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ICPMS FOR HEAVY METAL ANALYSIS OF MILK AND MILK PRODUCTS – A REVIEW

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ABSTRACT

Dairy products, such as milk, are an essential component of the human diet and are regarded as whole foods since they are rich in all the macronutrients and minerals. Although they are necessary for the body's healthy development and upkeep, too much of these metals, especially heavy metals, can harm the body and lead to pathological illnesses. People are now worried about difficulties with food safety involving chemical, physical, and microbiological dangers. Toxic effects can be brought on by heavy metals like cadmium (Cd), lead (Pb), arsenic (As), and mercury (Hg). These metals are metallic materials with high density that need attention. Analytical methods like inductively coupled plasma mass spectrometry (ICP-MS) can be used to detect trace components in bodily fluids. Even though some labs still employ antiquated techniques like atomic absorption and atomic emission, they have shifted to ICP-MS, particularly in the last decade. Clinical scientists must comprehend the analytical facets of ICP-MS, including the potential for spectral and non-spectral interference, as well as approaches that can be employed to minimize or reduce the issue, as this change will continue.

KEYWORDS: ICPMS, Heavy Metals, Spectrometry.

1. INTRODUCTION

Since ancient times, milk has been regarded as nature's most complete food (Park et al., 2009), and it continues to be a significant part of the diets of more than 6 billion people worldwide (Haug et al., 2007, Visioli et al., 2014, Mcgrane et al., 2011). As it contains essential macronutrients like carbohydrates, proteins, and fats as well as micronutrients like vitamins (like vitamins) like riboflavin, B5, and B12 and minerals, milk is also regarded as an important, nearly complete food for kids and adults. Secondary dairy ingredients like cheese and butter are included in many dishes. As these minerals form the foundation of life, milk typically contains significant levels of sodium (Na), potassium (K), calcium (Ca), and phosphorus (P). The majority of the chair's 118 components, which must be combined in the appropriate amount for development and ongoing improvement, are made of metal. Consuming certain metals in the right amounts is essential for human existence. For instance, iron is a crucial component of hemoglobin, which aids in the movement of oxygen throughout the body. Along with being essential nutrients, salt, potassium, magnesium, copper, and zinc are other crucial minerals that contribute to a variety of bodily processes. (Fadi, Abou-Shakra, et al. 2018). In order for our body to function properly, we must keep the proper ingredients at the proper levels. The quantity of the major ingredient is crucial; it must be at levels that are secure enough to support work but not too high to pollute. This implies that fact-checking is crucial. There are some substances, nevertheless, that are dangerous even in little amounts. For instance, heavy metals like lead (4), cadmium (5), the metalloids mercury (3) and arsenic (2) have been linked to a variety of health issues. (Jaishankar and colleagues et al.,2014). As it is produced from the mammary gland, milk can contain a variety of foreign chemicals that can be harmful to milk and dairy products. Lead (Pb) and mercury (Hg) have adverse effects on human health, these effects can be transmitted from outside contaminated soil to plants and grass, results in toxic in cows and human milk. Dairy products may get contaminated with toxins as a result of milk processing.

Fig. 1: Dairy and processed dairy products (Bakies., 2020).

2. Heavy Metals and Their Source in Milk

In general, heavy metals are regarded as being extremely toxic and damaging to the environment. Today's focus is on food safety issues include microbiological, chemical, and physical dangers. Important contaminants in the pharmaceutical sector include heavy metal residues of cadmium (Cd), lead (Pb), arsenic (As), mercury (Hg), and others. Due to ongoing industrialization and urbanization, heavy metal pollution has grown to be a significant cause of environmental harm. Although heavy metals naturally occur, the use of untreated sewage and industrial wastewater to irrigate crops has increased the amount of heavy metals in foods. Animals exposed to pesticides, herbicides, feeding grounds, canals, or sewer systems as well as heavy metals may also produce milk that is contaminated Heavy metals are generally considered very dangerous and harmful to the environment. Food safety issues such as microbiological, chemical and physical hazards are the focus today. Cadmium (Cd), lead (Pb), arsenic (As), mercury (Hg) and other heavy metal residues are important pollutants in the pharmaceutical industry. Heavy metal pollution has become an important source of environmental damage due to continuous industrialization and urbanization. Heavy metals exist in nature and their content in foodstuffs has increased due to the use of untreated sewage and industrial wastewater to irrigate crops. Heavy metals can also pass into milk from contaminated animals near canals or sewer systems, pesticides and herbicides, and feeding grounds (Caiet al., 2009; Iftikhar et al., 2014). Şimşek et al., (2000) Contaminated soil is an important source of cadmium and lead, which can be stored in food, milk. Heavy metals become contaminants in foods for various reasons and cause health problems (Table 1).

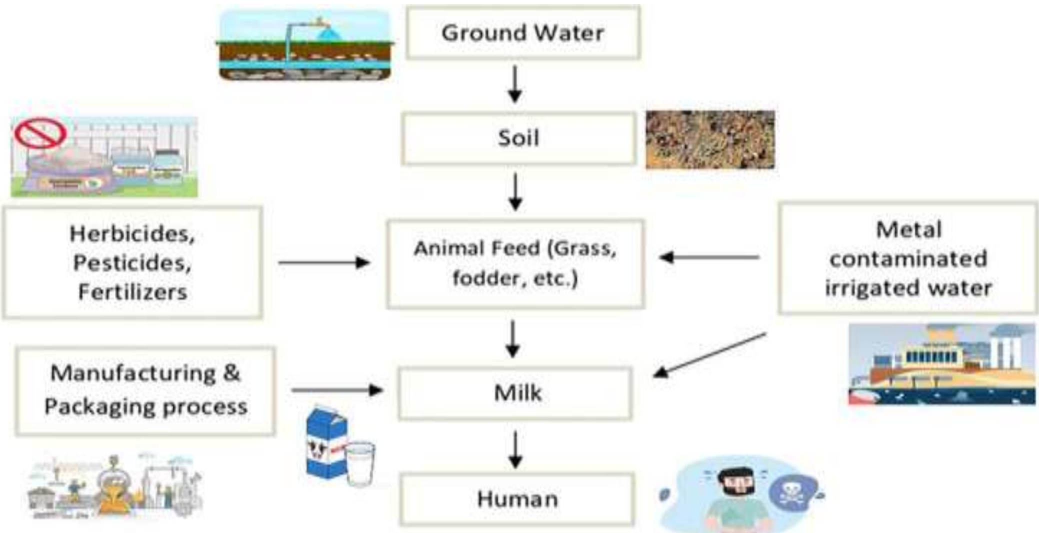

Fig. 2: Source of metals (Aggarwal et al., 2022).

The authenticity and traceability of milk and dairy products have been proven in several investigations. The features of 12 cows and 6 cows were investigated by Benincasa et al. in 2008. To distinguish between the two species, all animals were treated equally in the same place. In actuality, the authors' interpretations of the two memes are different from one another. By identifying the stable isotope ratios and the compositional elements of C, H, N, and O using the IRMS and ICP-MS techniques, respectively, Kalpage et al. published a study in 2022 examining the geographical origin of milk from various regions of Sri Lanka. The stable isotopes of 15N, 13C (found in boeuf casein), 15N, 18O, and 2H (found in whole milk) and Metal concentrations of Li, Al, Cr, Mn, Fe, Co, Ba, and Sr may be useful indicators of geographical differences. According to the authors, factors such as the animal's body (breeding, lactation, etc.), diet, and supplements may have an impact on the outcome.

Tedesco et al. (2021) and Aceto et al. (2017) looked into the effect of trace and rare earth elements in milk samples from various regions of Italy along the supply chain in a study that was comparable to theirs. Lanthanide has been demonstrated to have an almost constant concentration during the manufacture of milk, making it a viable pathogen.

The data gathered for research on cheese and dairy products in general reflect the local environment because it is assumed that iron is unaffected by the production process. Stable isotope ratios (13C/12C, 15N/14N, 18O/16O, 2H/1H and 87Sr/86Sr), elemental composition (Ca, Mg, Na, K, Cu, Mn, Mo, I), and radioactive elements (90Sr, 234U, 238U) were studied in 2003 by Pillonel et al. Different quantities of molybdenum and salt indicate different types of cheese. Camin et al. (2015), an international team of researchers, conducted a study on the topic. Seven hard cheese samples were evaluated for their H, C, N, and S stable isotope ratios and various concentration points in accordance with the IUPAC procedure and ISO 5725/2004 and 13528/2005. The isotopic and/or elemental analyses were conducted at thirteen separate laboratories. The identification of stable isotopes of H, C, N, and S as well as Li, Na, Mn, Fe, Cu, Se, Rb, Sr, Mo, Ba, Re, Bi, and U offers evidence of the origin of the two cheeses.

Table 1: Provides a summary of the literature on the authenticity and traceability of milk and milk products. (Mazarakioti et al., 2022).

1.	Milk and Dairy (Cow and Buffalo Milk)	P, S, K, Ca, V, Cr, Mn, Fe, Co, Zn, Ga, Rb, Sr, Mo, Cs and Ba	Italy	(Benincasa et al., 2008)
2.	Milk and Dairy (Cow Milk)	Li, Al, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Sr, Cd, Ba, Pb, and Bi	Sri Lanka	Kalpage et al., 2022
3.	Milk and Dairy (Cow and Goat Milk)	Al, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Sr, Cd, Cs, Ba, Pb, U, La, Ce, Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Yb, Lu, and Y	Italy	(Tedesco et al., 2021),
4.	Milk and Dairy (Cow Milk)	Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Rb, Sr, Y, Zr, Sn, Sb, Ba, La, Ce, Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu, Pb, Th, and U	Italy	(Aceto et al., 2017)
5.	Milk and Dairy (Cheese)	Ca, Mg, Na, K, Cu, Mn, Mo, and I	Finland, England, Germany, Austria, France, and Switzerland	(Pillonel et al., 2003)
6.	Milk and Dairy (Cheese)	Li, Na, Mn, Fe, Cu, Se, Rb, Sr, Mo, Ba, Re, Bi, and U	Italy	(Camin et al., 2015)

3. ADVERSE EFFECTS OF HEAVY METALS ON HUMAN HEALTH

Any metallic element that is dangerous or poisonous even at modest densities (5 g/cm3) is considered a heavy metal. (2011) Sani et al. Even at very low concentrations, heavy metals are cumulative poisons that can be harmful. They actually don't have any known metabolic functions, but when they're present in the body, they disturb cellular functions normally, which has harmful consequences on a number of organs (Al-Maylay et al., 2014).

A sizeable amount of heavy metals that are present in both plants and animals end up in food, damaging both the quality of the finished products and people's health (Table 2).

Table 2: Toxic Effects of Metals on Human Health.

Heavy metals	Human health consequences	Reference
Mercury	Memory issues increased heart rate, tremors, kidney, brain and liver damage	Zahir et al., 2005
Arsenic	Ulcer, liver problems an d kidney damage	Kapaj et al., 2006
Chromium	DNA damage, Lung Cancer	Baccarelli, et al., 2009
Lead	Abortion on the spur of the moment causes nervous system damage, kidney & brain damage and liver problems.	Duruibe, et al., 2007
Cadimium	Cancer, lung insufficiency disturbance in liver and kidney	Bernard, et al., 2008

4. HEAVY METAL STANDARD FOR MILK AND MILK PRODUCTS

Controlling heavy metals in milk is important because milk is consumed by people of all ages and children and the elderly are more likely to be exposed to heavy metals. For this reason, many regulatory agencies have set limits for heavy metals. To meet the list, Dairy and food stores need to check milk and dairy products for large particles, insects, and contaminants (such as heavy metals) to meet labeling requirements, monitor products for eating well, and prevent infection from toxic products. In Europe, regulations such as Council Regulation (EC) No 1881/2006 set maximum levels of certain pathogens in food. Similarly, the Food Safety and Standards Act (FSSRI) in India specifies the maximum level allowed for various food products. In the United States, Law 65 regulates air pollution as the maximum daily limit. The value of sample ranges from ng/L to percent, presents a challenge for ICP-MS equipment in laboratories to find samples that pass and work efficiently (Górska-Warsewicz et al., 2019).

4.1 Regulations and standards for milk and milk products

4.1.1 European Union (EU) COMMISSION REGULATION (EC) No 1881/2006

Regulations for the dairy industry are set forth by European Union legislation. The law outlines the prerequisites for the importation of milk and milk products for human consumption into the EU. More than 30 changes have been made to the regulation. This legislation establishes upper limits for specific pollutants in food.

4.1.2 FOOD SAFETY AND STANDARDS AUTHORITY OF INDIA (FSSAI) Regulations

These regulations may be called the Food Safety and Standards (Contaminants, toxins and Residues) Regulations, 2011. These regulations came into force on or after 5th August, 2011.

4.1.3 CODEX GENERAL STANDARD (CODEX STAN 193-1995)

This standard contains the main principles approved by the Codex Alimentarius Commission for the assessment of pathogens and toxins in food and feed, and specifies the highest levels and sampling schedules for pathogens and toxicants occurring in food and feed that CAC recommends should be used for products on the international market. The standard covers the highest levels of bacteria and toxic substances that occur in food only if the bacteria in the food can be transferred to food of animal origin and is a public health concern.

Table 3: Food Safety and Standards Authority of India (FSSAI), CODEX standard and EU recommended limit for milk and dairy products.

Heavy metals	Standards for milk and milk product		
	FSSAI (mg/l)	CODEX (mg/l)	EU (European Union) (mg/l)
Mercury	1	0.5	-
Arsenic	0.1	0.2	-
Lead	0.02	0.02	0.02
Cadmium	0.15	0.2	-
Copper	30	-	-
Tin	250	-	-

5 ANALYTICAL METHODS FOR DETECTION OF HEAVY METALS

The dangers of heavy metals to human health require the development of cost-effective, sensitive, fully selective and portable sensors and methods. Heavy metal detection methods such as atomic absorption spectrometry (AAS), atomic fluorescence spectrometry (AFS), laser-induced breakdown spectrometry, inductively coupled Optical emission spectrometry, Inductively coupled plasma mass spectrometry (ICP-MS), inductively coupled plasma emission spectrometry (ICP-MS), etc. (Palisoc et al., 2021) Many of these methods are expensive, require state-of-the-art equipment and trained personnel, which affects the measurement of the field well.

5.1 Atomic Absorption Spectrometry (AAS)

AAS was one of the first commercially developed methods for analysis. It was created in 1952 and first launched in 1960. This is a test that measures the concentration of an element by measuring the amount of light (light intensity) absorbed from an element's atom cloud at a characteristic wavelength. As the number of atoms in the light path increases, the amount of light absorbed increases in the estimate. The main disadvantage of this method is limited sensitivity, only one point can be measured at a time, and limited linearity. It also requires small size (1-3 mL) and has issues with refractory materials (Kuai et al., 2023).

5.2 Atomic fluorescence Spectrometry (AFS)

These analytical methods are often used to detect and measure metals. This is a very sensitive method based on the use of the unique fluorescent spectrum of each particular metal. Low concentrations of antimony, arsenic, bismuth, cadmium, germanium, lead, selenium, tellurium, tin and zinc can be detected using AFS; some of these metals can be detected in the parts per billion (ppb) range. The disadvantage of this method is that it must be combined with chromatography to provide information about the chemical composition of the analyzed substance during the separation of the drug. Especially for product samples, sample preparation is often difficult and time consuming. The analysis will affect the chemical reaction due to the chemical nature of the test substance and other aspects of the structure (matrix) that can reduce the free atoms created (Feng et al., 2022).

5.3 Laser-induced breakdown spectroscopy (LIBS)

Laser Induced Decay Spectroscopy (LIBS) is a fast, portable, atomic spectroscopy technique used to measure the concentration of important elements in solids, liquids, or air, or to record chemical signatures (fingerprints) of substances. Each LIBS spectrum contains information not only about the composition of each natural element, but also about some isotope ratios and the atomic structure of the material. LIBS technology is widely used in the rapid detection of heavy metals due to its advantages such as simple operation, simultaneous detection of many elements, element diversity and state, and no need for quantitative samples. However, the development of LIBS is limited by the three main limitations. First, the laser does not interact with the sample in exactly the same way for each laser pulse, there is a significant difference in intensity from shot to shot. Second, fundamental analysis using univariate or multivariate calibration cannot achieve the accuracy or precision of multivariate methods such as ICP-MS or XRF. Finally, as with any spectroscopic technique, the spectrum produced by a LIBS instrument is unique to that instrument and may differ slightly for the same sample analyzed on a similar instrument (Yang et al., 2022).

5.4 Inductively Coupled Plasma – Optical Emission Spectroscopy (ICP OES)

ICP-OES (Inductively Coupled Plasma-Optical Emission Spectroscopy) is a technique that can determine the composition of samples (usually dissolved in water) using plasma and a spectrometer. The technology has been used commercially since 1974. It is an analytical technique used to determine the value of something in a sample. The basic ICP-OES principle uses the fact that atoms and ions can absorb energy to move electrons from the ground state to the excited state. In ICP-OES, the energy source is heated by an argon plasma operating at 10,000 Kelvin. ICP-OES has been in commercial use around the world for almost half a century and has proven to be a very popular method for the analysis of samples, mainly due to its efficiency, many points of analysis and the reliability of the results it produces. Common problems with ICP-OES include false positives, sample drift, agreement limitations, and misidentification. (Nizio et al., 2012).

5.5 Inductively coupled plasma mass spectrometry (ICP-MS)

Considering the limitations of techniques mentioned above, here we describe a simple method that allows the identification and analysis of many elements, such as toxic elements, harmful elements, as well as elements important to health. Inductively coupled plasma mass spectrometry is unique in its ability to measure high velocities and high concentrations of different elements in the same sample. it an important method for identifying and measuring the potential of metal impurities (Ernstberger et al., 2018). It can be used to detect metals with a parts per million limit (Wilschefski et al., 2019). Since its introduction in the 1980s, inductively coupled plasma mass spectrometry (ICP-MS) has evolved to become arguably the most versatile, element-specific detection technique. In parallel, because of the fast developments in the field of elemental speciation, the utilization concept of ICP-MS has undergone a significant change (Pröfrock., 2012).

4.5.1 A BRIEF OVERVIEW OF ICP-MS

A single quadrupole ICP-MS consists of six main part: the sample introduction system, inductively coupled plasma (ICP), interface, ion optics, mass analyzer and detector. Figure 1 shows a simple block diagram of the instrument. The liquid sample is first nebulized in the sample guide to create a fine aerosol, which is then sent to the argon plasma. The high-temperature plasma atomizes and ionizes the sample, creating ions that are then extracted from the interface area into a series of electrostatic lenses called ion optics. Ion optics focuses the ion beam and directs it to the quadrupole mass analyzer. The mass analyser separates ions according to their mass-charge ratio (m/z), and these ions are measured at the detector (Pappas, et al., 2012).

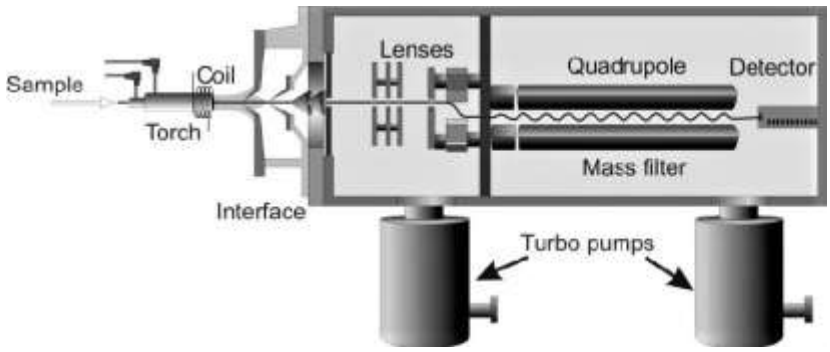

Fig. 3: Cross section schematic of an ICP-MS (Košler et al., 2003).

Understanding the basic principle of ICPMS

ICP-MS is a well-established technique for trace and ultratrace quantitative analysis and determination of isotope ratios of different isotopic elements. The usefulness of ICP-MS has been proven over the past decade. The advantages of ICP-MS include low sensitivity, high speed and a wide range of applications. Today, ICP-MS can be considered a mature technology. (Wilshefski et al., 2019). The ICP-MS is usually equipped with a liquid phase sampling system (nebulizer). It can be combined with chromatographic separation techniques.

Laser ablation is an important tool for detecting particles prior to ICP-MS detection. The analytical tools of ICP-MS are concerned with ion generation in inductively coupled plasmas and the sensitivity of ion detectors (Bocca et al., 2017). 2010; Psychogios et al., 2011). An important feature of the ICP-MS is that the output of the ICP is carried out by air pressure.

The process is versatile and solutions can be easily combined with different aspects including laser ablation, electrothermal evaporation, chemical manufacturing or high performance liquid chromatography (HPLC). Ion Strength ICP Mass Spectrometry Reflects the number of detected ions (counts per second or cps) obtained during a series of analytical steps (Gonnen et al., 2017)., 2000). These steps include: (i) conversion of the supplied sample (ii) delivery of aerosol/gas to the blood, (iii) nebulization of specific compounds after high temperature ionization and cooling of atoms in the blood, (iv) ion exchange. The ions transported from the plasma operating at atmospheric pressure to a large separator (analyzer) operating in high vacuum are extracted with ion optics, (v) separated according to the mass-charge ratio (m/z) and (vi) separated. The ions are detected by a detector that converts the ion flux into an electrical signal (cps). absorption rate, and the results of fractionation, Acid concentration or particle size distribution - for dry aerosols produced by laser cutting or electrothermal evaporation (Gonnen et al., 2000; Rodrigues et al., 2008; Dombovári et al., 2001; Vanhaecke et al., 2001).

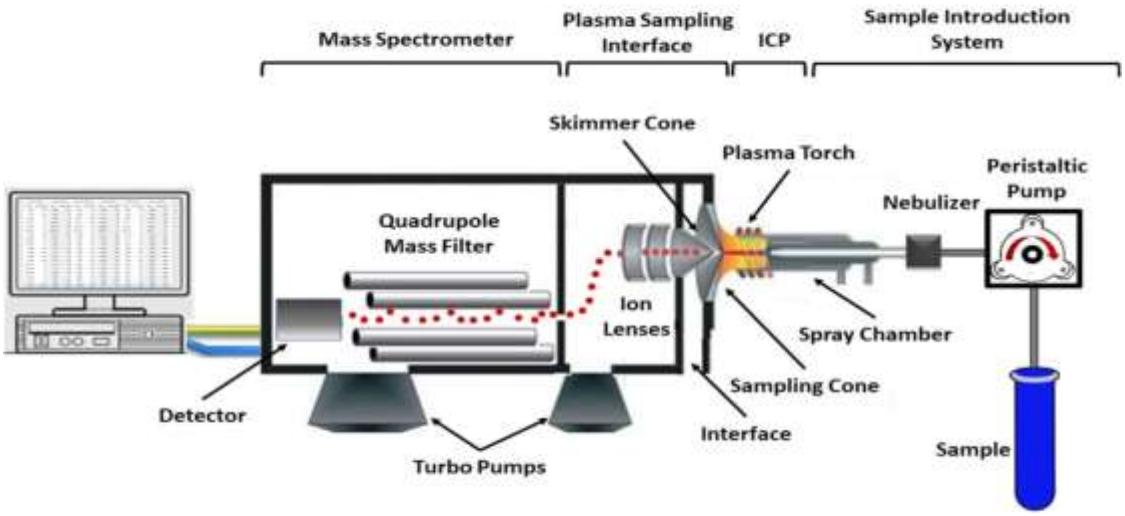

Fig. 4: Schematic diagram of the main components of an ICP-MS (Mazarakioti et al., 2022)

When the aerosol enters the hot plasma, some particles evaporate before the gaseous species undergo atomization and ionization. The effectiveness of this process depends on the nature of the drug and the state of the blood plasma. It should be noted that not all particles evaporate completely, but some of the largest particles and/or droplets can pass through the plasma without completely evaporating. Most commercial products use argon. Therefore, plasma consists mainly of argon atoms, and the structure contains many argon ions, electrons and species.

When all these (particles, steam, atoms and ions) are formed in a hot plasma, they disperse when they cross the plasma field. The ions formed in the plasma are transported to the mass analyzer and separated according to their mass-charge ratio (m/z). Finally, ions of comparable charge arrive at the detector and are counted (Novak et al., 2014). Elemental mass spectrometers generally cover the mass range of 6 to 254 a .Is this true? Therefore, they can often identify isotopic ions. The strength of the electrical signal is related to the ions produced in the blood and delivered by the ICP-MS ion optics. The ion-forming activity is affected by the temperature of the blood as well as the ionization energy of the specific material. Logic using the Saha-Eggert equation (Navas-Acien et al., 2017) , 2011), the degree of ionization of the drug depends on the plasma. Generally, ICP is considered a positive ion source. Assuming a plasma temperature of about 6000 K and an electron density of 1015 cm-3, the ionization efficiency is about 0.99 for sodium and 10-6 for chlorine. Of course, the element's ionization efficiency (signal-to-noise ratio) affects the signal-to-noise ratio. It is worth noting that the signal strength and sensitivity depend not only on the ionization efficiency, but also on the sampling rate, sample transmission/distribution efficiency, and finally the extraction and transmission efficiency of the ion channel of the spectrometer. Substrate effects on chemical and physical reactions can occur at any stage of the above process. These effects are related to sampling, isobaric effects and spectral effects. This effect can be caused by doubly charged ions or groups of ions. The first is slightly different, but the second should be based on blood testing (Novak et al., 2017). 2014; Pete et al., 2009; Jorabchi et al., 2006).

Working Procedure of ICPMS

Before beginning elemental analysis by ICP-MS, ensure any necessary maintenance has been carried out. Prepare the samples, ensuring all appropriate safety precautions are followed. Sample preparation may be as simple as acidifying a water sample to ensure all the elements are chemically stable. In case of Milk, contains high levels of Total Dissolved Solids (TDS), including organic and inorganic components. While microwave sample preparation breaks down the organic constituents, the inorganic salts remain in solution at high concentrations. Still some elements are chemically unstable and require a particular solvent or acid to ensure they give reliable data. For example, mercury (Hg) is not chemically stable in nitric acid (HNO_3) alone, so hydrochloric acid (HCl) is usually added to samples when mercury is a required analyte. ICP-MS has a very wide measurement range (from sub-ppt to 100s or 1000s of ppm), but data accuracy will be improved if the analytes are measured within the range of the calibration standards for each element. ICPMS is a multi-element technique with large analytical range and high sample throughput. It requires low sample volume having simple sample preparation. New technology ICPMS provide high-resolution and tandem mass spectrometry (triple-quadrupole) instruments with a very high level of interference control.

CONCLUSION

Heavy metals are generally considered very dangerous and harmful to the environment. Food safety issues such as microbiological, chemical and physical risks are a concern today. Cadmium (Cd), lead (Pb), arsenic (As), mercury (Hg) and other heavy metal residues are important pollutants in the chemical industry. Polluted soil is an important source of cadmium and lead, which can be stored in milk from food. Heavy metals have become contaminants in foods for many reasons and cause health problems. ICPMS is an efficient technology to determine the amount of heavy metal contamination in milk and milk products. Nowadays, it is efficiently used for fortified milk testing to ensure that the fortified milk carry required level of vitamins upon fortification.

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