*. For this purpose, a head fitted with a 5 mm probe was used. The absorbance was detected at 273 nm [6]. To determine the sodium concentration *in situ*, Spectro Genesis ICP-OES (Spectro Anal. Ins. GmbH, Kleve, Germany) was employed using the parameters outlined in Table 4. The results showed that the two measurement methods yielded similar results for immediate release pellets (Fig. 2).

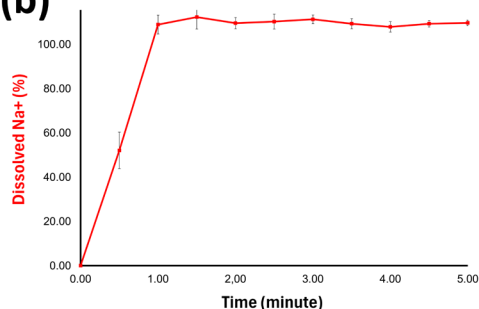
Table 4 ICP-OES settings

Parameters	Settings
Radio frequency power	1350 W
Auxiliary Ar flow rate	0.80 l/min
Pneumatic nebulizer Ar flow rate	0.85 l/min
Pump speed	2 step
Wavelengths	589.59 nm
Coolant flow	0.80 l/min
Light tube	0.90 l/min
Optic flush	1.00 l/min
Optic temperature	29.91 °C (29.0–31.0 °C)
Osc. exhaust	222.2 imp/s (min 170.0)
Osc. impedance	5875 Ohms
HVPS current	583 mA
HVPS voltage	3425 V
Flow optic flush	1.00 L/min
Flow light tube	0.90 L/min (0.8–1.8)
Nebulizer pressure	2.48 bar (2.0–4.0)
Main Ar pressure	7.01 bar (6.0–8.0)

(a)



(b)



(c)

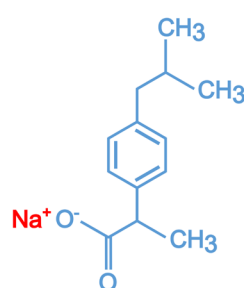
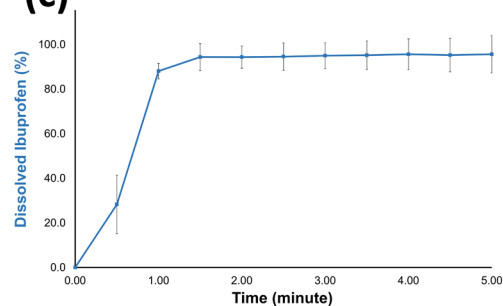


Fig. 2 Schematic drawing of in situ UV fiber optics and ICP-OES methods for dissolution testing measurements of pellets (a) sodium ion (b) and propionic acid derivate (c) release profile of layered pellets ($n = 3$)

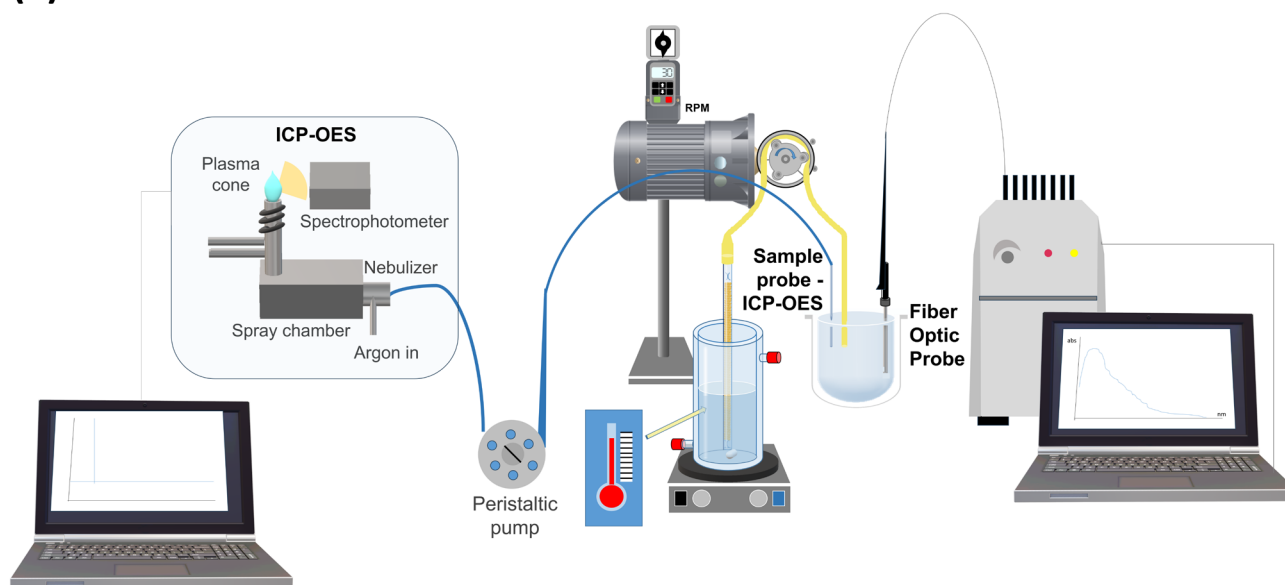
Straws were produced as a dosage form using small spherical particles. The pharmacopoeia does not provide a specific method for investigating pharmaceutical straws; however, several research groups have studied these drug forms [164, 165]. Accurately measured 1000 mg of pellets were filled into transparent PP-based straws (19 cm height, 0.9 cm diameter; VitaSip Kft., Cegléd, Hungary) and sealed using a custom-made straw-closing machine. Fig. 3 illustrates the measurement setup used to simulate straw usage. The medicated straw was placed in 250 mL of purified water, and the liquid was aspirated through the straw by a peristaltic pump (Locost Kft., Tiszaalpár, Hungary) into 250 mL of hydrochloric acid medium (pH 1.2, 37 °C), simulating stomach conditions. The concentrations of ibuprofen and sodium were determined using the same instruments and settings as those used for analyzing pellet release in this medium. Our results demonstrate that

ICP-OES with *in situ* sample probing, alongside the *in situ* Fiber Optic UV System, is an equally effective method for *in vitro* dissolution studies and the investigation of innovative drug forms such as medicated straws.

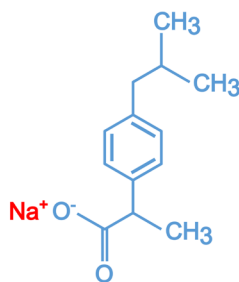
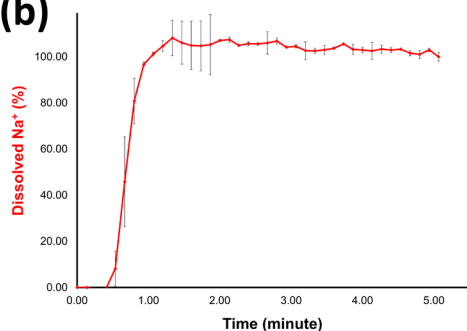
6 Conclusion

Over the last 50 years, ICP-OES became a key analytical technique with a wide range of applications across various scientific fields. Owing to its sensitivity, the elemental components can be detected even at ppm and ppb levels. This article primarily focuses on the pharmaceutical industry, where elements determined by IPC-OES may occur as impurities or as salts of active substances. Their qualitative and quantitative analysis in raw materials and dosage forms plays a crucial role in ensuring the safety and efficacy of pharmaceutical products.

(a)



(b)



(c)

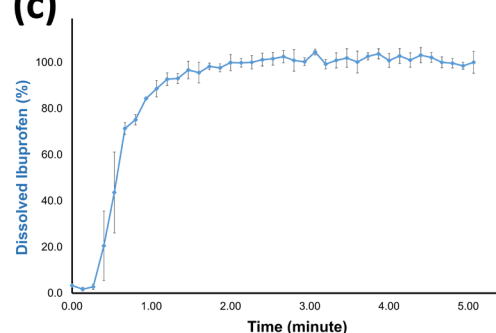


Fig. 3 Schematic drawing of the apparatus for simulating the sipping of liquid through the medicated straw (a) sodium ion (b) and propionic acid derivative (c) release profile from medicated straw ($n = 3$)

Nomenclature

AAS:	Atomic Absorption Spectrophotometry
AF-NP:	Auranofin-nanoparticle
CVAAS:	Cold Vapor Atomic Absorption Spectrometry
CVG-ICP-MS:	Chemical vapor generation inductively coupled plasma mass spectrometry
DES:	Deep Eutectic Solvent
DLLME-ICP-OES:	Dispersive Liquid-Liquid Microextraction Inductively Coupled Plasma Optical Emission Spectrometry
DRC-ICP-MS:	Dynamic Reaction Cell Inductively Coupled Plasma Mass Spectrometry
ETAAS:	Electrothermal Atomic Absorption Spectrometry
ETV-ICP-OES:	Electrothermal Vaporization Inductively Coupled Plasma Optical Emission Spectrometry
FI-ICP-MS:	Flow Injection Inductively Coupled Plasma Mass Spectrometry
FI-ICP/SF-MS:	Flow Injection Inductively Coupled Plasma/Sector Field Mass Spectrometry
GC:	Gas chromatography
GC-ICP-MS:	Gas Chromatography Inductively Coupled Plasma Mass Spectrometry
GC-MS:	Gas Chromatography Mass Spectrometry
GFAAS:	Graphite Furnace Atomic Absorption Spectrometry

HGAAS:	Hydride Generation Atomic Absorption Spectrometry
HPLC:	High Performance Liquid Chromatography
HPLC-ICP-MS:	High Performance Liquid Chromatography Inductively Coupled Plasma Mass Spectrometry
HVPS:	High Voltage Power Supply
ICP-OES-USN:	Inductively Coupled Plasma Optical Emission Spectrometry Ultrasonic Nebulizer
LA-ICP-MS:	Laser Ablation Inductively Coupled Plasma Mass Spectrometry
LA-ICP-AES:	Laser Ablation Inductively Coupled Plasma Atomic Emission Spectrometry
LC-MS:	Liquid Chromatography Mass Spectrometry
LC-NMR:	Liquid Chromatography Nuclear Magnetic Resonance
LC-NMR-MS:	Liquid Chromatography Nuclear Magnetic Resonance Mass Spectrometry
LIBS:	Laser-induced breakdown spectroscopy
MIP OES:	Microwave-induced Plasma Optical Emission Spectrometry
NMR:	Nuclear magnetic resonance
PTFE:	Polytetrafluoroethylene (teflon)
SF-MS:	Sector Field Mass Spectrometry
SP-ICP-MS:	Single Particle Inductively Coupled Plasma Mass Spectrometry

References

- [1] Ayre, A., Varpe, D., Nayak, R., Vasa, N. "Impurity Profiling of Pharmaceuticals", *Advance Research in Pharmaceuticals and Biologicals*, 1(2), pp. 76–90, 2011. [online] Available at: https://arastirmax.com/en/system/files/dergiler/160852/makaleler/1/2/arastrmx_160852_1_pp_76-90.pdf [Accessed: 26 January 2025]
- [2] Görög, S., Bajbák, M., Balogh, G., Brlik, J., Csehi, A., Dravecz, F., Gasdag, M., Horváth, P., Laukó, A., Varga, K. "Drug impurity profiling strategies", *Talanta*, 44(9), pp. 1517–1526, 1997. [https://doi.org/10.1016/S0039-9140\(96\)02179-0](https://doi.org/10.1016/S0039-9140(96)02179-0)
- [3] Warad, T. A., Bhusnure, O. G., Gholve, S. B. "Impurity Profile of Pharmaceuticals Ingredient: A Review", *Journal of Pharmacy Research*, 10(7), pp. 523–533, 2016. [online] Available at: https://www.researchgate.net/profile/Dr-Omprakash-Bhusnure/publication/306256352_Impurity_Profile_of_Pharmaceuticals_Ingredient_A_Review/links/57b5183508aeddbf36e6f64e/Impurity-Profile-of-Pharmaceuticals-Ingredient-A-Review.pdf [Accessed: 26 January 2025]
- [4] International Conference on Harmonisation "Draft Revised Guidance on Impurities in New Drug Substances", Food and Drug Administration, Washington, DC, USA, No. 00-18151, 2000. [online] Available at: <https://www.federalregister.gov/documents/2000/07/20/00-18151/international-conference-on-harmonisation-draft-revised-guidance-on-impurities-in-new-drug> [Accessed: 26 January 2025]
- [5] International Conference on Harmonisation "Draft Revised Guidance on Impurities in New Drug Products", Food and Drug Administration, Washington, DC, USA, No. 00-18150, 2000. [online] Available at: <https://www.federalregister.gov/documents/2000/07/19/00-18150/international-conference-on-harmonisation-draft-revised-guidance-on-impurities-in-new-drug-products> [Accessed: 26 January 2025]

- [6] International Conference on Harmonisation "Guidance on Impurities: Residual Solvents", Food and Drug Administration, Washington, DC, USA, No. 97-33639, 1997. [online] Available at: <https://www.federalregister.gov/documents/1997/12/24/97-33639/international-conference-on-harmonisation-guidance-on-impurities-residual-solvents> [Accessed: 26 January 2025]
- [7] Roy, J. "Pharmaceutical impurities—A mini-review", AAPS PharmSciTech, 3(2), 6, 2002. <https://doi.org/10.1208/pt030206>
- [8] Ahuja, S. "Impurities Evaluation of Pharmaceuticals", Marcel Dekker, 1998. ISBN 0824798848
- [9] Görög, S. (ed.) "Identification and Determination of Impurities in Drugs", Elsevier Science, 2000. ISBN 9780080534404
- [10] Ohls, K., Bogdain, B. "History of inductively coupled plasma atomic emission spectral analysis: from the beginning up to its coupling with mass spectrometry", Journal of Analytical Atomic Spectrometry, 31(1), pp. 22–31, 2016. <https://doi.org/10.1039/C5JA90043C>
- [11] Manousi, N., Zachariadis, G. A. "Development and Application of an ICP-AES Method for the Determination of Nutrient and Toxic Elements in Savory Snack Products after Autoclave Dissolution", Separations, 7(4), 66, 2020. <https://doi.org/10.3390/separations7040066>
- [12] Ghosh, S., Prasanna, V. L., Sowjanya, B., Srivani, P., Alagaraja, M., Banji, D. "Inductively Coupled Plasma – Optical Emission Spectroscopy: A Review", Asian Journal of Pharmaceutical Analysis, 3(1), pp. 24–33, 2013. [online] Available at: <https://ajpa-online.com/HTMLPaper.aspx?Journal=Asian%20Journal%20of%20Pharmaceutical%20Analysis;PID=2013-3-1-6> [Accessed: 26 January 2025]
- [13] Pilaniya, K., Chandrawanshi, H. K., Pilaniya, U., Manchandani, P., Jain, P., Singh, N. "Recent trends in the impurity profile of pharmaceuticals", Journal of Advanced Pharmaceutical Technology & Research, 1(3), pp. 302–310, 2010. <https://doi.org/10.4103/0110-5558.72422>
- [14] Iacocca, R. G., Toltl, N., Allgeier, M., Bustard, B., Dong, X., Foubert, M., Hofer, J., Peoples, S., Shelbourn, T. "Factors Affecting the Chemical Durability of Glass Used in the Pharmaceutical Industry", AAPS PharmSciTech, 11(3), pp. 1340–1349, 2010. <https://doi.org/10.1208/s12249-010-9506-9>
- [15] Dong, X., Iacocca, R. G., Bustard, B. L., Kemp, C. A. J. "Investigation of Stainless Steel Corrosion in Ultrahigh-Purity Water and Steam Systems by Surface Analytical Techniques", Journal of Materials Engineering and Performance, 19(1), pp. 135–141, 2010. <https://doi.org/10.1007/s11665-009-9430-x>
- [16] Iacocca, R. G., Allgeier, M. "Corrosive attack of glass by a pharmaceutical compound", Journal of Materials Science, 42(3), pp. 801–811, 2007. <https://doi.org/10.1007/s10853-006-0156-y>
- [17] Ahuja, S., Alsante, K. M. (eds.) "Volume 5: Handbook of Isolation and Characterization of Impurities in Pharmaceuticals", Elsevier Inc., 2004. ISBN 978-0-12-044982-8
- [18] Hanć, A., Komorowicz, I., Iskra, M., Majewski, W., Baralkiewicz, D. "Application of spectroscopic techniques: ICP-OES, LA-ICP-MS and chemometric methods for studying the relationships between trace elements in clinical samples from patients with atherosclerosis obliterans", Analytical and Bioanalytical Chemistry, 399(9), pp. 3221–3231, 2011. <https://doi.org/10.1007/s00216-011-4729-5>
- [19] Sims, J., Smith, A., Patel, D., Batchelor, R., Carreira, J. "Automated Sample Preparation for ICP Analysis of Active Pharmaceutical Ingredients and Intermediates", JALA: Journal of the Association for Laboratory Automation, 16(5), pp. 377–380, 2011. <https://doi.org/10.1016/j.jala.2010.10.006>
- [20] Zachariadis, G. A., Michos, C. E. "Development of a slurry introduction method for multi-element analysis of antibiotics by inductively coupled plasma atomic emission spectrometry using various types of spray chamber and nebulizer configurations", Journal of Pharmaceutical and Biomedical Analysis, 43(3), pp. 951–958, 2007. <https://doi.org/10.1016/j.jpba.2006.09.018>
- [21] Goncalves, D. A., Gu, J., dos Santos, M. C., Jones, B. T., Donati, G. L. "Direct determination of chromium in empty medicine capsules by tungsten coil atomic emission spectrometry", Journal of Analytical Atomic Spectrometry, 30(6), pp. 1395–1399, 2015. <https://doi.org/10.1039/C5JA00100E>
- [22] Correale, J., Chiquete, E., Milojevic, S., Frider, N., Bajusz, I. "Assessing the potential impact of non-proprietary drug copies on quality of medicine and treatment in patients with relapsing multiple sclerosis: the experience with fingolimod", Drug Design, Development and Therapy, 8, pp. 859–867, 2014. <https://doi.org/10.2147/DDDT.S66398>
- [23] Raghuram, P., Raju, I. V. S., Sriramulu, J. "Heavy metals testing in active pharmaceutical ingredients: an alternate approach", Pharmazie, 65(1), pp. 15–18, 2010. <https://doi.org/10.1691/ph.2010.9222>
- [24] Thiab, S., Wainwright, M., Riby, P. "The development of analytical procedures using ICP-OES and ICP-MS for the analysis of trace metals in pharmaceutical formulations", British Journal of Pharmacy, 2(2), pp. S2–S4, 2017. <https://doi.org/10.5920/bjpharm.2017.12>
- [25] Smichowski, P., Marrero, J., Gómez, D. "Inductively coupled plasma optical emission spectrometric determination of trace element in PM₁₀ airborne particulate matter collected in an industrial area of Argentina", Microchemical Journal, 80(1), pp. 9–17, 2005. <https://doi.org/10.1016/j.microc.2004.07.023>
- [26] Rodríguez Giraldo, Y., Rodríguez Sánchez, E., Torres, L. G., Montenegro, A. C., Pichimata, M. A. "Development of validation methods to determine cadmium in cocoa almond from the beans by ICP-MS and ICP-OES", Talanta Open, 5, 100078, 2022. <https://doi.org/10.1016/j.talo.2021.100078>
- [27] Karapınar, H. S. "Evaluation of some toxic metal levels in urban treatment waters", Avrupa Bilim Ve Teknoloji Dergisi, 21, pp. 301–306, 2021. <https://doi.org/10.31590/ejosat.771787>

- [28] Vogt, D., Vogt, T., Wolf, B., Neuroth, M., Otto, M. "Direct determination of organic and inorganic oxygen in coals from the Argonne Premium sample program by solid sampling electrothermal vaporization inductively coupled plasma optical emission spectrometry", *Fuel*, 196, pp. 185–194, 2017.
<https://doi.org/10.1016/j.fuel.2017.01.043>
- [29] Müller, A., Pozebon, D., Dressler, V. L. "Advances of nitrogen microwave plasma for optical emission spectrometry and applications in elemental analysis: a review", *Journal of Analytical Atomic Spectrometry*, 35(10), pp. 2113–2131, 2020.
<https://doi.org/10.1039/D0JA00272K>
- [30] Khan, K. F. "Application, principle and operation of ICP-OES in pharmaceutical analysis", *The Pharma Innovation Journal*, 8(11), pp. 281–282, 2019. [online] Available at: <https://www.thepharmajournal.com/archives/2019/vol8issue11/PartE/8-11-19-350.pdf> [Accessed: 26 January 2025]
- [31] Ido, K., Matsushita, R., Fujii, S.-I., Miyashita, S.-I., Umemura, T., Hokura, A., Inagaki, K. "Multiple-channel Concentric Grid Nebulizer for Online Standard Addition in Inductively Coupled Plasma Optical Emission Spectrometry", *Analytical Sciences*, 36(6), pp. 717–721, 2020.
<https://doi.org/10.2116/analsci.19P385>
- [32] Aziz, A., Broekaert, J. A. C., Laqua, K., Leis, F. "A study of direct analysis of solid samples using spark ablation combined with excitation in an inductively coupled plasma", *Spectrochimica Acta Part B: Atomic Spectroscopy*, 39(9–11), pp. 1091–1103, 1984.
[https://doi.org/10.1016/0584-8547\(84\)80195-0](https://doi.org/10.1016/0584-8547(84)80195-0)
- [33] Wellinger, M., Wochele, J., Biollaz, S. M. A., Ludwig, C. "Online elemental analysis of process gases with ICP-OES: A case study on waste wood combustion", *Waste Management*, 32(10), pp. 1843–1852, 2012.
<https://doi.org/10.1016/j.wasman.2012.05.015>
- [34] Mosqueda, Y., Pomares, M., Pérez-Cappe, E. L., Miranda, A., Fariñas, J. C., Larrea, M. T. "Determination of major, minor and trace elements in cobalt-substituted lithium nickelate ceramic powders by inductively coupled plasma optical emission spectrometry", *Analytical and Bioanalytical Chemistry*, 386(6), pp. 1855–1862, 2006.
<https://doi.org/10.1007/s00216-006-0788-4>
- [35] Hill, S. J. (ed.) "Inductively Coupled Plasma Spectrometry and its Applications", Blackwell Publishing Ltd, 2006. ISBN 9781405135948
<https://doi.org/10.1002/9780470988794>
- [36] Barnard, T. W., Crockett, M. I., Ivaldi, J. C., Lundberg, P. L., Yates, D. A., Levine, P. A., Sauer, D. J. "Solid-state detector for ICP-OES", *Analytical Chemistry*, 65(9), pp. 1231–1239, 1993.
<https://doi.org/10.1021/ac00057a021>
- [37] Trevizan, L. C., Nóbrega, J. A. "Inductively coupled plasma optical emission spectrometry with axially viewed configuration: an overview of applications", *Journal of the Brazilian Chemical Society*, 18(4), pp. 678–690, 2007.
<https://doi.org/10.1590/S0103-50532007000400003>
- [38] Silva, J. C. J., Baccan, N., Nóbrega, J. A. "Analytical Performance of an Inductively Coupled Plasma Optical Emission Spectrometry with Dual View Configuration", *Journal of the Brazilian Chemical Society*, 14(2), pp. 310–315, 2003.
<https://doi.org/10.1590/S0103-50532003000200020>
- [39] Kroukamp, E. M., Wondimu, T., Forbes, P. B. C. "Metal and metalloid speciation in plants: Overview, instrumentation, approaches and commonly assessed elements", *TrAC Trends in Analytical Chemistry*, 77, pp. 87–99, 2016.
<https://doi.org/10.1016/j.trac.2015.10.007>
- [40] Barin, J. S., Mello, P. A., Mesko, M. F., Duarte, F. A., Flores, E. M. M. "Determination of elemental impurities in pharmaceutical products and related matrices by ICP-based methods: a review", *Analytical and Bioanalytical Chemistry*, 408(17), pp. 4547–4566, 2016.
<https://doi.org/10.1007/s00216-016-9471-6>
- [41] Houk, R. S., Thompson, J. J. "Inductively coupled plasma mass spectrometry", *Mass Spectrometry Reviews*, 7(4), pp. 425–461, 1988.
<https://doi.org/10.1002/mas.1280070404>
- [42] Nölte, J. "ICP Emission Spectrometry: A Practical Guide", WILEY-VCH GmbH., 2021. ISBN 9783527346578
<https://doi.org/10.1002/9783527346578>
- [43] Reddy, D. N., Al-Rajab, A. J., Reddy, G. R. "Biomedical and Pharmaceutical Applications of Inductively Coupled Plasma-Mass Spectrometry (ICP-MS)", In: Bobbarala, V. (ed.) *Drug Discovery - Concepts to Market*, InTechOpen, 2018, pp. 131–144. ISBN 978-1-78923-697-2
<https://doi.org/10.5772/intechopen.74787>
- [44] Nageswara Rao, R., Kumar Talluri, M. V. N. "An overview of recent applications of inductively coupled plasma-mass spectrometry (ICP-MS) in determination of inorganic impurities in drugs and pharmaceuticals", *Journal of Pharmaceutical and Biomedical Analysis*, 43(1), pp. 1–13, 2007.
<https://doi.org/10.1016/j.jpba.2006.07.004>
- [45] Antes, F. G., Mesko, M. F., Barin, J. S., Moreira, C. M., Flores, É. M. M., Dressler, V. L. "Development of multi-elemental method for quality control of parenteral component solutions using ICP-MS", *Microchemical Journal*, 98(1), pp. 144–149, 2011.
<https://doi.org/10.1016/j.microc.2010.12.010>
- [46] Al-Ammar, A. S., Northington, J. "Accuracy improvement in the determination of palladium in pharmaceuticals by eliminating volatility error when using ICP-MS coupled with direct introduction of sample dissolved in organic solvents", *Journal of Analytical Atomic Spectrometry*, 26(7), pp. 1531–1533, 2011.
<https://doi.org/10.1039/c0ja00218f>
- [47] Muller, A. L. H., Oliveira, J. S. S., Mello, P. A., Muller, E. I., Flores, E. M. M. "Study and determination of elemental impurities by ICP-MS in active pharmaceutical ingredients using single reaction chamber digestion in compliance with USP requirements", *Talanta*, 136, pp. 161–169, 2015.
<https://doi.org/10.1016/j.talanta.2014.12.023>

- [48] Nam, K. H., Isensee, R., Infantino, G., Putyera, K., Wang, X. "Microwave-Induced Combustion for ICP-MS: A Generic Approach to Trace Elemental Analyses of Pharmaceutical Products", *Spectroscopy*, 26(4), pp. 2–7, 2011. [online] Available at: <https://www.spectroscopyonline.com/view/microwave-induced-combustion-icp-ms-generic-approach-trace-elemental-analyses-pharmaceutical-product> [Accessed: 26 January 2025]
- [49] Rudovica, V., Viksna, A., Actins, A. "Application of LA-ICP-MS as a rapid tool for analysis of elemental impurities in active pharmaceutical ingredients", *Journal of Pharmaceutical and Biomedical Analysis*, 91, pp. 119–122, 2014. <https://doi.org/10.1016/j.jpba.2013.12.025>
- [50] Barin, J. S., Tischer, B., Picoloto, R. S., Antes, F. G., da Silva, F. E. B., Paula, F. R., Flores, E. M. M. "Determination of toxic elements in tricyclic active pharmaceutical ingredients by ICP-MS: a critical study of digestion methods", *Journal of Analytical Atomic Spectrometry*, 29(2), pp. 352–358, 2014. <https://doi.org/10.1039/c3ja50334h>
- [51] Simitchiev, K., Stefanova, V., Kmetov, V., Andreev, G., Kovachev, N., Canals, A. "Microwave-assisted cloud point extraction of Rh, Pd and Pt with 2-mercaptobenzothiazole as preconcentration procedure prior to ICP-MS analysis of pharmaceutical products", *Journal of Analytical Atomic Spectrometry*, 23(5), pp. 717–726, 2008. <https://doi.org/10.1039/b715133k>
- [52] Kaczala, S., Costa, A. B., Posselt, E. L., Barin, J. S., Flores, E. M. M., Dressler, V. L. "Element Determination in Pharmaceuticals Using Direct Solid Analysis-Electrothermal Vaporization Inductively Coupled Plasma Optical Emission Spectrometry", *Journal of the Brazilian Chemical Society*, 26(3), pp. 475–483, 2015. <https://doi.org/10.5935/0103-5053.20150300>
- [53] Lin, M.-L., Jiang, S.-J. "Determination of trace Cr, Mo, Pd, Cd, Pt and Pb in drug tablets by ultrasonic slurry sampling electrothermal vaporization inductively coupled plasma mass spectrometry", *Journal of Analytical Atomic Spectrometry*, 26(9), pp. 1813–1818, 2011. <https://doi.org/10.1039/c1ja10100e>
- [54] Tu, Q., Wang, T., Welch, C. J. "High-throughput metal screening in pharmaceutical samples by ICP-MS with automated flow injection using a modified HPLC configuration", *Journal of Pharmaceutical and Biomedical Analysis*, 51(1), pp. 90–95, 2010. <https://doi.org/10.1016/j.jpba.2009.08.012>
- [55] Fischer, L., Zipfel, B., Koellensperger, G., Kovac, J., Bilz, S., Kunkel, A., Venzago, C., Hann, S. "Flow injection combined with ICP-MS for accurate high throughput analysis of elemental impurities in pharmaceutical products according to USP <232> / <233>", *Journal of Pharmaceutical and Biomedical Analysis*, 95, pp. 121–129, 2014. <https://doi.org/10.1016/j.jpba.2014.02.016>
- [56] Middlemost, E. A. K. "Rare earth element geochemistry: Paul Henderson (editor). Developments in geochemistry, vol. 2. Elsevier Science Publishers B.V., Amsterdam—Oxford—New York—Tokyo, 1984, xii + 510 pp., US \$84.75 (U.S.A. and Canada)/Dfl. 220.00 (rest of world) (hardcover)", *Chemical Geology*, 48(1–4), pp. 362–363, 1985. [https://doi.org/10.1016/0009-2541\(85\)90062-2](https://doi.org/10.1016/0009-2541(85)90062-2)
- [57] Whitfield, M. "Interactions between phytoplankton and trace metals in the ocean", In: Plön, S., Davy, S. K. (eds.) *Advances in Marine Biology*, Elsevier, 2001, pp. 1–128. ISBN 978-0-12-026141-3 [https://doi.org/10.1016/S0065-2881\(01\)41002-9](https://doi.org/10.1016/S0065-2881(01)41002-9)
- [58] Shaheen, M. E., Tawfik, W., Mankola, A. F., Gagnon, J. E., Fryer, B. J., El-Mekawy, F. M. "Assessment of contamination levels of heavy metals in the agricultural soils using ICP-OES", *Soil and Sediment Contamination: An International Journal*, 32(6), pp. 665–691, 2023. <https://doi.org/10.1080/15320383.2022.2123448>
- [59] Blixen Bang, B., Thiodjio Sendja, B., Medellín-Castillo, N. A., Loredó Portales, R., Labrada Delgado, G. J., Carranza Alvarez, C., Germain Hurbert, B. B., Leyva Ramos, R., Reyes López, S. Y. "Chemical speciation of lead adsorbed onto volcanic ashes by ICP-OES and XANES", *Suplemento de la Revista Mexicana de Física*, 3(1), 010602, 2022. <https://doi.org/10.31349/SuplRevMexFis.3.010602>
- [60] Widiastuti, E. L., Afifa, A. D., Tugiyono, T., Umar, S., Mumtazah, D. F., Hadi, S. "Plankton diversity and its heavy metal content in Ratai Bay of Pesawaran district, Lampung, Indonesia", *Journal of Water & Health*, 21(6), pp. 663–675, 2023. <https://doi.org/10.2166/wh.2023.209>
- [61] Rezić, I., Steffan, I. "ICP-OES determination of metals present in textile materials", *Microchemical Journal*, 85(1), pp. 46–51, 2007. <https://doi.org/10.1016/j.microc.2006.06.010>
- [62] Sanghapi, H. K., Ayyalasamayajula, K. K., Yueh, F. Y., Singh, J. P., McIntyre, D. L., Jain, J. C., Nakano, J. "Analysis of slags using laser-induced breakdown spectroscopy", *Spectrochimica Acta Part B: Atomic Spectroscopy*, 115, pp. 40–45, 2016. <https://doi.org/10.1016/j.sab.2015.10.009>
- [63] Saydut, A. "Microwave Acid Digestion for the Determination of Metals in Subbituminous Coal Bottom Ash by ICP-OES", *Energy Exploration & Exploitation*, 28(2), pp. 105–115, 2010. <https://doi.org/10.1260/0144-5987.28.2.105>
- [64] Jaron, I., Kudowska, B., Bulska, E. "Determination of Rare Earth Elements in Geological Samples by ICP-OES", *Atomic Spectroscopy*, 21(3), pp. 105–110, 2000.
- [65] Nuchdang, S., Injarean, U., Rattanaphra, D. "Evolution of rare earth elements, uranium and thorium in geological samples by ICP-OES and their characterization", *Journal of Physics: Conference Series*, 1285(1), 012025, 2019. <https://doi.org/10.1088/1742-6596/1285/1/012025>
- [66] Zhu, X., Lin, J., Gao, A., Wang, D., Zhu, M. "Simultaneous Determination of Rare Earth Elements in Aqueous Samples by Online Preconcentration System and Inductively Coupled Plasma Mass Spectrometry", *Atomic Spectroscopy*, 38(4), pp. 77–85, 2017. <https://doi.org/10.46770/AS.2017.04.001>
- [67] Petry, C. F., Pozebon, D., Bentlin, F. R. S. "Evaluation of ICP-OES Applicability for Trace Element Determination in Environmental Samples", *Atomic Spectroscopy*, 26(1), pp. 19–27, 2005. [online] Available at: https://www.researchgate.net/publication/344507853_Evaluation_of_ICP-OES_Applicability_for_Trace_Element_Determination_in_Environmental_Samples [Accessed: 26 January 2025]

- [68] Michalak, I., Chojnacka, K. "Multielemental analysis of macroalgae from the Baltic Sea by ICP-OES to monitor environmental pollution and assess their potential uses", *International Journal of Environmental Analytical Chemistry*, 89(8–12), pp. 583–596, 2009.
<https://doi.org/10.1080/03067310802627213>
- [69] Waqar, F., Jan, S., Mohammad, B., Hakim, M., Alam, S., Yawar, W. "Preconcentration of Rare Earth Elements in Seawater with Chelating Resin Having Fluorinated β -Diketone Immobilized on Styrene Divinyl Benzene for their Determination by ICP-OES", *Journal of the Chinese Chemical Society*, 56(2), pp. 335–340, 2009.
<https://doi.org/10.1002/jccs.200900049>
- [70] Abbasi, S., Keshavarzi, B., Moore, F., Hopke, P. K., Kelly, F. J., Dominguez, A. O. "Elemental and magnetic analyses, source identification, and oxidative potential of airborne, passive, and street dust particles in Asaluyeh County, Iran", *Science of The Total Environment*, 707, 136132, 2020.
<https://doi.org/10.1016/j.scitotenv.2019.136132>
- [71] Mujuru, M., McCrindle, R. I., Panichev, N. "Characterisation of coal slurries for introduction into ICP OES for multi-element determinations", *Journal of Analytical Atomic Spectrometry*, 24(4), pp. 494–501, 2009.
<https://doi.org/10.1039/b819963a>
- [72] Antes, F. G., Duarte, F. A., Mesko, M. F., Nunes, M. A. G., Pereira, V. A., Müller, E. I., Dressler, V. L., Flores, E. M. M. "Determination of toxic elements in coal by ICP-MS after digestion using microwave-induced combustion", *Talanta*, 83(2), pp. 364–369, 2010.
<https://doi.org/10.1016/j.talanta.2010.09.030>
- [73] Elsheikh, M. A. A., Hassan Mahmoud, M. H., Momen, A. A. "Determination of Selected Toxic Trace Elements in Agricultural Soil and Wells Water Samples by ICP-OES", *Oriental Journal of Chemistry*, 33(5), pp. 2263–2270, 2017.
<https://doi.org/10.13005/ojc/330514>
- [74] Chaves, E. S., dos Santos, E. J., Araujo, R. G. O., Oliveira, J. V., Frescura, V. L. A., Curtius, A. J. "Metals and phosphorus determination in vegetable seeds used in the production of biodiesel by ICP OES and ICP-MS", *Microchemical Journal*, 96(1), pp. 71–76, 2010.
<https://doi.org/10.1016/j.microc.2010.01.021>
- [75] Sneddon, E. J., Hardaway, C. J., Sneddon, J., Boggavarapu, K., Tate, A. S., Tidwell, S. L., Gary, D. P., Douvris, C. "Determination of selected metals in rice and cereal by inductively coupled plasma-optical emission spectrometry (ICP-OES)", *Microchemical Journal*, 134, pp. 9–12, 2017.
<https://doi.org/10.1016/j.microc.2017.04.009>
- [76] Granel, B., Izquierdo-Llopart, A., Sahuquillo, À., López-Sánchez, J. F., Saurina, J. "Characterization of Musts, Wines, and Sparkling Wines Based on Their Elemental Composition Determined by ICP-OES and ICP-MS", *Beverages*, 8(1), 3, 2022.
<https://doi.org/10.3390/beverages8010003>
- [77] Farahani, S., Eshghi, N., Abbasi, A., Karimi, F., Shiri Malekabad, E., Rezaei, M. "Determination of heavy metals in albumen of hen eggs from the Markazi Province (Iran) using ICP-OES technique", *Toxin Reviews*, 34(2), pp. 96–100, 2015.
<https://doi.org/10.3109/15569543.2015.1040166>
- [78] Kalayci, Ş. "Investigation of Arsenic Content in Field Pesticides Using Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES)", *Gazi University Journal of Science Part A: Engineering and Innovation*, 9(2), pp. 96–103, 2022.
<https://doi.org/10.54287/gujisa.1100870>
- [79] Cheng, G., He, M., Peng, H., Hu, B. "Dithizone modified magnetic nanoparticles for fast and selective solid phase extraction of trace elements in environmental and biological samples prior to their determination by ICP-OES", *Talanta*, 88, pp. 507–515, 2012.
<https://doi.org/10.1016/j.talanta.2011.11.025>
- [80] Harrington, J. M., Young, D. J., Essader, A. S., Sumner, S. J., Levine, K. E. "Analysis of Human Serum and Whole Blood for Mineral Content by ICP-MS and ICP-OES: Development of a Mineralomics Method", *Biological Trace Element Research*, 160(1), pp. 132–142, 2014.
<https://doi.org/10.1007/s12011-014-0033-5>
- [81] Jarić, I., Višnjić-Jeftić, Ž., Cvijanović, G., Gačić, Z., Jovanović, L., Skorić, S., Lenhardt, M. "Determination of differential heavy metal and trace element accumulation in liver, gills, intestine and muscle of sterlet (*Acipenser ruthenus*) from the Danube River in Serbia by ICP-OES", *Microchemical Journal*, 98(1), pp. 77–81, 2011.
<https://doi.org/10.1016/j.microc.2010.11.008>
- [82] Hall, A. G., King, J. C., McDonald, C. M. "Comparison of Serum, Plasma, and Liver Zinc Measurements by AAS, ICP-OES, and ICP-MS in Diverse Laboratory Settings", *Biological Trace Element Research*, 200(6), pp. 2606–2613, 2022.
<https://doi.org/10.1007/s12011-021-02883-z>
- [83] Park, Y. M., Choi, J. Y., Nho, E. Y., Lee, C. M., Hwang, I. M., Khan, N., Jamila, N., Kim, K. S. "Determination of macro and trace elements in canned marine products by inductively coupled plasma—optical emission spectrometry (ICP-OES) and ICP—mass spectrometry (ICP-MS)", *Analytical Letters*, 52(6), pp. 1018–1030, 2019.
<https://doi.org/10.1080/00032719.2018.1510938>
- [84] Dickinson, A. W., Power, A., Hansen, M. G., Brandt, K. K., Piliposian, G., Appleby, P., O'Neill, P. A., Jones, R. T., Sierocinski, P., Koskella, B., Vos, M. "Heavy metal pollution and co-selection for antibiotic resistance: A microbial palaeontology approach", *Environment International*, 132, 105117, 2019.
<https://doi.org/10.1016/j.envint.2019.105117>
- [85] Memon, A.-u.-R., Kazi, T. G., Afridi, H. I., Jamali, M. K., Arain, M. B., Jalbani, N., Syed, N. "Evaluation of zinc status in whole blood and scalp hair of female cancer patients", *Clinica Chimica Acta*, 379(1–2), pp. 66–70, 2007.
<https://doi.org/10.1016/j.cca.2006.12.009>
- [86] Siwulski, M., Mleczek, M., Rzymiski, P., Budka, A., Jasińska, A., Niedzielski, P., Kalač, P., Gąsecka, M., Budzyńska, S., Mikołajczak, P. "Screening the Multi-Element Content of *Pleurotus* Mushroom Species Using inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES)", *Food Analytical Methods*, 10(2), pp. 487–496, 2017.
<https://doi.org/10.1007/s12161-016-0608-1>

- [87] Siethoff, C., Feldmann, I., Jakubowski, N., Linscheid, M. "Quantitative determination of DNA adducts using liquid chromatography/electrospray ionization mass spectrometry and liquid chromatography/high-resolution inductively coupled plasma mass spectrometry", *Journal of Mass Spectrometry*, 34(4), pp. 421–426, 1999. [https://doi.org/10.1002/\(SICI\)1096-9888\(199904\)34:4<421::AID-JMS790>3.0.CO;2-I](https://doi.org/10.1002/(SICI)1096-9888(199904)34:4<421::AID-JMS790>3.0.CO;2-I)
- [88] Edler, M., Jakubowski, N., Linscheid, M. "Styrene oxide DNA adducts: quantitative determination using 31P monitoring", *Analytical and Bioanalytical Chemistry*, 381(1), pp. 205–211, 2005. <https://doi.org/10.1007/s00216-004-2925-2>
- [89] Axelsson, B.-O., Jörnten-Karlsson, M., Michelsen, P., Abou-Shakra, F. "The potential of inductively coupled plasma mass spectrometry detection for high-performance liquid chromatography combined with accurate mass measurement of organic pharmaceutical compounds", *Rapid Communications in Mass Spectrometry*, 15(6), pp. 375–385, 2001. <https://doi.org/10.1002/rcm.238>
- [90] Poirier, L., Nelson, J., Leong, D., Berhane, L., Hajdu, P., Lopez-Linares, F. "Application of ICP-MS and ICP-OES on the Determination of Nickel, Vanadium, Iron, and Calcium in Petroleum Crude Oils via Direct Dilution", *Energy & Fuels*, 30(5), pp. 3783–3790, 2016. <https://doi.org/10.1021/acs.energyfuels.5b02997>
- [91] Lienemann, C. P., Dreyfus, S., Pecheyran, C., Donard, O. F. X. "Trace Metal Analysis in Petroleum Products: Sample Introduction Evaluation in ICP-OES and Comparison with an ICP-MS Approach", *Oil & Gas Science and Technology - Rev. IFP*, 62(1), pp. 69–77, 2007. <https://doi.org/10.2516/ogst:2007006>
- [92] de Oliveira Souza, M., Ribeiro, M. A., Carneiro, M. T. W. D., Athayde, G. P. R., de Castro, E. V. R., da Silva, F. L. F., Matos, W. O., de Queiroz Ferreira, R. "Evaluation and determination of chloride in crude oil based on the counterions Na, Ca, Mg, Sr and Fe, quantified via ICP-OES in the crude oil aqueous extract", *Fuel*, 154, pp. 181–187, 2015. <https://doi.org/10.1016/j.fuel.2015.03.079>
- [93] Sánchez, R., Lefevre, J., Todolí, J.-L. "Direct elemental analysis of petroleum heavy fractions by means of ICP-OES equipped with a high temperature torch integrated sample introduction system", *Journal of Analytical Atomic Spectrometry*, 34(4), pp. 664–673, 2019. <https://doi.org/10.1039/C8JA00320C>
- [94] Hamilton, M. A., Rode, P. W., Merchant, M. E., Sneddon, J. "Determination and comparison of heavy metals in selected seafood, water, vegetation and sediments by inductively coupled plasma-optical emission spectrometry from an industrialized and pristine waterway in Southwest Louisiana", *Microchemical Journal*, 88(1), pp. 52–55, 2008. <https://doi.org/10.1016/j.microc.2007.09.004>
- [95] Uysal, K., Emre, Y., Köse, E. "The determination of heavy metal accumulation ratios in muscle, skin and gills of some migratory fish species by inductively coupled plasma-optical emission spectrometry (ICP-OES) in Beymelek Lagoon (Antalya/Turkey)", *Microchemical Journal*, 90(1), pp. 67–70, 2008. <https://doi.org/10.1016/j.microc.2008.03.005>
- [96] Suzuki, K. "Characterisation of airborne particulates and associated trace metals deposited on tree bark by ICP-OES, ICP-MS, SEM-EDX and laser ablation ICP-MS", *Atmospheric Environment*, 40(14), pp. 2626–2634, 2006. <https://doi.org/10.1016/j.atmosenv.2005.12.022>
- [97] de Paula, P. H. M., Mateus, V. L., Araripe, D. R., Duyck, C. B., Saint'Pierre, T. D., Gioda, A. "Biomonitoring of metals for air pollution assessment using a hemiepiphyte herb (*Struthanthus flexicaulis*)", *Chemosphere*, 138, pp. 429–437, 2015. <https://doi.org/10.1016/j.chemosphere.2015.06.060>
- [98] Khan, M. A., Khan, S., Khan, A., Alam, M. "Soil contamination with cadmium, consequences and remediation using organic amendments", *Science of The Total Environment*, 601–602, pp. 1591–1605, 2017. <https://doi.org/10.1016/j.scitotenv.2017.06.030>
- [99] Górecka, H., Chojnacka, K., Górecki, H. "The application of ICP-MS and ICP-OES in determination of micronutrients in wood ashes used as soil conditioners", *Talanta*, 70(5), pp. 950–956, 2006. <https://doi.org/10.1016/j.talanta.2006.05.061>
- [100] Gonçalves, D. A., de Souza, I. D., Rosa, A. C. G., Melo, E. S. P., Gonçalves, A.-M. B., de Oliveira, L. C. S., do Nascimento, V. A. "Multi-wavelength calibration: Determination of trace toxic elements in medicine plants by ICP OES", *Microchemical Journal*, 146, pp. 381–386, 2019. <https://doi.org/10.1016/j.microc.2019.01.021>
- [101] Lemos, V. A., de Carvalho, A. L. "Determination of cadmium and lead in human biological samples by spectrometric techniques: a review", *Environmental Monitoring and Assessment*, 171(1), pp. 255–265, 2010. <https://doi.org/10.1007/s10661-009-1276-z>
- [102] Yahaya, M., Shehu, A., Dabai, F. G. "Efficiency of Extraction of Trace metals from Blood samples using Wet Digestion and Microwave Digestion Techniques", *Journal of Applied Sciences and Environmental Management*, 17(3), pp. 365–369, 2013. <https://doi.org/10.4314/jasem.v17i3.4>
- [103] Puchyr, R. F., Bass, D. A., Gajewski, R., Calvin, M., Marquardt, W., Urek, K., Druyan, M. E., Quig, D. "Preparation of hair for measurement of elements by inductively coupled plasma-mass spectrometry (ICP-MS)", *Biological Trace Element Research*, 62(3), pp. 167–182, 1998. <https://doi.org/10.1007/BF02783969>
- [104] Alrobaian, M., Arida, H. "Assessment of Heavy and Toxic Metals in the Blood and Hair of Saudi Arabia Smokers Using Modern Analytical Techniques", *International Journal of Analytical Chemistry*, 2019(1), 7125210, 2019. <https://doi.org/10.1155/2019/7125210>
- [105] Lavilla, I., Costas, M., Miguel, P. S., Millos, J., Bendicho, C. "Elemental fingerprinting of tumorous and adjacent non-tumorous tissues from patients with colorectal cancer using ICP-MS, ICP-OES and chemometric analysis", *BioMetals*, 22(6), pp. 863–875, 2009. <https://doi.org/10.1007/s10534-009-9231-6>
- [106] Baj, J., Teresiński, G., Forma, A., Flieger, M., Proch, J., Niedzielski, P., Grochowski, C., ... Flieger, J. "Chronic Alcohol Abuse Alters Hepatic Trace Element Concentrations-Metallomic Study of Hepatic Elemental Composition by Means of ICP-OES", *Nutrients*, 14(3), 546, 2022. <https://doi.org/10.3390/nu14030546>

- [107] United States Pharmacopeia and the National Formulary "<232> Elemental Impurities-Limits", United States Pharmacopeia and National Formulary, Frederick, MD, USA, No. USP 39, 2023. [online] Available at: <https://www.usp.org/sites/default/files/usp/document/our-work/chemical-medicines/key-issues/c232-usp-39.pdf> [Accessed: 26 January 2025]
- [108] United States Pharmacopeia and National Formulary "<233> Elemental Impurities-Procedures", United States Pharmacopeia and National Formulary, Frederick, MD, USA, No. USP 38–NF 33, 2023. [online] Available at: <https://www.usp.org/sites/default/files/usp/document/our-work/chemical-medicines/key-issues/c233.pdf> [Accessed: 26 January 2025]
- [109] Majumdar, A. J., Dubey, N. "Applications of inductively coupled plasma-atomic emission spectrometry (ICP-OES) in impurity profiling of Pharmaceuticals", *International Journal of Pharmacy & Life Sciences*, 8(1), pp. 5420–5425, 2017. [online] Available at: <https://research.ebsco.com/c/qwz7kd/search/details/kmb6h3x-j?db=edb> [Accessed: 26 January 2025]
- [110] Resano, M., Flórez, M. D. R., Queral, I., Marguí, E. "Determination of palladium, platinum and rhodium in used automobile catalysts and active pharmaceutical ingredients using high-resolution continuum source graphite furnace atomic absorption spectrometry and direct solid sample analysis", *Spectrochimica Acta Part B: Atomic Spectroscopy*, 105, pp. 38–46, 2015. <https://doi.org/10.1016/j.sab.2014.09.013>
- [111] Tu, Q., Wang, T., Antonucci, V. "High-efficiency sample preparation with dimethylformamide for multi-element determination in pharmaceutical materials by ICP-AES", *Journal of Pharmaceutical and Biomedical Analysis*, 52(2), pp. 311–315, 2010. <https://doi.org/10.1016/j.jpba.2010.01.008>
- [112] Frey, O. R., Maier, L. "Polyethylene Vials of Calcium Gluconate Reduce Aluminum Contamination of TPN", *Annals of Pharmacotherapy*, 34(6), pp. 811–812, 2000. <https://doi.org/10.1345/aph.19306>
- [113] Jenke, D. R., Story, J., Lalani, R. "Extractables/leachables from plastic tubing used in product manufacturing", *International Journal of Pharmaceutics*, vol. 315, no. 1–2, pp. 75–92, Jun. 2006. <https://doi.org/10.1016/j.ijpharm.2006.02.011>
- [114] Van Caillie, M., Degenhart, H., Luijendijk, I., Fernandes, J. "Zinc Content of Intravenous Solutions", *The Lancet*, 312(8082), pp. 200–201, 1978. [https://doi.org/10.1016/S0140-6736\(78\)91934-7](https://doi.org/10.1016/S0140-6736(78)91934-7)
- [115] Van Hoecke, K., Catry, C., Vanhaecke, F. "Determination of elemental impurities in leachate solutions from syringes using sector field ICP-mass spectrometry", *Journal of Pharmaceutical and Biomedical Analysis*, 77, pp. 139–144, 2013. <https://doi.org/10.1016/j.jpba.2013.01.021>
- [116] Pinheiro, F. C., Barros, A. I., Nóbrega, J. A. "Evaluation of dilute-and-shoot procedure for determination of inorganic impurities in liquid pharmaceutical samples by ICP OES", *Microchemical Journal*, 146, pp. 948–956, 2019. <https://doi.org/10.1016/j.microc.2019.02.021>
- [117] da Silva, C. S., Pinheiro, F. C., do Amaral, C. D. B., Nóbrega, J. A. "Determination of As, Cd, Hg and Pb in continuous use drugs and excipients by plasma-based techniques in compliance with the United States Pharmacopeia requirements", *Spectrochimica Acta Part B: Atomic Spectroscopy*, 138, pp. 14–17, 2017. <https://doi.org/10.1016/j.sab.2017.10.004>
- [118] Jancevska, K., Petrushevski, G., Bogdanoska, M., Stafilov, T., Ugarkovic, S. "ICP-OES elemental impurities study on different pharmaceutical dosage forms of Ibuprofen using microwave-assisted digestion procedure", *Macedonian Journal of Chemistry and Chemical Engineering*, 40(1), pp. 43–50, 2021. <https://doi.org/10.20450/mjccce.2021.2100>
- [119] Druzian, G. T., Nascimento, M. S., Santos, R. F., Pedrotti, M. F., Bolzan, R. C., Duarte, F. A., Flores, E. M. M. "New possibilities for pharmaceutical excipients analysis: Combustion combined with pyrohydrolysis system for further total chlorine determination by ICP-OES", *Talanta*, 199, pp. 124–130, 2019. <https://doi.org/10.1016/j.talanta.2019.01.123>
- [120] Gomez, M. R., Cerutti, S., Sombra, L. L., Silva, M. F., Martínez, L. D. "Determination of heavy metals for the quality control in argentinian herbal medicines by ETAAS and ICP-OES", *Food and Chemical Toxicology*, 45(6), pp. 1060–1064, 2007. <https://doi.org/10.1016/j.fct.2006.12.013>
- [121] de la Calle, I., Menta, M., Klein, M., Séby, F. "Screening of TiO₂ and Au nanoparticles in cosmetics and determination of elemental impurities by multiple techniques (DLS, SP-ICP-MS, ICP-MS and ICP-OES)", *Talanta*, 171, pp. 291–306, 2017. <https://doi.org/10.1016/j.talanta.2017.05.002>
- [122] Mrmošanin, J., Pavlović, A., Mitić, S., Tošić, S., Pecev-Marinković, E., Krstić, J., Nikolić, M. "The Evaluation of ICP OES for the Determination of Potentially Toxic Elements in Lipsticks: Health Risk Assessment", *Acta Chimica Slovenica*, 66(4), pp. 802–813, 2019. <https://doi.org/10.17344/acsi.2018.4800>
- [123] Karacan, M. S., Çağran, F. "Multielement Determination in Fruit, Soaps and Coffee of Pistacia Terebinthus L. by ICP-OES", *Turkish Journal of Biology*, 33(4), pp. 311–318, 2009. <https://doi.org/10.3906/biy-0808-22>
- [124] Kalnicky, D. J., Kniseley, R. N., Fassel, V. A. "Inductively coupled plasma-optical emission spectroscopy: Excitation temperatures experienced by analyte species", *Spectrochimica Acta Part B: Atomic Spectroscopy*, 30(12), pp. 511–525, 1975. [https://doi.org/10.1016/0584-8547\(75\)80046-2](https://doi.org/10.1016/0584-8547(75)80046-2)
- [125] Meisel, T., Moser, J., Fellner, N., Wegscheider, W., Schoenberg, R. "Simplified method for the determination of Ru, Pd, Re, Os, Ir and Pt in chromitites and other geological materials by isotope dilution ICP-MS and acid digestion", *Analyst*, 126(3), pp. 322–328, 2001. <https://doi.org/10.1039/b007575m>
- [126] Paliulionyte, V., Meisel, T., Ramminger, P., Kettisch, P. "High Pressure Asher Digestion and an Isotope Dilution-ICP-MS Method for the Determination of Platinum-Group Element Concentrations in Chromitite Reference Materials CHR-Bkg, GAN Pt-1 and HHH", *Geostandards and Geoanalytical Research*, 30(2), pp. 87–96, 2006. <https://doi.org/10.1111/j.1751-908X.2006.tb00915.x>

- [127] Barnes, S.-J., Pagé, P., Zientek, M. "The Lower Banded series of the Stillwater Complex, Montana: whole-rock lithophile, chalcophile, and platinum-group element distributions", *Mineralium Deposita*, 55(1), pp. 163–186, 2020.
<https://doi.org/10.1007/s00126-019-00887-3>
- [128] Ishak, I., Rosli, F. D., Mohamed, J., Mohd Ismail, M. F. "Comparison of Digestion Methods for the Determination of Trace Elements and Heavy Metals in Human Hair and Nails", *Malaysian Journal of Medical Sciences*, 22(6), pp. 11–20, 2015.
- [129] Shen, K., Zhang, N., Yang, X., Li, Z., Zhang, Y., Zhou, T. "Dry Ashing Preparation of (Quasi)solid Samples for the Determination of Inorganic Elements by Atomic/Mass Spectrometry", *Applied Spectroscopy Reviews*, 50(4), pp. 304–331, 2015.
<https://doi.org/10.1080/05704928.2014.986735>
- [130] Maciel, J. V., Knorr, C. L., Flores, E. M. M., Müller, E. I., Mesko, M. F., Primel, E. G., Duarte, F. A. "Feasibility of microwave-induced combustion for trace element determination in *Engraulis anchoita* by ICP-MS", *Food Chemistry*, 145, pp. 927–931, 2014.
<https://doi.org/10.1016/j.foodchem.2013.08.119>
- [131] Abu-Samra, A., Morris, J. S., Koirtiyohann, S. R. "Wet ashing of some biological samples in a microwave oven", *Analytical Chemistry*, 47(8), pp. 1475–1477, 1975.
<https://doi.org/10.1021/ac60358a013>
- [132] Levine, K. E., Batchelor, J. D., Rhoades Jr., C. B., Jones, B. T. "Evaluation of a high-pressure, high-temperature microwave digestion system", *Journal of Analytical Atomic Spectrometry*, 14(1), pp. 49–59, 1999.
<https://doi.org/10.1039/a803895c>
- [133] CAS Element "Microwave Assisted Acid Digestion of Dediments, Sludges, Soils, and Oils", [pdf] United States Environmental Protection Agency, Washington, DC, USA, 2007. Available at: <https://www.epa.gov/sites/default/files/2015-12/documents/3051a.pdf> [Accessed: 26 January 2025]
- [134] Demirel, S., Tuzen, M., Saracoglu, S., Soylak, M. "Evaluation of various digestion procedures for trace element contents of some food materials", *Journal of Hazardous Materials*, 152(3), pp. 1020–1026, 2008.
<https://doi.org/10.1016/j.jhazmat.2007.07.077>
- [135] Sun, W., Gao, S., Wang, L., Chen, Y., Wu, S., Wang, X., Zheng, D., Gao, Y. "Microwave-assisted Protein Preparation and Enzymatic Digestion in Proteomics", *Molecular & Cellular Proteomics*, 5(4), pp. 769–776, 2006.
<https://doi.org/10.1074/mcp.T500022-MCP200>
- [136] Matusiewicz, H. "Wet digestion methods", *Comprehensive Analytical Chemistry*, 41, pp. 193–233, 2003.
[https://doi.org/10.1016/S0166-526X\(03\)41006-4](https://doi.org/10.1016/S0166-526X(03)41006-4)
- [137] Huang, L., Bell, R. W., Dell, B., Woodward, J. "Rapid Nitric Acid Digestion of Plant Material with an Open-Vessel Microwave System", *Communications in Soil Science and Plant Analysis*, 35(3–4), pp. 427–440, 2004.
<https://doi.org/10.1081/CSS-120029723>
- [138] Matusiewicz, H., Sturgeon, R. E. "Comparison of the efficiencies of on-line and high-pressure closed vessel approaches to microwave heated sample decomposition", *Fresenius' Journal of Analytical Chemistry*, 349(6), pp. 428–433, 1994.
<https://doi.org/10.1007/BF00322927>
- [139] Araújo, G. C. L., Gonzalez, M. H., Ferreira, A. G., Nogueira, A. R. A., Nóbrega, J. A. "Effect of acid concentration on closed-vessel microwave-assisted digestion of plant materials", *Spectrochimica Acta Part B: Atomic Spectroscopy*, 57(12), pp. 2121–2132, 2002.
[https://doi.org/10.1016/S0584-8547\(02\)00164-7](https://doi.org/10.1016/S0584-8547(02)00164-7)
- [140] International Conference on Harmonization "Guideline for Elemental Impurities", Food and Drug Administration, Washington, DC, USA, No. Q3D(R2), 2022. [online] Available at: https://database.ich.org/sites/default/files/Q3D-R2_Guideline_Step4_2022_0308.pdf [Accessed: 26 January 2025]
- [141] Agilent Technologies "USP <232>/<233> and ICH Q3D Elemental Impurities Analysis: The Agilent ICP-MS Solution", Santa Clara, CA, USA, 2021. [online] Available at: https://www.agilent.com/cs/library/whitepaper/public/ICP-MS-5991-8149EN-USP232_whitepaper.pdf [Accessed: 26 January 2025]
- [142] Sohail Arshad, M., Zafar, S., Yousef, B., Alyassin, Y., Ali, R., AlAsiri, A., Chang, M.-W., Ahmad, Z., Ali Elkordy, A., Faheem, A., Pitt, K. "A review of emerging technologies enabling improved solid oral dosage form manufacturing and processing", *Advanced Drug Delivery Reviews*, 178, 113840, 2021.
<https://doi.org/10.1016/j.addr.2021.113840>
- [143] Musazzi, U. M., Santini, B., Selmin, F., Marini, V., Corsi, F., Allevi, R., Ferretti, A. M., Prosperi, D., Cilurzo, F., Colombo, M., Minghetti, P. "Impact of semi-solid formulations on skin penetration of iron oxide nanoparticles", *Journal of Nanobiotechnology*, 15(1), 14, 2017.
<https://doi.org/10.1186/s12951-017-0249-6>
- [144] Berenguer, D., Sosa, L., Alcover, M., Sessa, M., Halbaut, L., Guillén, C., Fisa, R., Calpena-Campmany, A. C., Riera, C. "Development and Characterization of a Semi-Solid Dosage Form of Meglumine Antimoniate for Topical Treatment of Cutaneous Leishmaniasis", *Pharmaceutics*, 11(11), 613, 2019.
<https://doi.org/10.3390/pharmaceutics11110613>
- [145] Grotti, M., Leardi, R., Frache, R. "Combined effects of inorganic acids in inductively coupled plasma optical emission spectrometry", *Spectrochimica Acta Part B: Atomic Spectroscopy*, 57(12), pp. 1915–1924, 2002.
[https://doi.org/10.1016/S0584-8547\(02\)00161-1](https://doi.org/10.1016/S0584-8547(02)00161-1)
- [146] Flores, É. M. M., Barin, J. S., Mesko, M. F., Knapp, G. "Sample preparation techniques based on combustion reactions in closed vessels — A brief overview and recent applications", *Spectrochimica Acta Part B: Atomic Spectroscopy*, 62(9), pp. 1051–1064, 2007.
<https://doi.org/10.1016/j.sab.2007.04.018>
- [147] Stricker, A., Bergfeldt, T., Fretwurst, T., Addison, O., Schmelzeisen, R., Rothweiler, R., Nelson, K., Gross, C. "Impurities in commercial titanium dental implants – A mass and optical emission spectrometry elemental analysis", *Dental Materials*, 38(8), pp. 1395–1403, 2022.
<https://doi.org/10.1016/j.dental.2022.06.028>
- [148] Pinheiro, F. C., Aguirre, M. Á., Nóbrega, J. A., González-Gallardo, N., Ramón, D. J., Canals, A. "Dispersive liquid-liquid microextraction based on deep eutectic solvent for elemental impurities determination in oral and parenteral drugs by inductively coupled plasma optical emission spectrometry", *Analytica Chimica Acta*, 1185, 339052, 2021.
<https://doi.org/10.1016/j.aca.2021.339052>

- [149] Althoff, A. G., Williams, C. B., McSweeney, T., Gonçalves, D. A., Donati, G. L. "Microwave-Induced Plasma Optical Emission Spectrometry (MIP OES) and Standard Dilution Analysis to Determine Trace Elements in Pharmaceutical Samples", *Applied Spectroscopy*, 71(12), pp. 2692–2698, 2017.
<https://doi.org/10.1177/0003702817721750>
- [150] Pal, A. K., Raja, S. "Development and validation of a microwave-assisted digestion technique as a rapid sample preparation method for the estimation of selenium in pharmaceutical dosage forms by ICP-OES", *Archives of Razi Institute*, 79(1), pp. 68–82, 2024.
<https://doi.org/10.32592/ARI.2024.79.1.68>
- [151] Rujido-Santos, I., Naveiro-Seijo, L., Herbelo-Hermelo, P., Barciela-Alonso, M. D. C., Bermejo-Barrera, P., Moreda-Piñeiro, A. "Silver nanoparticles assessment in moisturizing creams by ultrasound assisted extraction followed by sp-ICP-MS", *Talanta*, 197, pp. 530–538, 2019.
<https://doi.org/10.1016/j.talanta.2019.01.068>
- [152] Alhusban, A. A., Ata, S. A., Shraim, S. A. "The Safety Assessment of Toxic Metals in Commonly Used Pharmaceutical Herbal Products and Traditional Herbs for Infants in Jordanian Market", *Biological Trace Element Research*, 187(1), pp. 307–315, 2019.
<https://doi.org/10.1007/s12011-018-1367-1>
- [153] Veeramachaneni, M., Jayavarapu, K. R. "Development and validation of new ICP-OES Analytical Technique to quantify the contents of Copper, Magnesium & Zinc in "Escitalopram Oxalate"", *Journal of Advanced Pharmacy Education & Research*, 3(4), pp. 516–523, 2013.
- [154] Tımrılı Zurnacı, M., Kucuk Tunca, A. "Determination of Some Metal Levels in Multivitamin Tablets by ICP-OES after Different Digestion Methods", *Latin American Journal of Pharmacy*, 36(4), pp. 679–685, 2017.
- [155] Lewen, N., Nugent, D. "The use of inductively coupled plasma-atomic emission spectroscopy (ICP-AES) in the determination of lithium in cleaning validation swabs", *Journal of Pharmaceutical and Biomedical Analysis*, 52(5), pp. 652–655, 2010.
<https://doi.org/10.1016/j.jpba.2010.02.015>
- [156] Lewen, N. "The use of atomic spectroscopy in the pharmaceutical industry for the determination of trace elements in pharmaceuticals", *Journal of Pharmaceutical and Biomedical Analysis*, 55(4), pp. 653–661, 2011.
<https://doi.org/10.1016/j.jpba.2010.11.030>
- [157] Lam, R., Salin, E. D. "Analysis of pharmaceutical tablets by laser ablation inductively coupled plasma atomic emission spectrometry and mass spectrometry (LA-ICP-AES and LA-ICP-MS)", *Journal of Analytical Atomic Spectrometry*, 19(7), pp. 938–940, 2004.
<https://doi.org/10.1039/b314732k>
- [158] Pinheiro, F. C., Barros, A. I., Nóbrega, J. A. "Microwave-assisted sample preparation of medicines for determination of elemental impurities in compliance with United States Pharmacopeia: How simple can it be?", *Analytica Chimica Acta*, 1065, pp. 1–11, 2019.
<https://doi.org/10.1016/j.aca.2019.03.016>
- [159] Wollein, U., Bauer, B., Habernegg, R., Schramek, N. "Potential metal impurities in active pharmaceutical substances and finished medicinal products – A market surveillance study", *European Journal of Pharmaceutical Sciences*, 77, pp. 100–105, 2015.
<https://doi.org/10.1016/j.ejps.2015.05.028>
- [160] Mulenós, M. R., Lujan, H., Pitts, L. R., Sayes, C. M. "Silver Nanoparticles Agglomerate Intracellularly Depending on the Stabilizing Agent: Implications for Nanomedicine Efficacy", *Nanomaterials*, 10(10), 1953, 2020.
<https://doi.org/10.3390/nano10101953>
- [161] Fakeha, F. K., Khaleequr, R., Arshiya, S., Shamsiya, K. "Development, Characterization, and *In Vitro* Antimicrobial Activity of *Lawsonia inermis* L. Leaves Hydroalcoholic Extract-Based Vaginal Suppositories", *Traditional and Integrative Medicine*, 8(1), pp. 16–25, 2023.
<https://doi.org/10.18502/tim.v8i1.12399>
- [162] Hussain, A., Altamimi, M. A., Imam, S. S., Ahmad, M. S., Alnemer, O. A. "Green Nanoemulsion Water/Ethanol/Transcutol/LabM-Based Treatment of Pharmaceutical Antibiotic Erythromycin-Contaminated Aqueous Bulk Solution", *ACS Omega*, 7(51), pp. 48100–48112, 2022.
<https://doi.org/10.1021/acsomega.2c06095>
- [163] Zhang, Y., Miyamoto, Y., Ihara, S., Yang, J. Z., Zuill, D. E., Angsantikul, P., Zhang, Q., Gao, W., Zhang, L., Eckmann, L. "Composite Thermoresponsive Hydrogel with Auranofin-Loaded Nanoparticles for Topical Treatment of Vaginal Trichomonad Infection", *Advanced Therapeutics*, 2(12), 1900157, 2019.
<https://doi.org/10.1002/adtp.201900157>
- [164] Farkas, B., Balogh, A., Farkas, A., Domokos, A., Borbás, E., Marosi, G., Nagy, Z. K. "Medicated Straws Based on Electrospun Solid Dispersions", *Periodica Polytechnica Chemical Engineering*, 62(3), pp. 310–316, 2018.
<https://doi.org/10.3311/PPCh.11931>
- [165] Király, M., Sántha, K., Kállai-Szabó, B., Pencz, K. M., Ludányi, K., Kállai-Szabó, N., Antal, I. "Development and Dissolution Study of a β -Galactosidase Containing Drinking Straw", *Pharmaceutics*, 14(4), 769, 2022.
<https://doi.org/10.3390/pharmaceutics14040769>