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Optimization of Sample Preparation Techniques for the Quantifications of Metal Ions by Atomic Absorption Spectrometry

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Abstract: Sample preparation is a crucial analytical tool that significantly contributes to the accuracy of analytical methods such as flame atomic absorption spectroscopy (FAAS), electrothermal atomic absorption spectrometry (ETAAS), and inductively coupled plasma optical emission spectroscopy. Therefore, analytical chemists focus on developing sample preparation methods to enhance the sensitivity of these technique measurements. To achieve this, they employ optimization techniques for sample preparation procedures and systems, utilizing multivariate techniques within experimental design frameworks. This not only saves time, cost, and reagents but also ensures improved accuracy. Nevertheless, newer methods of sample preparation are emerging that offer faster and more accurate alternatives to traditional techniques. This review aims to explore the fundamentals and applications of multivariate techniques within experimental design for sample preparation procedures and systems, specifically focusing on FAAS and ETAAS. The review covers various aspects including common errors encountered during sample preparation, different sample preparation methods (such as microwave-assisted extraction, ultrasound-assisted extraction, microwave acid digestion, pre-concentration and separation techniques, and slurry sampling), variables involved in sample preparation, and techniques of multivariate methods under experimental design. These techniques include full factorial design, fractional factorial design, Plackett-Burman design, Box-Behnken design, central composite design, and Doehlert design. The review also highlights the applications of multivariate methods in conjunction with newly developed sample preparation techniques, focusing solely on FAAS and ETAAS techniques.

Index Terms—Electrothermal atomic absorption spectroscopy, Experimental Design, Flame atomic absorption spectrometry, parameters (variables) in sample preparation, sample preparation.

1 INTRODUCTION

Both metallic and non-metallic elements are present in various inorganic and organic matrices, both simple and complex, which can be analyzed using Atomic Absorption Spectrometry (AAS). AAS stands out as a unique and important analytical tool, serving as the standard method for determining more than 70 elements, detectable at parts-per-million (ppm) and parts-per-billion levels, thereby offering high analytical sensitivities[1],[2]. Fig. 1. shows that, in AAS, when the correct wavelength of light is applied to an atom in its ground state, the atom may absorb the light energy and transition to an excited state, a phenomenon known as the atomic absorption process. The intensity of radiation absorbed by the atom is then quantitatively measured in AAS by passing through a specific resonant wavelength, referred to as atomic absorption measurement [3].

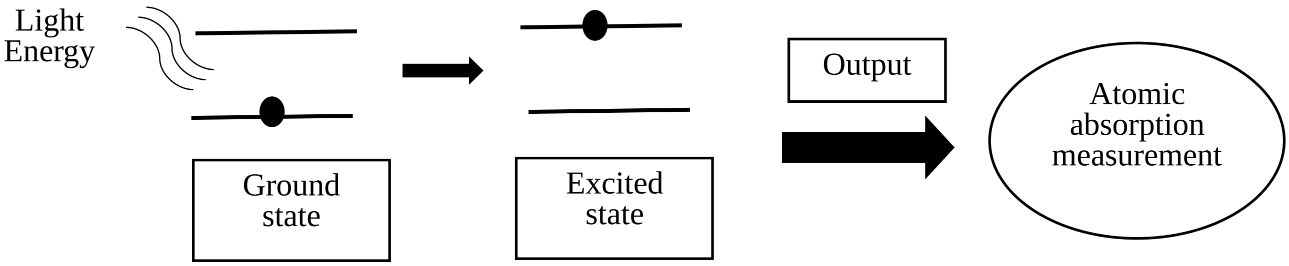

Fig 1. Sketch diagram of the atomic absorption process

The Atomic Absorption Spectrometry (AAS) technique comprises two main steps: the conversion (meaning volatilization and decomposition) of the sample into its constituent gas-phase atoms (atomization), and the subsequent adsorption of radiation by these neutral atoms [4]. Atomization can be achieved using flame, electrothermal, or plasma methods. Consequently, three analytical methods are generated: Flame Atomic Absorption Spectrometry (FAAS), Electrothermal Atomic Absorption Spectrometry (ETAAS), and Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) or Inductively Coupled Plasma Mass Spectrometry (ICP-MS) [3].

FAAS and ETAAS have become widely and frequently used techniques for trace metal analysis. ETAAS offers simplicity and high selectivity with relatively sensitive measurements, requiring smaller samples for routine analysis. FAAS, on the other hand, is successful for routine determination of most metals, providing simplicity, rapid analysis (10-15 seconds per sample), and relatively cheaper, robust, and easy-to-operate instrumentation, measuring at ppm concentration levels with good precision [5]. However, both techniques have drawbacks. ETAAS suffers from a low analytical range, low tolerance to chemical matrices, less precision, frequent maintenance, slower measurement time, greater operator skill requirements, higher matrix interferences, and relatively high cost for routine analysis. Similarly, FAAS has limitations including lower sensitivity, poor limit of detection, and the need for larger sample amounts [5],[6].

Among these disadvantages, the analytical sensitivity factor affects both techniques more significantly than other analytical techniques. Furthermore, sensitivity affects the precision and accuracy of measurements in both techniques. Poor analytical sensitivity in both techniques arises due to inefficiencies in atomization, sampling, and sample introduction processes. A consequence of the factors involved in the atomization step include nebulization, desolation, vaporization, dissociation, and ionization processes [5],[6],[7],[8]

Despite these challenges, the relationship between the limit of detection and accuracy is closely tied to sensitivity [9]. Therefore, sensitivity serves as a limiting factor in FAAS. Decreased sensitivity in FAAS measurements affects accuracy due to various factors including sample composition, sample preparation, instrumental system, and operator proficiency [10]. Sample preparation, in particular, significantly contributes to the limit of detection and sensitivity of both techniques, often leading to errors in spectroscopic analysis [11]. This review article discusses sample preparation errors that contribute to the underestimation or overestimation of analytical results. It also explores the use of experimental design tools to prevent such errors and develop new methods, such as the application of multivariate techniques.

1.1 Sample preparation

Simple or more complex sample preparation is always necessary for analysis by spectroscopic methods. However, such procedures are not unique to the spectroscopic field [10], [11]. The second step of the measurement process involves several stages, including drying, homogenization, grinding, and mineralization, ranging from simple dilution to partial and total dilution. The following scheme Fig. 2. shows the palanning of sample preparation to determine metals using FAAS and ETAAS techniques.

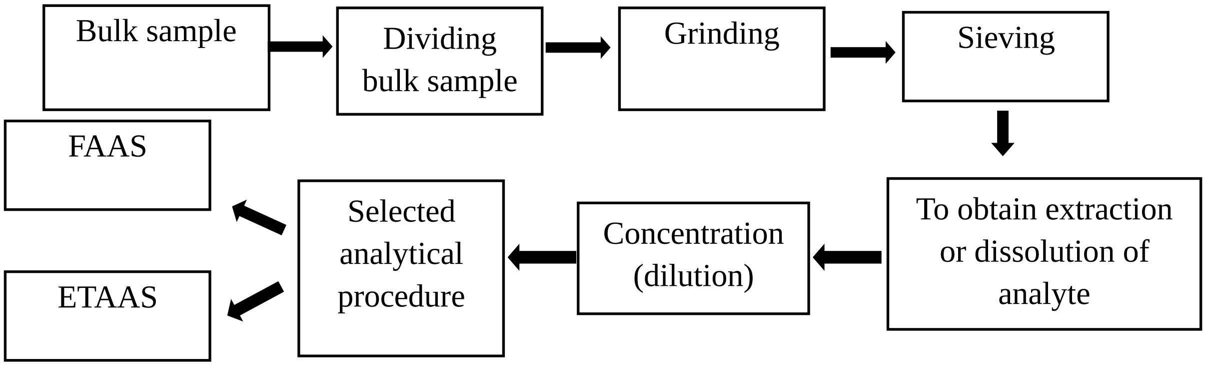

Fig 2. For the planning of sample preparation to determine metals using both techniques

Sample preparation plays a major role in converting a representative bulk sample into a suitable form for analysis. The choice of sample preparation method depends on extracting the analyte from the complex matrix. Therefore, this review will discuss numerous methods in sample preparation. Nevertheless, both random and systematic errors during sample preparation tend to be higher than those during the analysis process. So finally, the major target of sample preparation is to eliminate matrix interference, perform sample clean-up, and pre-concentrate the analyte to enhance the analyte’s response signal.

1.2 Errors during the sample preparation

In past years, some analysts claimed that the "contribution of sample preparation stage errors could be neglected," but most analysts recognized their importance. Many steps in sample preparation are carried out in the laboratory, and often the analyte concentration is relatively low in many samples. Therefore, errors in sample preparation directly affect the determination of element concentrations in FAAS and ETAAS. Consequently, analytical chemists focus on improving sample preparation methods to enhance instrumental (FAAS and ETAAS) performance [11].

Contamination is a critical concern due to the high risk it poses, especially in the presence of low levels of the analyte. Contamination can occur from the use of chemical compounds such as acids, spectrochemical buffers, and chemical modifiers with uncertain degrees of purity, as well as insufficiently distilled water [12]. Adsorption processes may result in the loss of the analyte. Failure to immediately acidify aqueous samples after sampling can lead to long-term adsorption of trace elements onto vessel walls, particularly with the use of old vessels [13]. Evaporation of the analyte often occurs due to the use of less viscous solutions. Incomplete decomposition of the matrix can affect the total loss of analytes, especially in organic matrices. Additionally, incomplete decomposition of organic matter, the use of inappropriate reagents (alkali metal hydroxides, carbonates, refluxing agents), and certain acids may interfere as nonspectral factors in the analytical determination in both techniques. Various parameters in sample preparation contribute to the loss and evaporation of analytes [11],[13]. Despite efforts, errors cannot be eliminated entirely but can be reduced through improved techniques. Analytical chemistry offers many sample preparation methods, and when the correct method is chosen, measurements in both techniques can be more accurate [14].

1.3 sample preparation methods

The objective of sample preparation is to break bonds and crystalline structures. The appropriate method is selected based on factors such as the nature of the analyte, analyte concentration levels, sample matrix, instrumental measurement technique, and required sample size. Sample preparation methods vary slightly between different techniques, and separation and detection procedures also follow the sample preparation techniques in analytical methods [12], [15],[16].

1.3.1 Decomposition techniques

There are two basic types of procedures in decomposition techniques: dry and wet decomposition. Both involve extracting the analyte of interest from an interfering matrix using complementary reagents/acids or heat [15] .

Acid Digestion or Wet Decomposition

Acid digestion is utilized for metal content determination or extracting metals from inorganic matrices using oxidizing agents or external heat sources. Various types of acids or acid combinations are employed, depending on the nature of the matrix and the analytical instrument used. Lower temperatures are often used under open systems to minimize volatile mineral loss [11],[17]

Wet Decomposition

Wet decomposition aims to achieve total decomposition and mobilization of selective analytes into solution. It may often adopt two approaches: determination of the total content of an element and fractionation of elements present in a given sample. Wet decompositions can be categorized as total decomposition, strong attack, and moderate attack, depending on the type and strength of acids used. These procedures are typically carried out in open systems, and various performances may exhibit different types of energy present in wet decomposition [12],[18]. Table 1 shows different energy types perform during the decomposition with various types of acids.

Table 1: Category of decomposition depends on energy

Energy type	Apparatus type	Type of using acids
Thermal energy	Bunsen burner Hot plate Digestion block Oven muffle	Combination of acids Ex: $HF+H_2SO_4$ H_2SO_4+HCl $HCl+HNO_3$ (depend on the sample)
Ultrasonic energy	Bath system	Diluted acid medium (normally)
Radiant energy (infrared radiation)		Nitric acid or hydrogen peroxide
Radiant energy (ultraviolet radiation)	Polarography Voltammetry	hydrogen peroxide
Radiant energy (microwave radiation)	Wave-guided type microwave digestion system Cavity microwave digestion system	Mixture of acids Ex; $HNO_3+H_2O_2$ $H_2SO_4+ H_2O_2$

Digestion can be carried out in open or closed vessels, which are performed under microwave radiation or classical heating blocks. Widely used closed systems improve oxidation efficiency, decrease digestion time, and are also successful for digesting different samples. However, silica residue-containing matrices are not suited for this technique. Materials are softened or solubilized using heat, chemical reagents, and moisture during the digestion process [12], [13].

1.3.2 Microwave Digestion

Microwave-assisted digestion (MAD) is an especially attractive and reproducible method for small samples. This technique is carried out using a focused microwave oven with reflux and polytetrafluoroethylene (PTFE) bombs, which are commercially available. Other systems, such as continuous flow systems, stopped-flow systems, ambient pressure systems, or pressurized systems, are also present. MAD performs better than traditional techniques, offering shorter acid digestion times, greater recovery of volatile elements, minimized contamination levels, and reduced reagent consumption [17], [18].

1.3.3 Microwave-assisted extraction (MAE)

MAE is a combination of microwave energy radiation and conventional solvent extraction. Microwave radiation heats the solution directly, significantly reducing extraction time and accelerating the extraction process. This modern and attractive extraction technique speeds up the leaching of the analyte. The temperature in the solution increases due to the dual mechanism of ionic conduction and dipole rotation. The choice of solvent for MAE depends on its dielectric constant. MAE is carried out under microwave systems, which can be multimode or single-mode systems. Unlike MAD, MAE uses organic solvents for extracting the analyte. This method achieves high efficiency with the same recovery in a shorter time and with less solvent consumption, offering advantages over traditional extraction methods [19]. The following diagram Fig. 3. Shows that microwave energy goes through the sample in MAE method.

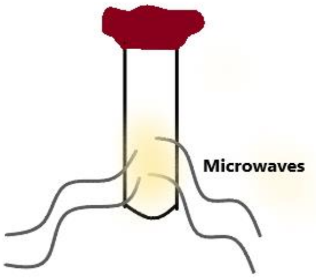

Fig 3. The sketch for the MAE method

1.3.4 Ultrasound-assisted extraction (UAE)

UAE is an efficient tool in analytical chemistry that can increase the extraction rate. Sample dissolution is accelerated by ultrasound, which raises the temperature more slowly than microwave-assisted digestion techniques. The mechanical effect of ultrasound occurs during the cavitation process, aiding in increasing the temperature of the reaction medium. Both organic and inorganic analytes from solid samples are susceptible to this technique.[20] The behavior of the both analyte during UAE showed in Table 2.

Table 2: Presence of the ultrasound waves, behavior of the organic analyte and inorganic analyte.

Organic analyte	Inorganic analyte
Partial or complete mineralization of the substrates	Getting excellent results from the diverse matrices
Adopt rigorous experimental control	To give the less decomposition risk

Major advantages of ultrasonic-assisted extraction include reductions in analysis time, lower reagent consumption, and absence of interfering species formation during sonication. Typically, an ultrasonic bath, ultrasonic probe, or cup-horn reactor can be used. Ultrasonic energy facilitates sample extraction when the sample is in dilute acid solution near room temperature and atmospheric pressure [21]. The diagram Fig. 4. illustrates that the ultrasonic energy passes via the sample (example: soil sample) in UAE method.

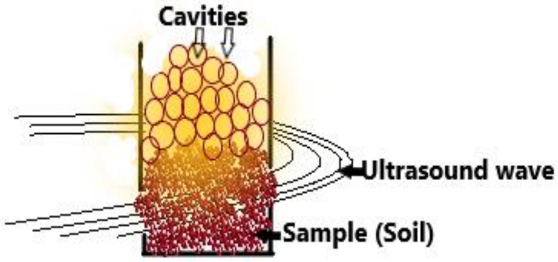

Fig 4. The sketch for the UAE method

1.3.5 Pre-concentration procedures and Separation

Pre-concentration methods are essential, as the determination of metals indirectly can be insufficiently sensitive in some analytical methods. Pre-concentration can be performed in online or offline systems and their comparison showed in Table 3.

Table 3: Comparing both the systems

On-line systems	Off-line systems
Possibility of automation	Happen in presence of higher pre-concentration factors
Increasing precision and accuracy	Relatively low the precision and accuracy
Minimizing sample consumption	Large consumption of sample
Reducing toxic residue in production and reagents	Maximizing the use of reagents
Less probability of sample contamination	Higher risk of sample contamination.

Precipitation, cloud point extraction (CPE), liquid-liquid extraction (LLE), solid-phase extraction (SPE), and ion exchange are used to obtain efficient, selective, and high purity products by separating metals [12]. Table 4 shows comparison of most popular pre-concentration methods such as LLE, SPE and CPE and the illustration of that techniques was shown in Fig. 5.

Table 4: Comparing of most popular pre-concentration methods

Technique	LLE	SPE	CPE
Features	Use for different solubility of elements in immiscible liquids Performing simple manner	Modern technique Use to overcome the limitation of LLE Following Liquid chromatography Always modified of the sorbent	Attractive method The ability to isolate the target analyte Entrap the analyte using uncharged micellar
Disadvantages	High consumption of	Sometimes obtain	

	solvent Sample contamination source analytical error and laborious routine	low recoveries	
Advantages	Increasing efficiency of atomization	Less risk of contamination Easy handling Reaching high enrichment factors (EF)	Use of water Faster operation Shorter extraction time Large recoveries High EF

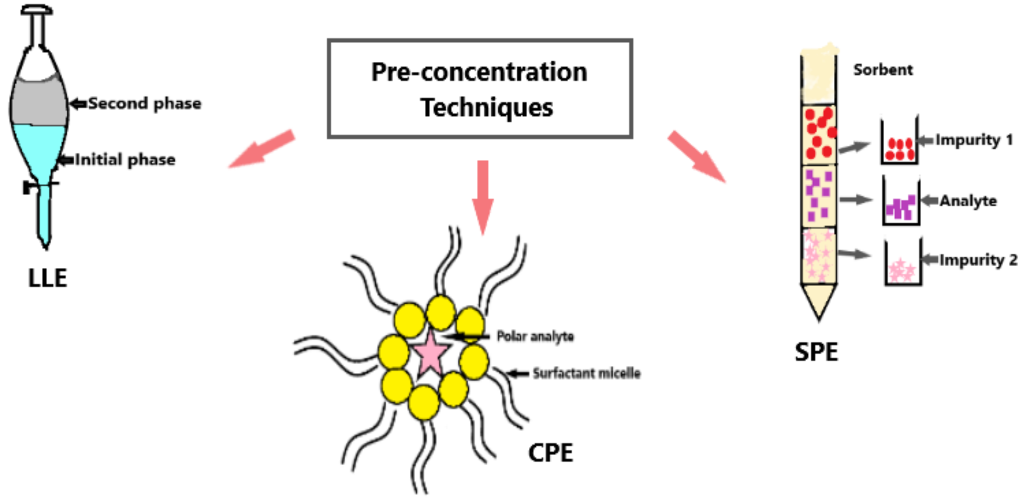

Fig. 5. Commonly used preconcentration techniques in applications of multivariate design in sample preparation

1.3.6 Slurry sampling

Slurry sampling is a special analytical procedure for solid samples. In this technique, solid samples are dispersed in a liquid phase that can be handled as solutions. Slurry sampling allows for the determination of analytes while reducing the risk of sample contamination and minimizing the loss of isolated analytes. It can be applied easily to both organic and inorganic samples, minimizing the use of reagents, and can be easily automated [22].

1.4 Parameters (variables) of sample preparation techniques

The goal of analytical chemists is to simplify sample procedures, which directly influences the accurate determination of analytes. Therefore, analytical chemists focus on developing sample preparation methods by minimizing processes and errors related to sample preparation [22]. Afterward, they introduce many parameters for different techniques that influence the total decomposition of the sample or the highest fraction of analyte in the sample. Different techniques with various parameters are presented in the Table 4.

Table 4: Uses of different parameters in different techniques

Sample preparation technique	Parameters (variables) of that technique	Reference
MAD	Compositions of the acid mixture Radiation time Microwave power the concentration of nitric acid the volume of nitric acid	Soylak, et al. [23] Soriano, et al. [24] Khajeh [25]
Slurry sampling	Type of extractor Its final concentration Time	Amorim, et al. [26]
UAE	Pre-sonication time Sonication time The temperature of the ultrasonic bath HNO_3 HNO_3: H_2O_2 Sample mass Particle size The volume of deionized water amplitude	Teixeira, et al. [21] Arain, et al. [27]
MAE	Temperature Irradiation power Irradiation time Concentration of acid	Khajeh [28] Khajeh [29]
Microwave acid digestion	Acid digestion volume Digestion temperature Digestion time Mass of sample Dummy Concentration of acids	Otero-Pazos, et al. [30]

If the parameters of sample preparation techniques are optimized quantitatively using the design of experiments (DOE), the detection of both techniques' measurements will be more accurate. Under these parameters, suitable best values can be obtained using different models [31]. Therefore, experimental design will be discussed in this review article.

Choosing the correct sample preparation method to apply with experimental designs contributes to obtaining accurate flame or ETAAS measurements. This helps achieve the golden goal of obtaining the best results in the shortest time, with minimal contamination, low reagent consumption, and minimal residue or waste [12].

1.5 Design of Experimental (DOE)

In analytical chemistry, the main goal of DOE is method optimization, which fulfills two steps: the screening step and the optimization step. The screening step involves studying many factors, and significant factors are chosen using models and the operator's intuition. The optimization step further studies factors to determine the best analytical performance, ultimately generating good analytical features [32].

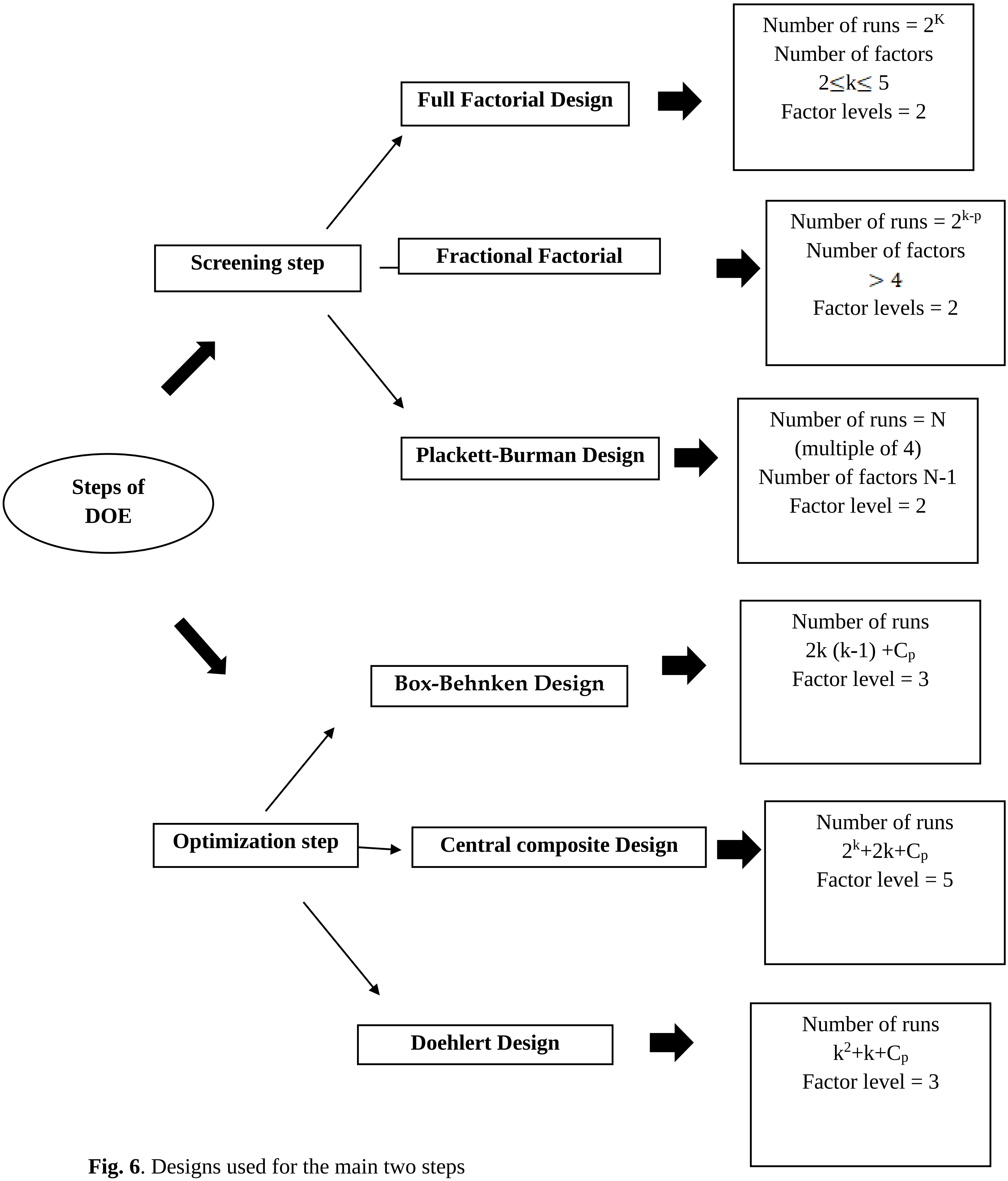

Fig. 6. Designs used for the main two steps
k=number of factors; C_p=number of center points.

There are two types of methods the univariate method and the multivariate method.[33] The comparison of the two methods in DOE was shown in Table 5.

Table 5: Comparing both DOE

Univariate method	Multivariate method
Studying each variable at a time	the study of several controlled variables at the same time
the higher number of runs	Less number of runs
large consumption of time	Save time
large consumption of reagents	Save reagents
High cost	Low cost

Multivariate techniques are applied to optimize the measurement process of FAAS or ETAAS in analytical chemistry to achieve the best possible analytical performance. Therefore, there are numerous applications of multivariate methods, such as optimization of instrumental parameters, sample preparation (including steps like pre-concentration methods), sampling, and sample introduction. In this review article, we focus on the application of sample preparation methods with published works in analytical chemistry involving FAAS and ETAAS using multivariate techniques.

2 APPLICATION OF MULTIVARIATE TECHNIQUES IN SAMPLE PREPARATION

Multivariate techniques encompass various steps of sample preparation, which can be divided into several parts, including optimization of digestion processes, extraction, and pre-concentration procedures. Furthermore, they are further categorized based on sample preparation techniques.

2.1 Optimization of microwave-assisted extraction method using the experimental design

Khajeh [29] investigated the development of a procedure for Zn and Cu by FAAS in food samples after extraction by a microwave system using response surface methodology (RSM). Additionally, Khajeh [28] proposed a focused MAE procedure for soybean samples to determine copper and zinc using FAAS. Khajeh, et al. [34] developed a procedure for Fe, Cu, Mn, and Zn in cabbage after MAE using RSM. Furthermore, Khajeh and Ghanbari [35] focused on the development of the MAE procedure for the determination of Zn, Pb, Mn, Fe, and Cu in snow trout samples (fish muscles) after extraction by a microwave system. Khajeh and Sanchooli [36] applied RSM to the development of a procedure for Zn and Cu in cereal samples by FAAS after extraction by a microwave system. Moreover, Khajeh, et al. [37] applied RSM to the development of a MAE procedure for Zn and Fe determination by FAAS in celery samples after extraction by a microwave system. Khajeh [25] proposed the use of a full factorial design and Box-Behnken design to optimize the extraction of Zn, Cu, and Fe in pistachio nut in a closed vessel system.

2.2 Optimization of microwave-assisted digestion method using the experimental design

Soylak, et al. [23] proposed the development of a MAD procedure for tea samples to determine Zn, Cu, and Ni using FAAS. Additionally, Khajeh [38] established a microwave-assisted method for the digestion of powdered milk for the determination of Cu and Zn employing FAAS. Santelli, et al. [39] employed a three-level Doehlert design to optimize the extraction of Zn, Fe, and Mn in food samples in a focused microwave system with a closed vessel for FAAS. Soriano, et al. [24] employed a three-variable Doehlert design to optimize after leaching with dilute acid in a microwave applied to multivitamin supplements for determination of Cu, Fe, Mn, and Zn using FAAS.

2.3 Optimization of ultrasound-assisted extraction method using the experimental design

da Silva Medeiros, et al. [40] investigated a simple analytical procedure based on UAE coupled with FAAS for the determination of Al, Cd, Cu, Ni, and Zn in soil samples. Additionally, Costa, et al. [41] established the development of a simple UAE procedure for the determination of Cu, Fe, Zn, and Mn in plant samples (stem, leaf) using FAAS. Machado, et al. [42] proposed a sample preparation method involving UAE for the determination of iron and zinc in infant formulas using FAAS. Silva, et al. [43] performed optimization of the development of the sample preparation method using UAE for the determination of Ca, Mg, Fe, and Zn in fish fillets dissolved in an alkaline medium (tetramethylammonium hydroxide) employing FAAS. dos Santos Alves, et al. [44] proposed the development of sample dissolution assisted by ultrasound energy in tetramethylammonium hydroxide (TMAH) media for the determination of Ca, Mg, Zn, and Fe in liquid and powdered cow milk by FAAS. Moreover, Teixeira, et al. [21] applied 25-2 fractional factorial designs and 23 central composite designs to develop an efficient ultrasound-assisted extraction for Cd, Co, Cr, Cu, Mn, Ni, Pb, and Zn determination in organic fertilizers by fast sequential FAAS. Barros, et al. [45] established an acid leaching method assisted by ultrasonic energy for the extraction of Cu, Mn, Ni, and Zn from rations for chicken nutrition employing FAAS. Jalbani, et al. [46] introduced a simple and rapid method based on ultrasound energy for the determination of aluminum in complex matrices of chocolate and candy samples by ETAAS. Arain, et al. [27] proposed a sample preparation method based on UDM of Cd and Ni from tobacco leaves grown in contaminated soil by ETAAS. Trindade, et al. [47] established the development of the ultrasound-assisted procedure to determine Fe and Ni in vegetable oil using high-resolution continuum source ETAAS.

2.4 Optimization of digestion by UV radiation method using the experimental design

The SPE procedure has been developed for the determination of cadmium in landfill leachate samples using FAAS by Sousa Filho, et al. [48]. Photooxidation degradation with UV radiation/H2O2 sampling technique has been developed for the determination of Fe, Zn, Mn, Ni, and Co in municipal solid waste landfill leachate using FAAS by Bezerra, et al. [49].

2.5 Optimization of slurry sampling method using the experimental design

Amorim, et al. [50] proposed the use of the Box-Behnken design as a multivariate optimization procedure for iron and zinc determination in starch samples (corn, rice, potato, and cassava) after slurry sampling using FAAS. Bezerra, et al. [51] employed slurry sampling as a sample treatment for the determination of Zn and Mn in tea leaves using FAAS. Amorim, et al. [26] established the development of a slurry sampling procedure to determine Fe and Mg in cassava starch using FAAS. Brandao, et al. [52] developed a slurry sampling method to determine Fe in fortified milk powder samples using high-resolution continuum source FAAS. Soares and Nascentes [53] evaluated this procedure for the determination of lead in hair dyes coupled with ETAAS. de Oliveira, et al. [54] introduced slurry sampling for the determination of Cd and Pb trace levels in cassava starch using ETAAS.

2.6 Optimization of microwave-assisted extraction method using the experimental design

Tuzen, et al. [55] developed a procedure for pre-concentration to determine trace levels of copper and nickel in food samples using solid-phase extraction (SPE) as a separation technique with Dowex Optipore SD-2 resin. An aqueous two-phase system without an extracting agent has been developed for pre-concentration of small amounts of Cd and Mn in food samples using FAAS by Neves, et al. [9]. A procedure for water and sediment matrix was developed by Meira and de Souza Dias [56] using a constrained mixture design to achieve optimization values of the proportions of a mixture composed of the disperser, extractor solvents, and complexing agent, and used a Doehlert matrix to obtain optimum values of their variables such as pH, the concentration of NaCl, and sonication time. Kolachi, et al. [57] proposed a methodology for determining zinc in an aqueous extract of medicinal plants using cloud point extraction with FAAS detection. Ferreira, et al. [58] developed a procedure for pre-concentration using cloud point extraction to determine copper and zinc in food samples using sequential multi-element FAAS. Altunay, et al. [59] proposed the use of multivariate optimization for the determination of Pb (II) in vegetables via FAAS after heat-induced deep eutectic solvent micro-extraction. Do Carmo, et al. [60] performed the optimization of an online preconcentration system, using Moringa oleifera husks as a biosorbent, for the determination of copper in gasoline using FAAS. Jalbani and Soylak [61] proposed a preconcentration procedure using a micro-extraction technique that combined Fe3O4 nanoparticles with surfactant-mediated solid-phase extraction for the determination of Cd (II) and Pb (II) in water and soil samples using FAAS. An on-line pre-concentration method was proposed for the determination of Zn(II) in alcohol fuel by [30]

2.7 Optimization of microwave-assisted extraction method using the experimental design

Otero-Pazos, et al. [62] developed a microwave acid digestion procedure for the determination of Cd, Co, Cr, Cu, Mn, Pb, and Zn from paper and board samples using both techniques. A Plackett-Burman design was performed for the optimization of experimental factors.

2.8 Summary of the recent applications of experimental design applied in the sample preparation

Table 6, 7, 8 show the summarization of the applications in recent publications of designs used in only screening step, designs used in only optimization step and designs used in both steps applied in sample preparation respectively.

Table 6: Application of only designs used in screening step applied in sample preparation

Experimental design	Optimum parameters	Matrix	Reference
Full factorial design	Composition of acids Radiation time Microwave power	Tea	Soylak, et al. [23]
Two-level factorial design	Concentration of HCl acid Sonication time Triton X-100 concentration	Fortified milk powder sample	Brandao, et al. [52]
Two-level full factorial design	pH, reagent Concentration Amount of resin on column	Water and Food samples	Tuzen, et al. [55]
Full factorial design	pH of sample Flow rate Adsorbate mass	Gasoline	Do Carmo, et al. [60]
Full factorial design	sorbent mass, pre-concentration time,	Alcohol fuel	Alves, et al. [63]

	volume of eluent, sample flow rate, sample pH, and eluent concentration		
Placket-Burman design	Acid digestion volume Digestion temperature Digestion time Mass of sample Dummy Concentration of acids	Paper and board samples	Otero-Pazos, et al. [30]

Table 7: Applications of only designs used in optimization step applied in sample preparation

Experimental design	Optimum parameters	Matrix	Reference
Box-Behnken design	Irradiation power Irradiation time Temperature	Wheat flour Corn flour	Khajeh [29]
Central composite design	Power Temperature Time Volume of nitric acid	Cabbage	Khajeh, et al. [34]
Box-Behnken design	Irradiation power Time Temperature	Celery	Khajeh and Sanchooli [36]
Doehlert design	Irradiation power Time Temperature	Cereal samples	Khajeh, et al. [37]
Doehlert design	Irradiation power, Time Composition of oxidant solution	Food sample	Santelli, et al. [39]
Doehlert design	Concentration of nitric Power Time	Multivitamin supplements	Soriano, et al. [24]
Central composite design	Concentration of HCl, HNO3, HF Extraction time	Soil	da Silva Medeiros, et al. [40]
Mixture design and Box – Behnken	Power Time Temperature	Plant	Costa, et al. [41]
Central composite	Concentration of	Infant formulas	Machado, et al. [42]

design	HNO_3 Sonication time Sonication amplitude		
Doehlert design	Volume of TMAH Sonication time Bath temperature	Fish fillets	Silva, et al. [43]
Central composite design	Sonication time Methyl ammonium hydroxide volume	Powered cow milk	dos Santos Alves, et al. [44]
Doehlert design	p^H buffer concentration, flow rate	Landfill leachate samples	Sousa Filho, et al. [48]
Constrained mixture design and Doehlert design	p^H irradiation time buffer concentration	Municipal solid waste landfill leachate	Bezerra, et al. [49]
Box-Behnken design	type extractor, final concentration of extracting solution, and sonication time	starch samples	Amorim, et al. [50]
Constrained mixture design	HCl, HNO_3, and Triton X-100 solutions	Tea leaves	Bezerra, et al. [51]
Box-Behnken design	solvent, final concentration, and time	Cassava starch	Amorim, et al. [26]
Doehlert design	pH Polymer molar mass Type of salt	Food sample	Neves, et al. [9]
Constrained mixture design Doehlert design	pH Concentration of NaCl Sonication time	Water Sediment	Meira and de Souza Dias [56]
Box-Behnken design	pH Reagent Concentration buffer concentration	Food samples	Tuzen, et al. [55]
Central composite design	pH of sample solution, amount of extraction solvent	Vegetables	Altunay, et al. [59]

	temperature ,and amount of ligand		

Table 8: Applications of designs used in both steps applied in sample preparation

Experimental design	Optimum parameters	Matrix	Reference
Full Factorial design Box-Behnken design	Irradiation power Extraction time Temperature Concentration of nitric acid	Soybean	Khajeh [28]
Fractional Factorial design Box-Behnken design	Irradiation power Extraction time Temperature Concentration of nitric acid	Fish Muscles	Khajeh and Ghanbari [35]
Full Factorial design Box-Behnken design	microwave power, temperature time volume of nitric acid	Pistachio nut	Khajeh [25]
Full Factorial design Box-Behnken design	Irradiation power, Volume of nitric acid, Digestion time Temperature	Powder milk	Khajeh [38]
Fractional factorial design Central composite design	extractor, volume of HF, time volume of extractor and amplitude	organic fertilizers	Teixeira, et al. [21]
Centroid-simplex mixture design Doehlert design	sample mass, sonication time final concentration of acid	Rations for chicken	Barros, et al. [45]
Placket-Burman design Central composite design	Presonication time, sonication time, temperature of ultrasonic bath, concentration of HNO_3, HNO_3, H_2O_2, sample mass, sample mass,	Tobacco leaves grown in contaminated soil	Arain, et al. [27]

	particle size		
Fractional Factorial design and Doehlert matrix design	Temperature of the Ultrasonic bath, Exposure time to Ultrasonic energy, Volumes of two acid mixtures HNO_3-H_2SO_4-H_2O_2(1+1+1) HNO_3-H_2O_2(1+1) sample mass	Chocolate and candy samples	Jalbani, et al. [46]
Full Factorial design and Doehlert design	Extraction time, Extraction temperature Sonication amplitude	Vegetable oil	Trindade, et al. [47]
Fractional Factorial design Central composite design	Pyrolysis temperature, Pyrolysis time atomization temperature.	Hair dye	Soares and Nascentes [53]
Fractional Factorial design and Central Composite design	atomization temperature pyrolysis temperature pyrolysis time	Cassava starch	de Oliveira, et al. [54]
Placket-Burman design Central composite design	Ligand concentration, pH Temperature	Aqueous extract of medicinal plant	Kolachi, et al. [57]
Placket-Burman design Central composite design	amount of absorbent P^H Concentration of nonionic	Water soil	Jalbani and Soylak [61]

4 CONCLUSION

The main achievement of all published studies is to apply the best optimized conditions of the system to the unique matrix to obtain greater analytical features, such as sensitivity, precision, accuracy, and lower limits of detection (LOD) and limits of quantification (LOQ) for FAAS and ETAAS techniques. Additionally, errors in sample preparation, types of sample preparation methods, and multivariate design were addressed.

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