



Review

Electrothermal vaporization–inductively coupled plasma–mass spectrometry: A versatile tool for tackling challenging samples

A critical review

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ABSTRACT

In this review, the literature on the subject of electrothermal vaporization–inductively coupled plasma–mass spectrometry (ETV–ICP–MS) published during the last decade is reviewed with a double purpose: an evaluation of the possibilities of this technique for dealing with very challenging analytical applications on the one hand, and the establishment of a reference guide for method development in ETV–ICP–MS on the other. First, a brief introduction, pointing out the milestones in the development of the technique will provide the reader with a better understanding of the present situation of ETV–ICP–MS and its future perspective. After a section on the basic processes occurring in the furnace and during analyte transport, a guide for method development for challenging analytical applications is proposed, based on the existing literature. Next, the latest contributions in the main application areas of the field are reviewed, with special attention to the most challenging ones: i.e. speciation, “thermal” resolution, enabling complex matrixes to be analyzed and spectral overlap to be avoided, and the direct analysis of slurries and solid samples. Finally, the advantages obtained by coupling an ETV unit to newer types of ICP–MS instrumentation, equipped with collision/reaction cells, time-of-flight (TOF) or sector field (SF) spectrometers, are also discussed.

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1. Introduction

Since the commercial introduction of ICP–MS, the development and improvement of sample introduction systems has been one of the main challenges for the scientists working in this field [1]. Since the beginning, sample introduction was carried out *via* pneumatic nebulization, which offered a simple and fast means of sample handling, relatively good stability, potential for automation and low cost. However, some negative aspects were also associated with this sample introduction system and, therefore, the efforts devoted to improving this part of the technique were well justified.

Very soon after the first ICP–MS paper appeared in the literature [2] (in 1980) and the first commercial instruments became available (in 1983), Gray and Date – some of the first scientists involved in the very early research in ICP–MS – pointed out the problem of high background signals coming from the water vapor introduced as a part of the nebulized aerosol and suggested that “the technique would benefit from the application of “dry” sample introduction techniques, including electrothermal atomization” [3]. Some months later, they described the coupling of an electrothermal vaporizer to an ICP–MS instrument for the first time [4], using a commercial vaporizer originally designed for coupling with an inductively coupled plasma–optical emission spectrometer (ICP–OES) [5].

ETV–ICP–MS was received with great enthusiasm by the scientific community owing to the potential advantages that the coupling could bring along. Besides the possibility to separate the volatilization of the sample matrix and that of the analyte in time (with the subsequent reduction of both spectral and non-spectral interferences), the sample introduction efficiency could be clearly improved compared to pneumatic nebulization (the efficiency of which is only about 1–2% [4]), improving even more the limits of detection (LODs) attainable. Only low sample volumes were required for analysis and the possibility for analyzing very demanding samples such as organics, slurries and even solid materials existed. This encouraged scientists to work on and with ETV–ICP–MS.

In 1985, the first ETV device specifically designed for working with an ICP–MS was presented by C.J. Park in his PhD thesis [6]. From this moment on, some publications related to ETV–ICP–MS started to appear in the literature. They mainly contained general descriptions of the technique’s features and some applications, using Park’s device or other in-house modified atomic absorption spectrometry (AAS) or ETV–ICP–OES vaporizers. A nice overview of the situation and papers presented in this first period can be found in [7].

Attracted by the optimistic conclusions reported in these works, some scientific manufacturers developed and commercialized ETV devices for combination with ICP–MS in the beginning of the 1990s [7]. This had a dramatic influence on the number of papers published on the topic in the following years, as can be seen in Fig. 1A. In 1992, the number of publications per year was doubled with respect to the papers published in 1991; and in 1994, the number of publications was five times higher (at that moment it was estimated that more than 100 commercial electrothermal vaporizers had been sold worldwide [8]). From this moment on, the rate of ETV–ICP–MS publications per year has only undergone few changes, with a limited but steady number of contributions in-between 20 and 30 per

year. However, by considering the tremendous increase in the number of ICP–MS-related publications in the same period [9], one can easily see that ETV–ICP–MS has been attracting less attention from the scientific community than in the period in which it was first introduced.

This situation contrasts with the highly optimistic predictions of most of the scientists actively working in the field of ETV–ICP–MS in the beginning of the technique’s life. On the 4th Surrey Conference on Plasma Source Mass Spectrometry in 1991, e.g., D.C. Grégoire foresaw an “unusually rapid popularization of ETV–ICP–MS among ICP–MS users” [10]. In fact, this “rapid popularization” never took place. The reasons were many. On the one hand, scientists realized that working with ETV–ICP–MS was not so straightforward and required a higher level of expertise. The work presented by D.J. Gray and coworkers in 1994 [11], stressing the need for careful optimization of the working conditions in ETV–ICP–MS in order to compensate for the different factors affecting stability and sensitivity with this technique, illustrates this statement. On the other hand, and also in the same period, important improvements in other sample introduction systems for ICP–MS were also accomplished (as reflected, for instance, in a special issue of *Spectrochimica Acta Part B* published in 1995, entirely devoted to advances in sample introduction in spectrochemistry [12]). As a result, some of the former “unique” ETV features, such as the capability of analyzing small sample volumes, were then matched and even surpassed by the newly developed introduction devices (e.g., microflow nebulizers), which, additionally, were in most cases easier to use than ETV. In fact, the actual market trends reflect this situation quite clearly, as several companies now produce these “alternative” introduction systems and, to the best of the authors’ knowledge, only one company is still manufacturing ETV units [13]. Also the evolution of ICP–MS instrumentation has contributed to the decline of ETV, as the feasibility of ETV systems to reduce some polyatomic interferences in ICP–MS was no longer a prime advantage since sector field ICP–MS instruments and quadrupole-based units equipped with collision/reaction cells were introduced onto the market. A combination of all these factors caused the analytical domain of ETV–ICP–MS to be considerably reduced in favor of some competing techniques, as summarized in Table 1.

These circumstances led to a noteworthy change in the original perspective on the position of ETV–ICP–MS in the beginning of the 2000s. ETV was no longer considered as a potential “standard” sample introduction system for ICP–MS, but its use was rather reserved to cope with particularly challenging analytical problems that could not be tackled easily with other strategies. This consideration is still valid today. An excellent review in this direction was written by Sturgeon and Lam in 1999 [14]. In their paper, also the feasibility of using chemical modifiers or other reagents used in electrothermal atomic absorption spectrometry (ETAAS) and ETV–ICP–OES to alter the volatility of either the analyte or the concomitant matrix in ETV–ICP–MS was highlighted, presenting the ETV as a *thermochemical reactor* for ICP–MS sample introduction. As indicated by these authors, this approach might alleviate space–charge matrix effects, minimize polyatomic ion interferences, permit direct speciation of trace element fractions in samples, as well as serve as a crucible for sample preparation. These outstanding features can explain why, in spite of the new sample introduction systems cited in Table 1 and

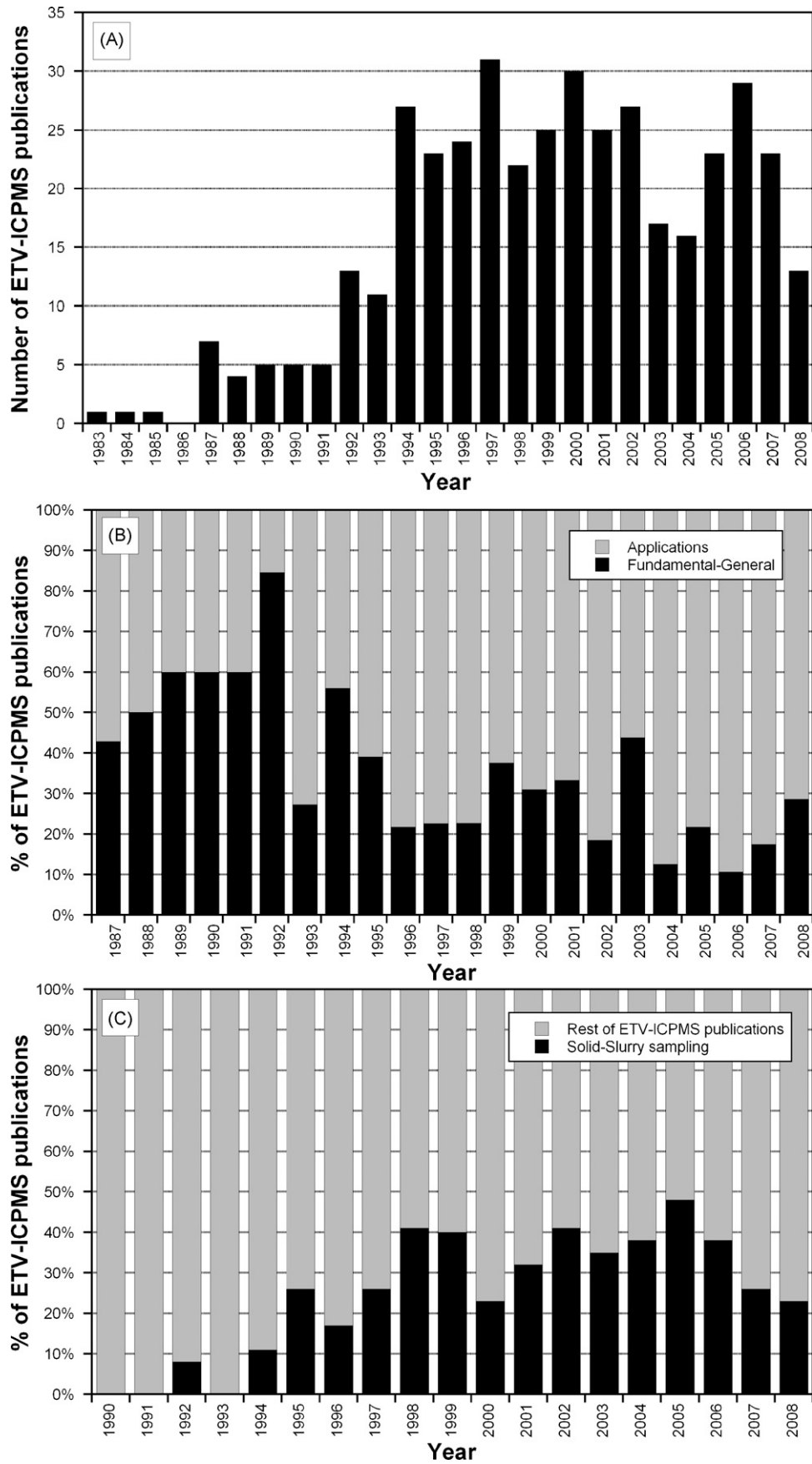


Fig. 1. Evolution of number and type of ETV-ICP-MS publications in scientific journals (Web of Science). (A) Total number of ETV-ICP-MS publications per year. (B) Percentage of applied and fundamental/general ETV-ICP-MS publications per year. (C) Percentage of solid sampling - ETV-ICP-MS publications per year.

Table 1
ETV versus competing sample introduction techniques and other improvements in ICP-MS.

Analytical situations where ETV-ICP-MS is advantageous	Alternative device/technique	Comments
Microsamples	- Micro-nebulizers (High Efficiency Nebulizer, MicroMist, Microconcentric nebulizer, etc.) [17] - Recirculating nebulizers [18]	LODs are normally lower for ETV than for nebulizers consuming the same amount of sample. These nebulizers are very prone to clogging.
Ultra-trace analysis (very low LODs needed). Enhanced transport efficiency needed.	- Ultrasonic nebulizers - Direct injection nebulizer	For both kinds of nebulizers sample efficiency is much higher than with conventional nebulizers (30–100%) [17,18]. However, LODs are only improved for simple samples because of the increased plasma loading. Desolvation units are needed with ultrasonic nebulizers; these also show low tolerance for viscous samples and samples with high concentration of dissolved solids. Both are not as robust as ETV.
Interference reduction power (mainly solvent-related interferences)	- Collision/reaction cell-ICP-MS - High resolution ICP-MS - Desolvation units	New-generation ICP-MS are available at lower prices.
Heavy matrix analysis - High total dissolved solids (slurries)	- Nebulizers with anti-clogging design (Babington, V-groove, etc.) [17] - High tolerance ICP-MS interface (modified cone: anti-clogging design)	The continuous aspiration of these solutions can create problems in the torch/interface. FIA systems could alleviate the problem.
- Organics	- Special introduction kits for organics: thermostat controlled spray chambers, additional gas ports for O ₂ , high tolerance cones with modified design. - Desolvation units.	Some systems might not be well suited for really heavy organics (e.g. crude oil).
- Solid samples	- Laser-ablation systems - Spark ablation systems - Glow discharge systems	ETV can accept all kind of samples: powders, pellets, conductive or non-conductive. Quantification with ETV is more flexible. ETV LODs are generally lower.

the interruption of the ETV production by the main manufacturers, ETV-ICP-MS still remains an excellent approach for some particular applications and did not disappear from the analytical literature.

As could be expected, this new situation has been reflected in the type of publications appearing in the field of ETV-ICP-MS in the last years. As seen in Fig. 1B, most papers presented in the last decade have been devoted to the development of particular applications, in contrast with the many fundamental papers published in the first years of the technique's life. Regarding the field of application, it is interesting to note the increasing number of articles devoted to the direct analysis of solid samples/slurries, as the prime example of a challenging/demanding sample. As shown in Fig. 1C, the number of solid sampling/slurry related publications accounts for about 40% of the total number of papers that appeared in the last decade. This confirms the idea shown in the most recent reviews on the field of ETV-ICP-MS published by Resano et al. [15] and Hu et al. [16], stressing that the main practical interest of ETV-ICP-MS could be, in fact, the direct analysis of solid samples.

The present review has a double goal. On the one hand, the possibilities of ETV-ICP-MS as a versatile tool for tackling challenging analytical problems will be discussed, reviewing the more significant publications presented in this field during the last decade. Moreover, and as an added value of the paper in comparison with some recent reviews on the subject (i.e. references [15] and [16]), this review also intends to serve as a reference guide for method development in ETV-ICP-MS applied to challenging analytical problems. For this purpose, some of the general aspects concerning the basic principles of the technique will be covered and briefly revised for a better understanding of the factors that need to be optimized during method development. General guidelines for using this technique and based on published results as well as on the authors' experience are provided in an easy-to-follow way, in

an attempt to bring the technique closer to newcomers. It is out of the scope of this review, however, to treat these general issues in detail, and the reader is referred elsewhere for further information. In this regard, a list of the most relevant reviews and general texts written concerning ETV-ICP-MS, with indication of the main focus selected in each case, is gathered in Table 2.

2. Basic principles of ETV-ICP-MS

In ETV-ICP-MS, a small amount of sample in liquid or solid phase (typically 5–40 μL in the case of liquid/digested samples or 0.1–5 mg in the case of solid samples) is placed in a conducting reservoir, acting as a resistor (such as a graphite furnace), which is subsequently heated resistively in order to vaporize the sample. The resulting sample vapor is transported into the ICP by a carrier gas (pure Ar in most cases) through a transport tube. Some electrothermal vaporizers have been described for direct insertion into the plasma (without transport tube) [31,32], but a detailed discussion of these devices is beyond the scope of this review.

As in ETAAS, different steps with different temperatures, durations and heating rates can be programmed. Addition of modifiers (chemical substances in liquid, solid or gaseous phase) in one or several steps of the program is also possible, opening a wide variety of possibilities for resolving challenging analytical problems as indicated in the introduction.

As a result of the discrete character of this sample introduction system, transient signals with typical durations ranging from 0.5 s to 5–6 s, in the case of the more refractory elements, are obtained. This fast transient character of the ETV signal poses some problems for data acquisition with the sequential mass spectrometers normally used for analysis, limiting to a certain extent the multi-element capabilities of the technique. On the other hand, it also

Table 2
Reviews and general texts on ETV–ICP–MS.

Year	Author	Focus	Reference
1992	J.M Carey, J.A. Caruso	General review on ETV–ICP–MS.	[19]
1995	L.K. Olson et al.	General review on alternative introduction systems for ICP–MS. Reports general possibilities of ETV–ICP–MS as seen in 1995.	[20]
1995	L. Moens et al.	Review on solid/slurry sampling by ETV–ICP–OES/MS	[21]
1998	P. Verrept et al.	Book chapter on solid sampling by graphite furnace techniques. Solid/slurry sampling ETV–ICP–MS/OES	[22]
1999	R. Sturgeon, R. Lam	ETV–ICP–MS as a thermo–chemical reactor.	[14]
2000	D.C. Grégoire	Book chapter on discrete sample introduction techniques to ICP–MS. General text about ETV–ICP–MS.	[23]
2000	V. Majidi et al.	Series of two reviews on furnace chemistry for ETV–related techniques (surface and gas phase chemistry)	[24,25]
2001	T. Kantor	ETV–ICP–MS/OES and laser ablation. General review with focus on transport efficiency issues.	[26]
2002	F. Vanhaecke et al.	Review on real-life applications by ETV–ICP–MS	[27]
2002	M.A. Belarra et al.	Tutorial review on direct solid sampling with Electrothermal vaporization/atomization	[28]
2003	A. Martin–Esteban et al.	ETV–ICP–MS for direct solid sampling	[29]
2005	F. Vanhaecke	Book chapter in general book about ICP–MS. General text about ETV–ICP–MS.	[30]
2007	B. Hu et al.	ETV–ICP–MS and ETV–ICP–OES. Chemical modification, preconcentration and separation techniques	[16]
2008	M. Resano et al.	ETV–ICP–MS/OES and GFAAS. General review with focus on solid sampling	[15]

offers the possibility to separate the signal for different analytes (of different volatility) in time, such that the selectivity can also be improved.

In the following sections, some general considerations about these basic principles will be discussed in a tutorial way. Additionally, the most important contributions related to these issues will be also reviewed.

2.1. Instrumentation

2.1.1. Electrothermal vaporizers

The construction and optimization of the design of electrothermal vaporizers has played an important role in the development of ETV–ICP–MS since the very beginning. Although this research line has never been totally abandoned, most of the efforts in this regard were done in the 1980s and beginning of the 1990s, before any commercial ETV unit specifically designed for ICP–MS was available. The variety of systems described in the literature is quite considerable and includes strips, coils, rods or furnaces made out of metals characterized by a high melting point (such as Ta, W or Pt) or graphite (including pyrolytic graphite and metal-coated graphite). An overview of some of these vaporization systems can be found in some of the publications listed in Table 2 [22,23].

Evolution of ETV–ICP–MS has led, however, to the unified trend of using graphite tube furnaces as vaporizers, even if the performance of some of the alternative devices mentioned before might be better for some particular applications (e.g., determination of carbide-forming elements). In fact, graphite furnaces are the best compromise solution to fully exploit the versatility of ETV as a sample introduction system, since they permit the vaporization of both liquid and solid samples with very different characteristics. Powders, pellets or highly viscous liquids, for instance, can be introduced in the graphite tubes in a more convenient way if compared with other systems, which in some cases cannot even handle this kind of samples. Moreover, the possibility of transferring some knowledge from the extensive graphite furnace atomic absorption spectrometry (GFAAS) literature available [10] probably favored the use of this kind of vaporizers over other alternatives.

In fact, most of the graphite furnaces used for introduction in ICP–MS are modifications of GFAAS devices, either adapted in-house or by commercial manufacturers. In all different designs, a flow of Ar is passed through the inside of the furnace transporting the vaporized sample to the plasma, either through one of the ends of the tube (end-on streaming systems) or through the transverse dosing hole in the middle of it (upwards streaming systems) [33]. Both systems have their advantages and disadvantages (which were critically compared by Kantor in [34]), but the critical parameter of

the furnace design is always the flow characteristics of the carrier gas, which strongly affect the sample transport efficiency to the ICP. This issue will be discussed in detail in Section 2.2.

Unlike for GFAAS devices, strict control of the thermal conditions inside the graphite vaporizers used for introduction into ICP–MS is not such a critical parameter [22]. In ETV–ICP–MS, only sample vaporization needs to take place in the furnace, while atomization and ionization are occurring in the plasma, and this leaves some freedom for improving other aspects like sample handling or transport efficiency.

The first description ever published for the design of the most frequently used commercially available ETV unit, the Perkin Elmer HGA-600 MS [35], is an interesting example on how a GFAAS furnace (HGA600) could be successfully adapted for an easy and convenient use with ICP–MS. The most important feature in this instrument (schematically depicted in Fig. 2) affecting the work with ICP–MS, is perhaps the fact that the carrier gas bypasses the furnace during all the temperature steps, but the analyte vaporization, avoiding the vapors originating during these previous steps to enter and contaminate the ICP–MS. As indicated by their developers [35], optimization of sample transport efficiency was not the prime goal. Conversely, more attention was spent to the ease of use and versatility regarding sample introduction. In fact, the possibility of coupling the HGA600 MS with the liquid (AS60 [35]) or slurry (USS100 [36]) auto-samplers developed for GFAAS or that of using *cup-in-tube* graphite tubes [37] for easy introduction of solid samples was an important contribution to its success.

As mentioned previously, research in the field of furnace design has never completely stopped, and several interesting contributions in this regard can be found in the recent literature. The group of Salin has been working on the development and application of an induction heating–electrothermal vaporization furnace (IH–ETV) for sample introduction in plasma sources, with the first corresponding paper appearing in 1997 [38]. The basic design of this device consists of a graphite cup that is inserted in a free-running induction furnace with modifications around the induction coil for easy sample introduction. The system is enclosed in a quartz chamber flushed with a carrier gas, which transports the sample vapors to the ICP. Advantages of this system are mainly to be situated in the field of solid sampling analysis, and include the possibility of using larger sample sizes owing to the use of larger graphite sample probes, improving LODs and minimizing sample homogeneity concerns. Further details on the design of and applications with this device can be found in the literature [39–41]. Hermann and coworkers developed an ETV graphite furnace for which streaming conditions were designed that provided maximum transport efficiency and minimum analyte loss. The setup includes the use of an

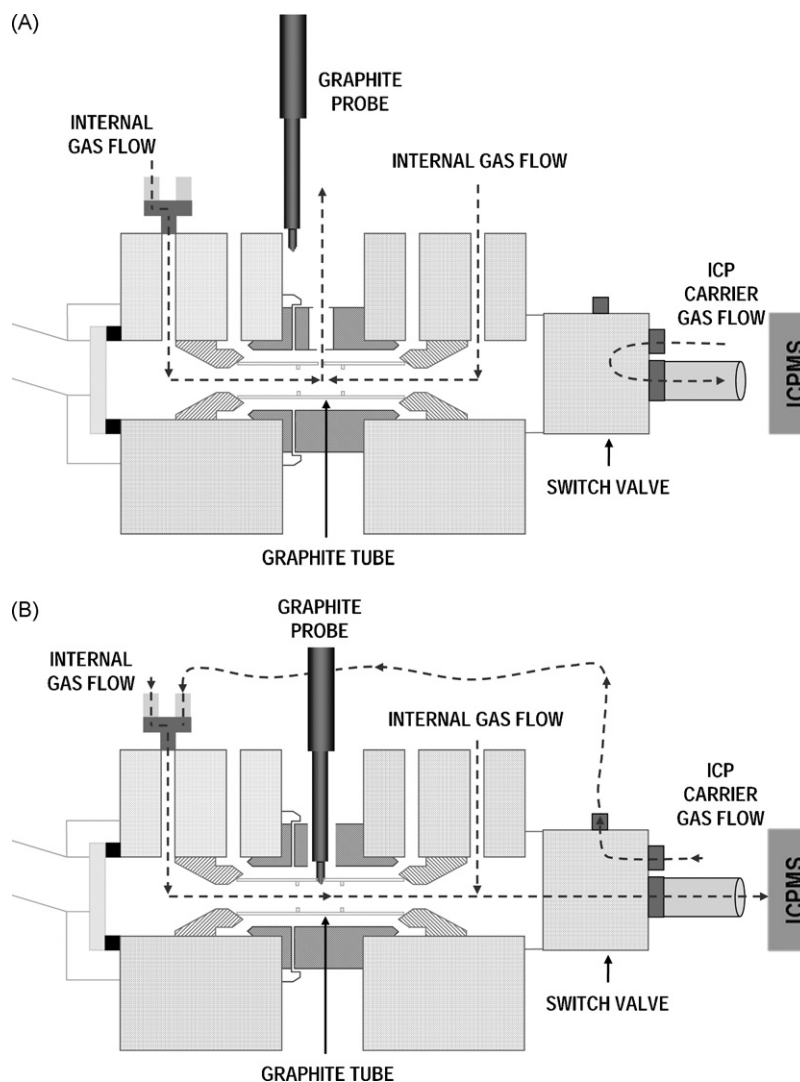


Fig. 2. Schematic representation of the Perkin Elmer HGA-600MS ETV unit. (A) Drying, pyrolysis and cleaning steps. (B) Vaporization step.

upstream configuration with the flow of carrier gas directed into a specially designed vertical tube in which a combination of gas flows reduces the analyte loss by minimizing the deposition that normally takes place at the cold parts of ETV systems. Although the coupling to ICP-MS instruments should, in principle, be possible, this device has been used in combination with ICP-OES only [42]. Holcombe's group designed an ingenious multiplexed ETV system in an effort to increase sample turn-around time [43]. An array of tungsten filaments (300 W) were used as ETVs. The thermal stages were multiplexed such that a vaporization event could take place every 20 s, increasing significantly the sample throughput for this setup.

In spite of the improvements brought along by the aforementioned contributions, none of the designed systems has found a commercial distribution. As indicated in the introduction, the only ETV commercial systems currently available are those manufactured by Spectral Systems [13], which are again mainly intended for solid sampling analysis.

2.1.2. Transport tubing

The design of the transport tube from the ETV to the ICP-MS has not received much attention from the ETV-ICP-MS scientific community, although the influence of tube length or diameter on the ETV signal has been studied in several publications, mainly focusing

on the study of sample transport efficiency [5,44–48]. These studies on transport efficiency will be discussed in more detail in Section 2.2, but the practical conclusion that can be drawn concerning the tubing design is that changes in the tube length and diameter are mainly affecting the peak shape (broadening) obtained, while little changes in the integrated total peak area are observed. The typical ETV setup uses about 50–70 cm of plastic tubing (Teflon® or Tygon® are mostly used), with an inner diameter of about 6 mm. Other factors, such as the carrier gas flow rate and/or the heating rate, can be adapted in view of optimum peak definition.

2.2. Furnace chemistry and transport efficiency

Since the first couplings of ETV with excitation/ionization sources (flames, ICPs) were realized, it was confirmed that the sample transport efficiency for this introduction technique was in all cases much higher than that of pneumatic nebulization. However, also from these first experiments, it became clear that the sample transport efficiency was a very variable parameter, influenced by numerous factors that affect to various degrees all ETV systems. As a result, identifying, quantifying and understanding the effects of these factors became a very active field of research for scientists working on ETV-ICP-MS, required as a tool for the eventual optimization of the working conditions with this technique.

2.2.1. Methods for evaluating transport losses and transport efficiency

The first aspect to be considered when tackling this issue is how to measure transport efficiencies and detect analyte losses in an ETV system. A comparative recap of some of the methods used for measurement of these values is presented in [49]. As shown in that paper, the methodologies used in this regard are numerous, and will not be treated in detail here. However, following the description made by Friese et al. in [50], a general description of these methods can be presented as follows (the reader is referred to the cited references for further information):

1. Methods trapping the analytes from the carrier gas stream using filters, wash bottles, bags or electrostatic deposition, and subsequent determination of the amounts of analyte collected by spectrometric or other analytical methods (e.g., particle counters or gravimetric measurements) [48,49,51–56].
2. So-called “indirect” methods, which are based on the quantification of analytes deposited in the vaporizer, the interface and the tubing after rinsing these components and collecting the deposited material for subsequent analysis [46]. Also radiotracer experiments, combining approaches 1 and 2, have been used [57–59].
3. Methods relating the signal intensities obtained in ETV to the signals obtained with a certain reference method, e.g., the pneumatic nebulization of solutions [50,60,61].

In this third group, some early studies can be included in which transport efficiency variations were assessed by direct monitoring of the change in the spectrometric signal (absorbance, MS-intensity or emission intensity) for a given analyte [62–64] upon modifying some factors known to influence this transport efficiency. This methodology, however, does not take into account the possible influence of the different factors studied on the behavior of the excitation source, but rather assumes that this influence is negligible (e.g., addition of modifiers or modification of the Ar flows change the ionization/atomization efficiency of ICPs, which is overlooked by these methods). Although this assumption could be essentially true for the particular cases considered in those papers, the scientists behind the investigation pointed out that this was not always the case. In this regard, later contributions in the field of ETV–ICP–MS included the monitoring of some plasma-related species in the ICP–MS (e.g., the Ar dimer [65–67]) to detect suppression or enhancement effects related with changes in the plasma conditions (the so-called plasma loading effects) or the processes occurring in the ICP–MS interface (the so-called space-charge effect). This approach permits to distinguish between these ICP–MS-related effects and transport efficiency-related effects [68,69], and has been used very often ever since as a valuable diagnostic tool for method development in ETV–ICP–MS. More details on this regard will be given in Section 2.3.

2.2.2. Factors influencing transport efficiency

By using the different methods described in the previous paragraphs, an important number of scientists tackled the problem of identifying, quantifying and understanding the factors having an influence on the sample transport efficiency for ETV–ICP–MS. In 1988, Kántor described the most accepted theory, explaining the process of analyte transport between the ETV and the ICP source based on aerosol science [62]. In short, it was concluded that for the ETV-generated aerosol to be transported to the ICP, it is necessary that rapid self-nucleation occurs to particles large enough as to be effectively transported by the carrier gas, but small enough to avoid coagulation and deposition in the transport path. Most of the papers written on sample transport efficiency for ETV–ICP–MS since then have been based on this theory.

In 1999, for instance, Grégoire and Sturgeon studied the analyte transport efficiency for a conventional commercially available ETV unit (Perkin Elmer HGA600 MS) without the addition of any foreign substance to the furnace (carriers or modifiers) and with a new graphite tube. They selected different analytes with different volatilities and made use of the typical experimental conditions used for real analysis by ETV–ICP–MS. Under these conditions, they found that sample transport efficiency to the plasma was approximately 10% only, with 70% of the total amount of vaporized analyte being lost in the switching valve of the ETV device, 19% in the transfer tube and 1% in the components comprising the torch assembly. Analyte transport to the plasma increased up to 25% with addition of a modifier/carrier (Pd/NaCl) [52]. This is only one of the examples that can be found in the literature attempting to measure the sample transport efficiency from the ETV and analyzing the factors having an influence on it. Even if the numbers presented in other previous or later publications with the same goal may be substantially different from the ones presented in this work, the main idea that can be drawn from all these studies is clear: the transport of the ETV-formed aerosol is never quantitative for any ETV device. Without any external help and following Kantor’s theory, the self-nucleation process can hardly take place within the aerosol itself and the analyte particles easily deposit onto the colder parts of the ETV interface that act as nucleation/condensation sites. However, this tendency can be greatly influenced by a number of external factors that can be studied and optimized for the best results to be obtained.

Although no firm consensus has been reached in this respect, a closer look at the published data permits a simplification to be made by classifying the factors influencing the sample transport efficiency in the following categories:

- (i) Streaming conditions/design of the experimental setup.
- (ii) Vaporization conditions/furnace chemistry including:
 - nature and state of the furnace substrate
 - heating conditions (fast or slow heating rates)
 - nature (volatility) of the analyte and the sample matrix and addition of foreign substances as modifiers/carriers (in gaseous, liquid or solid state)

2.2.2.1. Influence of streaming conditions and design of the ETV device. Self-evidently, the carrier gas flow rate used in the ETV device is having a great influence on the sample transport efficiency and needs to be carefully optimized for every ETV–ICP–MS method, as will be shown in Section 2.3. Besides this, some other technical aspects related with the streaming conditions and design of the ETV interfaces have been found to have a remarkable influence on the transport efficiency as discussed partly in Section 2.1. Apart from the comparison between upwards streaming and end-on streaming devices and the studies on the length and diameter of the transport tube mentioned there, maybe the most remarkable contribution in this regard is the addition of a cooling argon flow at the exit of the ETV system (before entering the transport tube) in order to promote the self-nucleation of the analyte vapors before they could reach the cool surfaces further downstream. This modification was introduced to graphite-tube-type ETV by Shen et al. [70]. Later, Ren and Salin modified this design by adding an internal sheath gas to provide a thin gas layer between the analyte vapor and the wall of the transport tube to further decrease the analyte vapor condensation on the tube wall [71]. The same idea has been used afterwards in many other designs with some additional improvements in recent years. Friese et al., for instance, following a previous design from Schäffer and Krivan for ETV–ICP–OES [57], optimized the sample transport efficiency for a commercial ETAAS furnace by bypassing part of the carrier gas introduced into the entrance of the tube to the exit of the tube and using a nozzle-shaped graphite tube instead of

the standard one. Under the best working conditions (also with the addition of trifluoromethane as carrier), they reported improved transport efficiencies in the range of 70–100% [50]. The design introduced by Hermann and coworkers cited in Section 2.1 [42] is also another example of the same principle. With the introduction of the *Axially Focused Convection* tube (AFC), a convection zone is created in the beginning of the transport path, where vapor condensation and aerosol formation can take place apart from the colder walls.

2.2.2.2. Influence of vaporization conditions/furnace chemistry. Even if the improvements in sample transport efficiency that can be derived from furnace design optimization are noteworthy, most of the efforts and studies have been made in the direction of ETV chemistry, most probably because this offers important chances for improvement, regardless of the ETV unit deployed.

(a) Influence of the furnace substrate

Several works have been conducted in order to establish the influence of the ETV substrate on the transport efficiency. In a series of two reviews published by Majidi et al. [24,25], a complete study is presented on how transport efficiencies vary with different substrates used in the ETV unit. Pt, Al, Ta and graphite surfaces are compared with respect to gas phase and surface chemistry. However, and considering that most of the times graphite furnaces are used in ETV–ICP–MS applications, most of the works on the influence of the furnace substrate study the effect of carbon particulates released from the graphite furnace during the vaporization step. Fonseca et al. [68,72] and Majidi and Miller-Ilhi [73] proved the positive effect on transport efficiency when oxygen ashing was used in the graphite furnace, as a result of the increased number of carbon particles leaving the furnace acting as carrier agents for the analyte vapors. Some quantitative studies on carbon losses in graphite furnaces, on the other hand, showed that the differential mass loss per analysis cycle varies markedly depending on the tube type (pyrocoated or not) and lifetime [74].

(b) Influence of the heating conditions

As indicated by Kántor in some of his works on sample transport efficiency in ETV coupled techniques [34,62], the effective vapor concentration in the furnace is the most important factor influencing the processes of aerosol formation and transport. This vapor concentration is strongly influenced by the heating rate of the sample, and this idea can be used for the optimization of the working conditions in ETV–ICP coupled techniques.

For the vaporization of single-element standard solutions, for instance, the interpretation of this statement is quite straightforward: a faster heating rate would lead to a higher vapor concentration in the ETV in a shorter period of time, which would result in a higher rate of self-nucleation in the vaporizer in that period and hence, in improved transport efficiency. Conversely, too high heating rates would have an adverse effect on the transport efficiencies as too high a vapor concentration would create conditions where coalescence of the particles begins to be important [62].

When complex matrixes and/or modifiers are also vaporized in the ETV, however, this interpretation needs to be reconsidered as other factors might have a remarkable influence. In this regard, it is clear that the heating rate will have an influence on the peak shape (e.g., peak broadening, location of the peak maximum or peak height) obtained for the analytes, concomitants and modifiers [75]. Taking this into account, one can easily conclude that, when multi-element standards, digested/solid samples or chemical modifiers are vaporized in the ETV, the applied heating rate will also influence the way in which all these “vaporization peaks” overlap and hence, the vapor con-

centration and rate of self-nucleation existing in the vaporizer at different moments. In these cases, an increased heating rate may not result in improved transport efficiencies due to a poor overlap between the analyte and modifier (carrier) vaporization peaks, as described by Hughes et al. for some multi-element determinations with seawater added as a carrier agent [64].

(c) Nature (volatility) of the analyte/sample matrix and addition of modifiers

One of the main disadvantages of ETV–ICP–MS is the variable transport efficiency shown by elements of different volatilities (the more volatile showing lower transport efficiencies than the more refractory ones [76]) or present in different matrixes (e.g., higher transport efficiencies for solid/slurries than for aqueous solutions [28]). This fact leads to very strong matrix effects observed in ETV–ICP–MS measurements, which obviously can be problematic. As indicated by Grégoire and Sturgeon [52], the addition of modifying reagents can help not only to improve but also to normalize the transport efficiency for all constituents. As a result, the influence of these matrix effects can be reduced, which simplifies the calibration process and improves the quality of the data obtained by means of ETV–ICP–MS.

Even if the influence on the transport efficiency of the furnace substrate or the heating conditions discussed above is worth studying, that of the addition of foreign substances to the ETV has received much more attention than the rest. In fact, a large number of works reporting on the use of different modifiers in gaseous, liquid or solid form in order to improve sample transport efficiency have been published in the 25 years of ETV–ICP–MS existence. Nowadays, the use of modifiers to act as a carrier agent is very extended and is even considered as mandatory by some scientists [26]. More details on the different modifiers proposed will be given in Section 2.3.2.

2.3. Working methodology and method development

As already indicated before, one of the main disadvantages related with the use of ETV–ICP–MS is the need for a careful selection of the working conditions in order to obtain quantitative results with sufficient quality. Several parameters need to be optimized both for the ETV device and for the ICP–MS unit. Selection of the optimum working conditions is not always an easy task for ETV–ICP–MS and requires considerable expertise, especially when challenging applications are considered. However, some general ideas and hints simplifying this process can be compiled and are presented in this section. A general protocol for method development summarizing these ideas is proposed in Fig. 3.

2.3.1. Optimization of ICP–MS parameters

2.3.1.1. Plasma tuning. As for any other sample introduction system, the ICP–MS working parameters need to be optimized when an electrothermal vaporizer is used. These parameters include the different lens voltages, the different gas flow rates (normally Ar), the RF power, the position of the torch with respect to the interface (if the instrument permits it) and of course, the data acquisition parameters. Considering the transient nature of the signals generated by ETV–ICP–MS systems, the optimization or “tuning” of some of these parameters (namely the lens voltages and the torch position) is normally done with a conventional nebulizer providing a steady-state signal in the ICP–MS. This optimization system is far from being ideal, as it has been proved that the presence of water in the central channel does have a great influence on how the plasma behaves [77]. Although the use of a dry steady-state signal for the optimization of these parameters would help improving the overall ETV–ICP–MS performance (as shown by Kreschollek and Holcombe with the use of a device built in-house generating a dry aerosol in

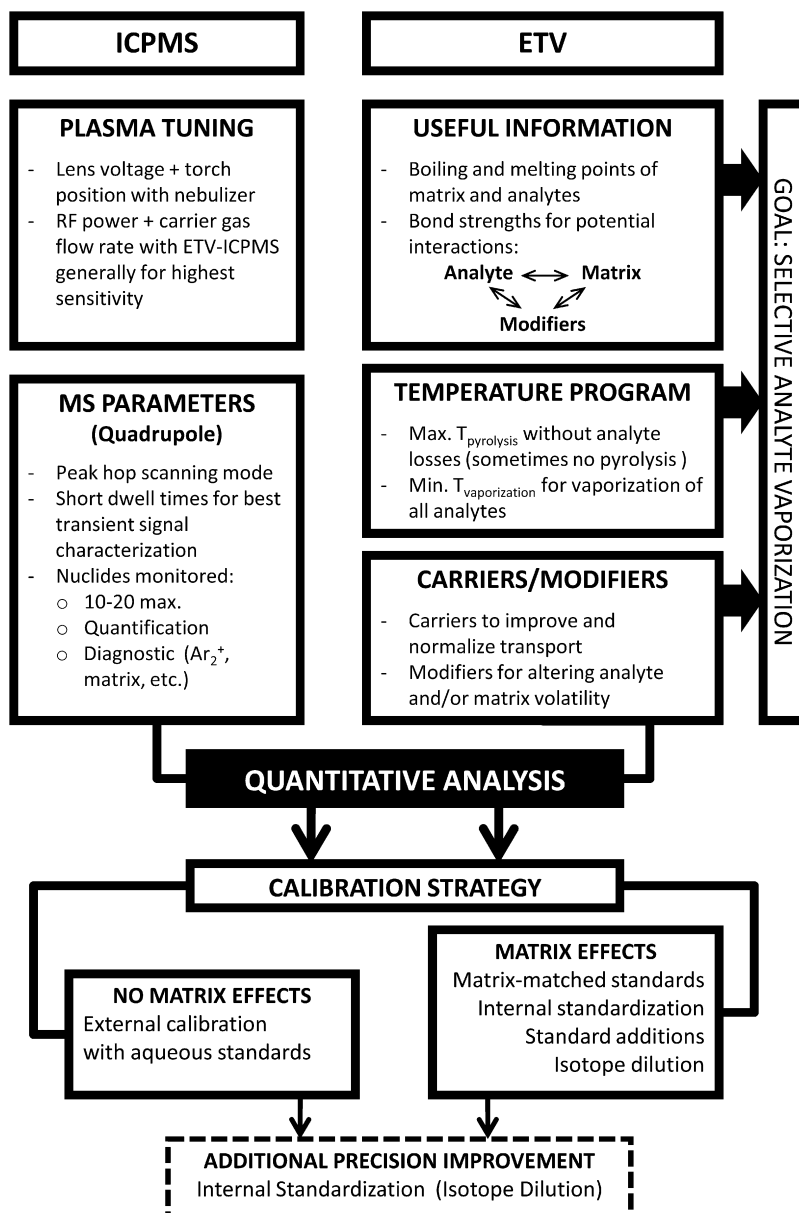


Fig. 3. ETV-ICP-MS method development.

a continuous way [78]), the use of nebulizers is still the most often used approach for practical reasons.

Optimization of the rest of the ICP-MS parameters, on the other hand, is normally done in a sequential way using the ETV-ICP-MS system. As for any other sample introduction system, the RF power and the carrier gas flow rate need to be optimized for each individual method, generally searching for the highest possible sensitivity. These parameters are finely optimized once the ETV program has been set.

2.3.1.2. Mass spectrometer parameters. Besides the optimization of these plasma parameters (which is not so different from the optimization needed when working with nebulizers or other sample introduction systems in combination with ICP-MS), the most critical issue at this point is the selection of the data acquisition parameters, especially if multi-element analysis is intended. Self-evidently, this point depends upon the type of mass spectrometer used for analysis. In this regard, it is important to point out that

most of the ICP-MS instruments available in most analytical laboratories are quadrupole-based instruments, and these are also the instruments that ETV systems are most often coupled to. For the sake of simplicity, we will refer to this kind of instruments in the following discussion.

Quadrupole-based mass spectrometers monitor only a single m/z at any given time and are scanned sequentially to produce a mass spectrum. Due to the fast transient nature of the signals produced by the ETV, the speed at which the m/z scans are acquired by the ICP-MS instrument must be maximized to obtain the best accuracy and precision possible. As a consequence, the so-called “peak jumping mode” (or equivalent) is normally preferred as the scanning mode and short dwell times per peak are selected for analysis [79] (10–20 ms are typical values, but even lower values can be deployed [80]).

The speed of scanning, however, will be ultimately limited by the number of nuclides monitored simultaneously, the higher this number, the longer the scan time and, in theory, the poorer the

accuracy and precision for the transient signal characterization [81]. As a consequence, it is generally accepted that the multi-element capabilities of ETV–ICP–MS are limited to a small number of elements only. However, there is no clear consensus on where exactly this limit can be set, probably because it is difficult to establish a general rule in this respect.

Resano et al. were the first who tried to systematically assess the limits in terms of multi-element capabilities of ETV–ICP–MS with a quadrupole-based instrument [82]. They experimentally demonstrated that the monitoring of up to 20 nuclides is still possible for the evaluation of typical ETV transient signals with a duration of 1.5–2 s without deterioration of the precision, accuracy and LODs achieved. Venable and Holcombe supported this conclusion later on and proposed a theoretical model that permitted to select the maximum number of nuclides that could be monitored for a given limit of precision [83]. Besides the proper selection of the data acquisition parameters, they included in their model the role played by the analyte sensitivity and the peak shape of the analyte signals, factors that were not fully evaluated in the work by Resano et al. In this regard, they showed how, by modifying the ETV signal shape and stretching it out with a simple experimental setup, it was possible to significantly increase the number of masses that could be monitored (with an increase from 21 to 68 m/z values in the examples presented in the work). In a later contribution, Björn et al. entered the discussion and pointed out how the multi-element capabilities of ETV–ICP–MS using scanning mass spectrometers were deteriorated if the peak characteristics of the transient signals would vary with the analyte amount or between calibration standards and samples [84]. They concluded their work clearly referring to the works presented by Resano and Venable, suggesting that “the promising multi-element potential of ICP–scanning MS for the monitoring of transient signals showed in those reports could have been exaggerated”.

After all these contributions, it seems clear that establishing a general limit for the number of nuclides that can be monitored simultaneously in quadrupole-based ETV–ICP–MS systems is complicated, as many factors depending on the particular method considered can influence this number. However, a closer look to the published data reveals that successful determinations in real samples have been carried out with the monitoring of up to 10–12 nuclides per ETV firing [85–87]; therefore, proposing a general limit of nuclides in the range of 10–20 should be adequate to stay on the safe side. In any case, the idea that the data acquisition parameters must be carefully optimized for every particular situation still remains the most important point to retain for successful method development.

Finally, and considering that the multi-element capabilities have been often indicated as one of the main advantages of ETV–ICP–MS over the similar (but cheaper) technique of GFAAS [28], it is worth pointing out that several approaches have been described in the literature for extending these capabilities, including coupling of the ETV to newer types of ICP–MS instrumentation, better suited for transient signal characterization. A closer look to this issue will be given in Section 3.5.

2.3.1.3. Selection of nuclides: quantification and diagnostic purposes. A proper selection of the nuclides monitored, taking into account potential spectral interferences is, obviously, also needed in ETV–ICP–MS for successful method development. In this regard, it is important to remind that the typical solvent or matrix-related spectral interferences appearing in the ICP–MS when using pneumatic nebulizers might be virtually eliminated when using ETV for sample introduction, provided that a suitable ETV program is selected. In fact, the combination of temperature programming and/or chemical modification often permits selective analyte vaporization, thus enabling the selection of nuclides otherwise suffering from the occurrence of isobaric and/or polyatomic spectral interferences in

the mass spectrometer. This fact has permitted, for instance, V determination at ppt levels in calcite and seawater matrixes [88], Sr isotope ratio determination without Rb separation [89] and other challenging applications to be developed with ETV–ICP–MS systems as will be shown in Section 3.

Apart from the nuclides selected for quantification purposes, very often some additional nuclides are monitored for diagnostic or correction purposes. Similarly to conventional pneumatic nebulization (PN)–ICP–MS, these would include nuclides used as internal standards (more details on internal standardization will be given in Section 2.3.3) or nuclides used for mathematical correction of spectral interferences. The particular nature of ETV–ICP–MS, however, makes it advisable to select some other diagnostic nuclides helping in the process of method development or improving quality control once the method is developed.

In this category, matrix-related nuclides can be used for monitoring matrix vaporization, helping in the process of temperature program optimization. Monitoring of $^{13}\text{C}^+$ in the analysis of organic samples is a typical example used in these situations [90]. On the other hand and as previously mentioned, very often when modifiers or carriers are added for improving transport efficiency or achieving selective analyte vaporization, “loading” effects in the plasma can be observed, resulting in enhancement or suppression of the analytical signal. The same can be said for the vaporization of heavy matrixes or solid samples. In these cases, monitoring of some plasma-related signals is strongly recommended to detect such effects. Monitoring of the argon dimer at m/z 80 or other argides (e.g., ArC^+) have been proposed in the literature for this purpose [67,69]. The role of such signals can be merely qualitative (i.e. indicating that a change in the vaporization conditions used, e.g., the heating rate, the modifiers used or the pyrolysis temperature selected, is needed) or even quantitative, as some researchers have proposed their use as internal standards, correcting for matrix effects or sensitivity drift [67,87].

Also in some of the cases where temperature programming or chemical modification is used for selective analyte vaporization, some additional diagnostic signal can be monitored for surveying the process in every ETV firing. This could permit eventual rejection of measurements not fulfilling the quality requirements. A good example for this situation is the direct determination of Zn in TiO_2 solid samples presented by Aramendía et al. [91]. In that work, temperature programming was used to separate the vaporization of Zn from that of Ti, thus avoiding the matrix-related polyatomic TiO^+ interferences, which affect to different extents all of the Zn isotopes. While $^{66}\text{Zn}^+$ was used for quantification purposes, monitoring of $^{64}\text{Zn}^+$ permitted the detection of matrix co-vaporization affecting the accuracy of the determination. In fact, firings where too large deviations for the m/z 64 to m/z 66 ratio were detected (indicating significant matrix co-vaporization) were discarded and the corresponding results not used in the final calculations.

2.3.2. ETV program optimization

The ultimate goal of all the methods that use electrothermal vaporization/atomization (e.g., GFAAS, ETV–ICP–OES/MS) is to achieve a selective atomization/vaporization of the analyte, free from solvent or matrix co-vaporization [28]. As already indicated in this manuscript, this requisite is particularly important in the case of ETV–ICP–MS in order to minimize the frequently observed spectral and non-spectral interferences. Moreover, selective analyte vaporization may also help simplifying the calibration protocol for quantitative analysis, allowing the use of aqueous standards for quantitative analysis of complex samples (e.g., heavy matrixes and solids). To achieve this goal, it is essential to optimize the temperature program, including chemical modification if necessary. This is certainly one of the crucial points of ETV–ICP–MS method development, especially when very demanding samples (e.g., heavy

matrixes such as oils or solid samples) or challenging applications (e.g., direct speciation analysis or reduction of isobaric interferences) as those discussed in this review are considered. In fact, if the ETV is regarded as a thermochemical reactor for in-situ pre-treatment of the samples as proposed by Sturgeon and Lam [14], a careful optimization of the ETV program is probably the most important step for method development. Some practical comments on the goals and available tools for ETV program optimization will be given in the following paragraphs.

2.3.2.1. Goals of ETV program optimization. From a practical point of view, the prime goals to consider for analyte-selective vaporization and ETV program optimization would be: (i) solvent removal (if present); (ii) assurance of minimal transport of matrix components with the analyte; (iii) complete removal of remaining residues in the vaporizer to avoid memory effects; and (iv) normalized transport of the analyte regardless of the nature of the samples/standards, thus allowing reliable quantitative results to be obtained.

Solvent removal (typically water) and cleaning of the vaporizer after analyte vaporization can be easily achieved by programming a drying and a cleaning stage, respectively (more details in next section). Conversely, gathering general rules for assuring minimal transport of matrix components with the analyte may seem difficult, considering the large variety of analytical situations that can benefit from the use of this technique. Fortunately, most of them can be fitted in one of the following two situations: either the sample matrix is selectively vaporized in a previous step (pyrolysis) before the vaporization of the analyte and its transport to the plasma, or it is removed from the vaporizer following the preceding selective vaporization of the analyte at lower temperatures [14,28]. In either case, a proper selection of the temperature program is often not enough to achieve separate vaporization of matrix and analyte. For this reason, chemical modifiers are often used to react with the analyte and/or the matrix components to maximize the differences in volatility between them and achieve the final goal of selective analyte vaporization.

Goal number iv regarding normalized transport efficiency for the analyte is normally accomplished by adding a suitable modifier with carrier effect, as discussed in Section 2.2.2.

2.3.2.2. Tools for ETV program optimization: gathering information. As shown in Fig. 3, collection of information on melting and boiling points for the different analytes and matrix or solvent components, as well as bond strengths or equilibrium constants for existing analyte-matrix interactions or potential analyte/matrix-modifier reactions can be a good starting point for successful ETV program optimization. However, even if this information can be helpful, it is important to bear in mind that all these reactions and interactions will proceed within the reducing atmosphere of the graphite tube, so some unexpected effects might be observed. In this regard, the extensive literature available on GFAAS method development is very useful and the results observed there can generally be adapted, with some adjustments, for use with ETV-ICP-MS [10,14].

2.3.2.3. Tools for ETV program optimization: temperature programming. Conversion of the sample to analyte vapor is generally done in several separate steps in the ETV unit. For graphite furnaces, a range of temperatures varying from room temperature to around 2700–2800 °C can be selected (the maximum temperature is limited by the thermal stability of the graphite [23]). Heating rates ranging from 1 °C s⁻¹ up to 2000 °C s⁻¹ are available. Relatively long periods can be selected for low or moderate temperatures (several minutes if required), while only a few seconds (10–30 s maximum) can be programmed at the highest temperatures. In any case, maintenance of high temperatures for longer periods is normally not necessary and would result in too short tube lifetimes.

As for any graphite furnace-based technique, the different steps usually programmed in the graphite furnace can be organized in four categories, known as drying, pyrolysis, vaporization and cleaning. Each of the steps is designed to perform a specific function, but at the same time, other undesirable effects may occur. These 4 steps can be optimized individually for achieving a particular vaporization goal. As a general rule, selection of the different temperatures can be done according to the following criteria:

- *Drying step:* Temperature slightly above the boiling point of the solvent and below that of the analyte in the predominant chemical form. Not too vigorous heating rate to avoid analyte losses by explosive boiling of the sample.
- *Pyrolysis step:* Maximum temperature possible to remove matrix without removing the analytes (that might be stabilized with a modifier).
- *Vaporization step:* Normally minimum temperature possible to vaporize all the analytes without undesired matrix or substrate co-vaporization. Higher temperatures might be used for better signal definition. Addition of modifiers can promote vaporization at lower temperatures.
- *Cleaning step:* Short step at high temperature to remove any sample residue. Assisted cleaning (addition of modifiers) might be desirable in order to reduce the cleaning step temperature or duration, thus extending the tube lifetime.

For conventional applications (e.g., analysis of digested samples), these four steps are normally programmed sequentially in the order indicated above. For more challenging applications on the other hand, these steps can be seen as independent actions that can be skipped or used more than once, in different orders, with cooling steps and/or addition of different modifiers in-between, depending on the particular goal pursued for each application. Many examples of successful temperature programming application can be found in the literature, as will be shown in Section 3.

2.3.2.4. Tools for ETV program optimization: addition of modifiers. At this point of the manuscript, it is quite clear that foreign substances (different from the samples or standards) can play different roles when incorporated in an ETV-ICP-MS method: either they are added in order to improve and/or normalize the transport efficiency of the analyte from samples and standards, or they are added to intentionally modify the vaporization properties of matrix and/or analytes.

The use of modifiers in electrothermal devices was first proposed for GFAAS in the 1970s and was then extensively deployed for this technique before ETV-ICP-MS was introduced [92,93]. As a heritage of this extensive use, it is not surprising that the addition of modifiers for ETV-ICP-MS was already reported since the very beginning of the technique's life [94,95]. However, when adapting these modifier-based strategies for ETV-ICP-MS, some fundamental differences appeared and needed to be evaluated. In 1992, Ediger and Beres systematically tested the performance of several typical graphite furnace modifiers for use with ETV-ICP-MS, proving their positive effect on analyte sensitivity and giving for the first time some insights on their mechanism of action [35]. Since then, several dedicated studies have been presented on the evaluation of different modifiers for ETV-ICP-MS [8,59,64,96] and many examples of successful modification for different applications have been reported in the literature. A summary with the most common modifiers proposed for this technique with their observed effect, comments and some general references reporting their use is gathered in Table 3.

According to the information reported in all these works, the following general ideas can be indicated for selection and work with modifiers in ETV-ICP-MS.

Table 3
Chemical modifiers often use in ETV–ICP–MS.

Modifier	Use/effect	References
Halogenating agents - Gas phase (CHF_3 , CCl_4 , CCl_2F_2 , HCl , Cl_2) - Solid phase (PTFE powder/slurry) - Liquid (dissolved) phase (HF , HCl , NH_4F , HF , NH_4F , NH_4Cl)	- Promotion of the vaporization of refractory elements and/or carbide-forming elements (both analytes and matrix components) - Improvement of transport for these elements. Lower LOD. - Assisted cleaning. Lower memory effects. - Halocarbons may improve plasma conditions	[14], [16] (Review), [26] (Review), [59], [97], [98], [99]
PGMs and other metals - Added as nitrates, chlorides, pre-reduced in the GF, alone or as mixtures - Pd (most often), Rh, Ir, Au, $\text{Mg}(\text{NO}_3)_2$, $\text{Mg}(\text{NO}_3)_2 + \text{Pd}(\text{NO}_3)_2$, $\text{Ni}(\text{NO}_3)_2$	- Stabilization of volatile analytes - Transport efficiency improvement (carrier effect)	[8] [23], [35], [59], [96], [100]
Seawater (NASS-3 CRM)	- Multicomponent physical carrier	[64]
Chelating agents - EDTA, organic diacids, polyhydroxy compounds, etc.	- Promotion of the vaporization of complexed elements at lower temperatures - Selective reactions/vaporizations. Potential use for speciation.	[16] (Review) [101]
Carbon-producing reagents - Ascorbic acid, citric acid, Triton x-100, CCl_4	- Release of C particles in the furnace thus improving transport efficiency - Improvement of plasma energetic conditions	[8] [69]
Specific reagents for matrix digestion: - NH_4NO_3 - O_2 mixed in the Ar gas during pyrolysis	- Elimination of Cl from the matrix - Improvement of organic matrix removal at lower temperature. Generation of C particles from the GF improving transport efficiency.	[102] [72], [73]

- The reagents to be used as modifiers must be of high purity if the extremely low LODs of the technique are to be retained [8].
- The effect of the added modifier on the plasma (e.g., loading) needs to be controlled. Selection of (a) plasma-related signal(s) for diagnostic purposes is advised.
- The effect of the added modifier in forming additional spectral interferences needs to be controlled. The relatively large amounts of modifier added (μg amounts) may result in unexpected interferences *via* reaction with plasma gas species (i.e. generation of argide species) [8].
- The amount of modifier added must be carefully optimized in order to achieve the desired effect regardless of the sample concentration, while at the same time avoiding undesired plasma loading effects.

As already commented on in Section 2.2, the use of modifiers for ETV–ICP–MS is very extended and according to some scientists even compulsory if quantitative results are to be obtained [26]. No truly universal modifier can be suggested, and, thus, carrying out a specific optimization in order to select the right modifier considering the final effect intended is recommendable. Nevertheless, some guidance can be given as to what modifiers should be checked first. For instance, Pd is a very effective modifier for both stabilizing volatile analytes during the pyrolysis, as well as for normalizing their transport to the ICP. On the other hand, when refractory analytes are targeted, the use of halogenating agents is very popular, since these often allow a more efficient vaporization of this type of analytes at substantially lower temperatures.

2.3.3. Calibration methodologies for quantitative analysis

As for any other sample introduction system used in combination with ICP–MS, several possibilities for calibration are possible for obtaining quantitative results in ETV–ICP–MS analysis. These can be summarized as follows:

- External calibration with aqueous standards. Only possible if no significant matrix effects are observed.

- External calibration with aqueous standards, together with internal standardization, the latter used for improving shot-to-shot precision and for correction of matrix effects.
- External calibration with matrix-matched standards (e.g., solid standards for solid sampling), used for matrix effects correction. This approach can also benefit from internal standardization for improving shot-to-shot precision.
- Single or multiple standard additions. Used when (strong) matrix effects occur. This approach can also benefit from internal standardization for improving shot-to-shot precision.
- Isotope dilution. Used for correction of matrix effects and for improving the shot-to-shot precision.

In theory, the possibility for achieving a selective vaporization of the analyte after a proper optimization of the ETV program (as described in the previous section) should minimize the existence of matrix effects, permitting the use of the simplest external calibration strategy for all kind of samples, even for solids. In practice, even if careful optimization of the ETV program is carried out, matrix effects cannot be fully eliminated in many cases, especially when very demanding samples or solids are considered. In these cases, other calibration methodologies being able to deal with these matrix effects are needed. It is not surprising that calibration is often one of the crucial points for discussion in ETV–ICP–MS papers reporting quantitative applications.

Matrix effects observed in ETV–ICP–MS can be due to two main processes: suppression or enhancement effects caused by plasma loading or space-charge effects when, in spite of a careful ETV program optimization, the sample matrix is partially or totally co-vaporized with the analyte on the one hand, and different transport efficiencies are observed for samples and calibration standards (even if carrier agents are added to normalize the transport) on the other. In both cases, use of a suitable internal standard can help correcting for the influence of these effects. Finding this suited internal standard, however, is not self-evident in ETV–ICP–MS. Just as the analyte signals obtained with this technique, the matrix effects for ETV–ICP–MS also show a transient behavior. This effect can be eas-

ily appreciated in Fig. 4 for instance, where matrix co-vaporization for direct I determination in NIST SRM 1549 Milk Powder caused a signal suppression (detected *via* the Ar dimer) *only* between seconds 2 and 5 of the vaporization process [103]. If a suitable internal standard is to be used for correction of this matrix effect, it is clear that, even more important than meeting the general prerequisites of a mass number and ionization potential close to that of the target analyte [104], the internal standard should show similar vaporization behavior in the ETV under the set of conditions used. In the particular case presented in Fig. 4, Pd co-vaporization with the sample at 2500 °C resulted in quasi-simultaneous peaks obtained for the analyte and the internal standard that were thus affected by the matrix effects in exactly the same way. As a result, the use of the $^{106}\text{Pd}^+$ signal as internal standard permitted to correct for this matrix effect.

In the case of matrix effects caused by variations in analyte transport efficiencies between samples and calibration standards, this transient character can be also observed. In these cases, proper selection of the internal standard among the elements showing the same vaporization behavior to that of the analyte(s) is also compulsory. An example of this situation is presented in the work by Aramendía et al. [91] where partial co-vaporization of the solid

titanium dioxide matrix enhanced analyte transport to the ICP-MS, although it did not affect the plasma conditions. In that particular case, sample co-vaporization was not constant along the vaporization step but followed an increasing trend, being more apparent at the end of the step than at the beginning. As a result, analytes of higher volatility (released earlier from the ETV) were less affected by the matrix effect than the more refractory ones released at the end of the vaporization stage. A combination of two internal standards (Te and Pd) with different volatilities and released at different times from the vaporizer helped to solve the problem in that case.

Other examples of the use of internal standards for correction of matrix effects can be found in the literature, mainly for solid sampling applications. In this regard, the use of the Ar dimer signal as internal standard proposed by Vanhaecke et al. in [67], as a means to avoid the sometimes difficult task of finding a suitable internal standard for ETV-ICP-MS, is worth pointing out. Similarly, the use of the signal stemming from the added chemical modifier (Pd^+ in these examples) as a suitable internal standard proposed by Resano et al. in several works [103,105] can be highlighted.

Besides this ability of internal standards to correct for (moderate) matrix effects, monitoring the signal intensity variation for internal references can also help improving shot-to-shot precision, also when no matrix effects are detected. This strategy is especially helpful in very long measurement sessions for heavy matrices, where clogging of the cone orifices or other effects causing sensitivity drifts may be an issue. Also in this context, the general solutions described above, i.e. the use of the Ar_2^+ signal [87], or that of the signal stemming from the added chemical modifier (Pd^+) [106], have been proposed.

Of course, there are other calibration strategies that can help correct for matrix effects. When possible, the use of matrix-matched standards would be the more straightforward solution for this problem. Unfortunately, this approach is not generally possible or even advisable for many applications, like the case of solid sampling analysis. In this case, the use of solid reference materials for calibration is not always possible due to unavailability of certified reference materials (CRMs) with a suitable matrix composition. Besides, its use would introduce an additional important source of uncertainty: the lack of homogeneity of many of these standards at the mg level. In spite of that, this calibration approach was successfully used in some early works in solid sampling (SS)-ETV-ICP-MS [107]. The traditional (single/multiple) standard addition method, on the other hand, can also be used for dealing with (strong) matrix effects [14,27,91,103,108] where the use of a suitable internal standard may also help improving shot-to-shot repeatability [67].

Even if all the abovementioned methodologies can provide reliable quantitative results even for the most complicated samples, isotope dilution as a calibration technique is always the most powerful option, provided that the prerequisites for its use are fulfilled (i.e. at least two isotopes free from spectral interferences available for the target analyte and perfect isotopic equilibration between the sample and the enriched spike [109]). In fact, isotope dilution can even correct for severe matrix effects that vary from one firing to another; moreover, shot-to-shot repeatability is assured by the perfect internal standard, i.e. an isotope of the target analyte itself. This calibration methodology was very often used in the beginning of the technique's life, with the idea that its use was almost compulsory for obtaining quantitative results of sufficient quality, due to the high imprecision introduced by the discrete character of this sample introduction system [11,110]. With the evolution of ETV-ICP-MS, this statement was proved wrong. However, the idea that this is the calibration technique providing the best quantitative results is still valid, and therefore it has been used in many challenging applications ever since, both for digested and solid/slurry

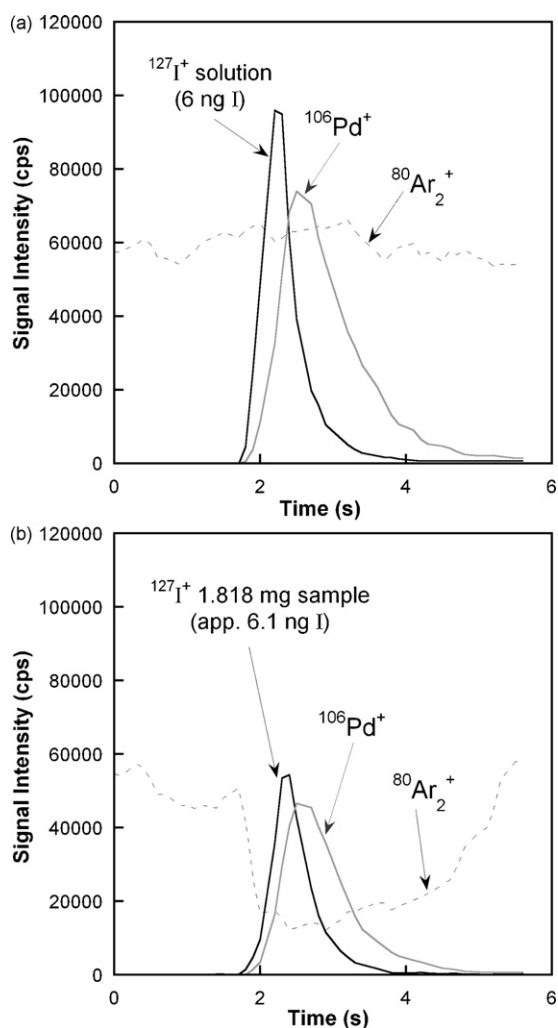


Fig. 4. Correction of matrix effects (detected by monitoring the Ar dimer) by using $^{106}\text{Pd}^+$ signal as internal standard (from [103]). Comparison of the signal profiles obtained for the vaporization of I from (a) an aqueous standard solution and (b) a solid sample, NIST SRM 1549 Milk Powder. (a) 6 ng I solution with 0.5 μg Pd: I peak area = 57 480 counts, Pd peak area = 85 730 counts; (b) 1.818 mg of sample (\approx 6.1 ng I) with 0.5 μg Pd: I peak area = 35 750 counts, Pd peak area = 49 810 counts.

sample analysis [111–118]. The main challenge in the latter case is of course the isotopic equilibration between the sample and the spiked standard, which is usually added in the form of an aqueous solution. A careful optimization of the ETV program with the use of matrix modification if necessary is, again, crucial for achieving this goal [97].

3. Applications

As stated before, even if ETV has failed to become a “standard” sample introduction system to ICP-MS, its excellent features and great versatility have proven very useful in challenging applications, as becomes evident from a closer revision of the literature published to date in this field. In this section, selected examples of the most interesting ETV-ICP-MS applications published in the last decade will be presented. A comprehensive review of these applications is beyond the scope of this critical review, and the reader is referred elsewhere for a more detailed coverage [15].

3.1. Analysis of liquid samples and solutions: ETV-ICP-MS for complex matrices and/or challenging analytes

When liquid samples or solutions need to be analyzed, PN is, in principle, the method of choice. As mentioned before, the transient signals generated by ETV lead to a deteriorated repeatability and limited multi-element capabilities. However, there are some particular situations where the use of ETV for this kind of samples might be preferable.

The first example among these situations is the ultra-trace analysis of samples with complex matrices that would need special preparation protocols for analysis with PN but can be directly (or with minimum pre-treatment) analyzed in the ETV. The benefits derived from the use of ETV and the subsequent reduction or elimination of any sample pre-treatment are many: the risks of analyte losses or contamination are significantly reduced, the LODs are improved by avoiding or minimizing the dilution of the sample and the total time of analysis is also shortened. Several examples of this kind of application can be found in the recent literature. Bettinelli et al., for instance, used ETV-ICP-MS for the determination of 18 trace elements in bee honey, which is considered an indicator of environmental pollution [119]. Due to the rather complex composition of honey and the low content of trace elements, sample preparation is generally the crucial step in the analytical procedure for this matrix with special concern for contamination. By using ETV-ICP-MS, a contamination-free sample preparation by simple dilution with water was possible. External calibration *versus* aqueous standards (with the addition of an internal standard for improvement of the precision) was also possible after optimization of the furnace program.

The same approach has been used for the determination of different analytes in vegetable oil samples [120] or fuel-oils (e.g., gasoline, diesel and biodiesel) [121–123]. In these cases, 10-fold diluted oil-in-water emulsions were prepared in order to benefit from the use of conventional devices for handling of liquid samples (e.g., pipettes, auto-samplers). Addition of other reagents to the emulsions was also necessary, like emulsifying agents (Triton X-100 in the cited examples) or nitric acid (in order to transform all the organometallic species of the target analytes into inorganic species). Straightforward calibration *versus* aqueous standards (using either external calibration, standard additions or isotope dilution) was also possible in all cases after optimization of the ETV program. Even simpler approaches have also been used for the analysis of other fuel types such as ethanol, only requiring addition of diluted nitric acid to transform all organometallic

species into inorganic species [113,124]. Straightforward calibration *versus* aqueous standards (external calibration or isotope dilution) was also possible after optimization of the ETV program with addition of chemical modifiers for the determination of some volatile elements. In this way, very sensitive and fast methods of analysis could be developed for these challenging samples.

This ability of the ETV to directly deal with (heavy) organic matrices has also been used for the direct analysis of organic-phase pre-concentrates containing different analytes after their extraction from different samples. In these instances, the possibility of micro-sampling offered by the ETV permitted to extend the pre-concentration factor even further by reducing the volume of the extractant. Xia et al., for instance, [125] developed a method for the single-drop micro-extraction of Be, Co, Pd and Cd from digested biological samples and subsequent analysis by ETV-ICP-MS. The digested sample was continuously flowing through a small PFA extraction chamber (0.2 mL) and a 10 μ L micro-syringe was used to insert the extraction solution: benzoylacetone (BZA). 3–5 μ L of BZA were pushed out of the syringe to form a drop that was then situated just above the PFA tubing outlet in the extraction chamber. As the fresh sample solution flowed around the micro-droplet continuously, the trace analytes were continuously extracted from the sample solution into the solvent drop. After 10 min of extraction, enrichment factors between 40 (for Pd) and 180 (for Cd) were achieved. Once the extraction was finished, the droplet was directly injected in the ETV and the analytes were vaporized at low temperatures (800–1000 °C) owing to the BZA acting as a chemical modifier. Calibration was carried out *versus* aqueous standards also subjected to micro-extraction. Further examples of other pre-concentration procedures *via* micro-extraction and subsequent analysis by means of ETV-ICP-MS can also be found in the literature. The synergistic extraction of rare earth elements (REEs) from environmental samples with only 2 mL of extraction solution (hexamethylene + two chelating agents) and subsequent vaporization at low temperatures in the ETV proposed by Yin et al. [126], or the pre-concentration of platinum group metals (Rh, Pt, Au, Pd) from biological samples after cloud point extraction with *O,O*-diethyl-dithiophosphate and Triton X-114 proposed by Mesquita da Silva et al. [127] are two of the existing examples.

This ability of ETV to deal with extremely low sample volumes has also been used in many other pre-concentration strategies. In-column micro-extractions for trace element determination in small quantities of biological or environmental samples (e.g., urine, serum, fish otoliths) have been presented [128–130]. In other instances, the graphite tube itself (or some of the graphite parts) has served as a pre-concentrator. Hermann et al. [131], for instance, used commercially available graphite platforms to collect atmospheric aerosols by electrostatic precipitation that were then directly analyzed by means of ETV-ICP-MS and other graphite furnace-based techniques. Another typical example of this kind of application is the well-established methodology (already described in the early 90s) for determination of hydride forming elements after trapping of their hydrides in pre-reduced Pd (or other platinum group metals) inside the GF [132]. In the recent literature, this methodology has been extended to the direct analysis of sediment slurries by Vieira et al. [133].

Apart from the abovementioned applications, the use of ETV-ICP-MS is also very well suited for analysis of radioactive samples with high activity. The small sample volumes required for the analysis with ETV is a great advantage for assuring safe handling of this kind of samples [132]. The use of ICP-MS for determination of long-lived radionuclides is especially indicated for beta-emitters, for which the use of conventional beta-counting methods might be compromised by the usually complicated sample pre-treatment needed for elimination of other beta-emitters and the rather long counting times required (e.g., >1 day) [134,135]. The main problem

when using ICP-MS, however, is the occurrence of spectral interferences, which very often leads to the necessity of additional sample pre-treatment for analyte isolation if PN is used as sample introduction system. In these cases, the ability of ETV to deal with spectral interferences (as already mentioned in this manuscript before and discussed in detail in Section 3.4), may help to further simplify the analytical procedure, thereby increasing safety. This strategy proved successful, e.g., for the determination of ^{79}Se in solutions of fission products with Pd as chemical modifier [136]; that of ^{135}Cs and ^{137}Cs in the presence of Ba with KSCN as modifier [137]; or that of ^{99}Tc without ^{99}Ru separation with sodium chlorate and nitric acid as modifiers [132].

Last but not least, the suitability of ETV-ICP-MS for determination of challenging analytes with high ionization potential (IP) is worth mentioning. The possibility of separating the vaporization of the analyte from the ETV from its ionization in the ICP improves the efficiency of the process and the attainable LODs. The most challenging example in this regard is probably the determination of fluorine in aqueous samples by means of this technique proposed by Okamoto [138]. With one of the highest ionization potentials in the periodic table, the ionization efficiency for fluorine in Ar plasmas is normally very poor. This fact compromises the LODs achievable for this element by means of ICP-MS. By using ETV as sample introduction system, however, an absolute LOD of 0.29 μg for the aqueous fluoride ion could be obtained. Tetramethylammonium hydroxide was used as chemical modifier in order to prevent premature analyte losses during the drying step, and optimized temperature conditions were needed for reduction of the $^{18}\text{OH}^+$ interference.

3.2. Solid and slurry sampling

As already indicated in the introduction, most of the scientists working in the field of ETV-ICP-MS agree on the fact that the direct analysis of solid samples and slurries is one of the main fields of application of this analytical technique nowadays. The reasons favoring the use of these solid sampling/slurry strategies have been recently analyzed in the review by Belarra et al. [28], and can be summarized as follows. On the one hand, the direct production of an analytical signal from a solid sample (or a minimally pre-treated slurry) offers a number of important advantages, resulting from the elimination of the dissolution step:

- (i) the risk of contamination and analyte loss is considerably reduced;
- (ii) sensitivity increases, as samples are barely (slurries) or not diluted at all;
- (iii) analysis time is considerably reduced;
- (iv) normally, a smaller amount of sample is needed;
- (v) the use of hazardous reagents, harmful for personal and instrumentation, is not required, resulting in both economic and environmental benefits.

However, also some drawbacks apply:

- (i) calibration is not always easy due to the occurrence of matrix effects
- (ii) larger uncertainties can be expected for the results obtained due to, among other reasons, the lack of homogeneity observed at the mg-level for many samples and the small sample quantities used for analysis
- (iii) sample manipulation might be complicated, especially for direct solid sampling.

- (iv) limited linear dynamic range, which can be problematic as dilution is not easily possible

In spite of the disadvantages cited, there are many analytical situations in which the global balance is clearly positive towards the use of slurry and direct solid sampling strategies. These would include, e.g., analysis of samples very difficult to digest, determination of analytes very prone to contamination or losses, situations where only a very limited amount of sample is available or extremely low analyte contents are expected, or cases where the expeditiousness of the analysis is of prime importance. As could be expected considering the great number of ETV-ICP-MS papers devoted to slurry and solid sampling analysis that have been published in the last decade (see Fig. 1), many different examples of these situations can be found in the recent literature covering all fields of application. A recap of these publications organized according to the kind of sample analyzed is presented in Table 4.

Finally, it is worth stressing that, compared to other analytical techniques with solid sampling capabilities, ETV-ICP-MS is much more versatile, especially when quantitative analysis is intended. Compared to LA-, glow discharge (GD-) or spark ablation-coupled techniques, GF vaporizers allow all kind of samples for analysis: powders, pellets, conducting and non-conducting, transparent or opaque samples can be, with no exception, vaporized in an ETV unit. Moreover, calibration is an issue much easier to cope with, as discussed in Section 2.3.3. Regarding detection, ICP-MS-based techniques permit multi-element and isotopic information to be obtained in a fast and convenient way, and generally lower LODs can be achieved if compared to AAS or ICP-OES techniques [15]. The only point where this technique might be at a disadvantage is the ease of sample handling. In fact, introduction of solid samples in the GF is not always an easy task, especially if in-house adapted furnaces are used, and this is one of the reasons why preparation of slurries was abundantly used for this technique. Although the only ETV system commercially available nowadays [13] is equipped with an automated device for handling of solid samples, its limited presence in the analytical laboratories supports the aforementioned statement. Anyway, this is more a commercial issue rather than a technological one, because there are automated solid sampling accessories available for GFAAS (e.g., SSA-61 from Analytik Jena) that perform very reliably and could be also deployed in combination with ETV devices.

3.3. Potential for speciation/fractionation studies

Elemental speciation aims at the separation, identification and quantification of the different chemical forms in which the elements of interest are present in a given sample. Most often, powerful separation techniques (e.g., liquid or gas chromatography, electrophoresis or extraction techniques) coupled to different detection systems, including ICP-MS, are used for this purpose. In this context, ETV-ICP-MS has also been used as detection technique for speciation and fractionation studies of different elements in different samples. Chéry et al. reported on the separation of selenium-containing proteins by means of polyacrylamide gel electrophoresis (PAGE) with the subsequent detection and quantification of selenium in the protein spots by ETV-ICP-MS [161,162]. For this purpose, the bands of the gel were cut in fragments that were directly inserted into the ETV. External calibration with the use of Te as internal standard for correction of matrix effects was applied. Chen et al. [163] reported a method for speciation of Al in human serum using capillary electrophoresis separation with on-line UV and off-line ETV-ICP-MS detection. Al-citrate, Al-transferrin and Al-albumin could be efficiently separated and quantified by ETV-ICP-MS under optimized conditions for spiked serum samples, although the applicability

Table 4
Selected solid and slurry sampling applications published in the last decade.

Sample	Analytes	Sampling mode	Calibration	Comments	References
Industrial and advanced materials (metals, polymers, ceramics and other)					
Steelmaking fuel dust	As, Bi, Cd, Mo, Sb, Se, Sn, Te, Ti, V	Slurries	AS ^a	Rh added as modifier (carrier)	[85]
Coal	As, Ge, Hg, Pb, Sb, Se, Sn	Slurries	AS, ID ^b	Chemical vapor generation and trapping in an Ir-treated tube	[139]
Coal, coal fly ash	Cd, Hg, Pb, Tl	Slurries	ID	Pd, Au and Ir used as modifiers	[117]
Fluorocarbon polymer	Cr, Cu, Fe, K, Mn, Pb, Zn	Solid sampling	AS	Pd (chemical modifier) also used as internal reference	[106]
Polyvinyl chloride, poly-styrene	Cr, Cd, Pb	Slurries	SA ^c , ID	NH ₄ NO ₃ added as modifier. Use of dynamic reaction cell	[140]
Polyamide	Mn, Si	Solid sampling	AS	Pd added as modifier	[141]
Bisphenol A	S	Solid sampling	AS	Pd and HNO ₃ as modifiers	[142]
Polyethylene	Al, Ba, Cd, Cu, Mn, Pb, Ti	Solid sampling	AS, SA	Pd added as modifier. Multi-element monitoring evaluated	[143]
Polyethylene terephthalate	Co, Mn, P, Ti	Solid sampling	SA	Pd + ascorbic acid added as modifiers	[144]
Al ₂ O ₃	Cu, Fe, Ga	Slurries	SA	ICP-MS with array detector	[145]
Nb ₂ O ₅	Cu, Cr, Mn, Ni, Ta, Ti, W	Slurries	SA	PTFE added as modifier	[146]
TiO ₂	As, Cd, Hg, Pb, Sb, Zn	Solid sampling	AS, SA	Pd added as chemical modifier and also used as internal reference. Te added as internal reference	[91]
Ancient porcelain	Rare earth elements	Slurries	AS	PTFE added as modifier	[147]
Thermographic material	Al, Mg, Mn, Ni, Sb, Ti, Zr	Solid sampling	AS	HF and HCl as modifiers	[98]
Biological samples					
Human hair	Tl	Solid sampling	ID	Study of the longitudinal distribution of Tl	[115]
Human hair	Hg	Solid sampling	SS ^d	Single hair strand analysis. Induction heating vaporizer	[40]
Botanical and animal samples	Co, Cu, Fe, Ni, Zn	Slurries	SA	Use of DRC for alleviating spectral interferences	[148]
Fish samples	Cd, Hg, Pb	Slurries	SA, ID	EDTA used as modifier	[149]
Milk powder	Cd, Cr, Pb, Zn	Slurries	ID	Use of DRC for alleviating spectral interferences	[150]
Rice flour	Cd, Cr, Cu, Hg, Pb	Slurries	SA, ID	Use of DRC for alleviating spectral interferences	[151]
Fish CRMs	Hg	Solid sampling	ID (gas phase)	Direct speciation of methylmercury and inorganic mercury	[90]
Milk powder, animal tissue polyethylene	Cr	Solid sampling	AS, SA	In-situ microfusion, Pd added as modifier and used as internal reference	[105]
Milk powder, hay powder, typical diet	I	Solid sampling	AS	Pre-reduced Pd used as modifier and as internal reference	[103]
Various botanical and animal CRMs	Pb	Solid sampling	AS	In-situ sample fusion with (NH ₄) ₂ HPO ₄ and tetramethylammonium hydroxide	[152]
Various biological CRMs	B	Solid sampling	ID	NH ₄ F.HF as chemical modifier	[97]
Various CRMs	Se	Slurries	ID	In-situ fusion with NaOH	[153]
Environmental samples					
Tunnel dust, aerosol, grass	Pt, Rh	Solid sampling	SA	Separation in time of interfering polyatomic ions	[154]
Arctic air particles	Ag, Cd, Co, Fe, Mn, Ni, Pb, Sb, Sn	Solid sampling	AS	Particles collected on graphite filters directly introduced into the ETV	[155]
Sediment CRMs	Cd, Cu, Pb, Se, Tl	Slurries	ID	Different ETV programs for the different analytes	[156]
Various CRMs	Hg, Tl	Slurries	AS	KMnO ₄ as chemical modifier	[157]
Sludge	Hg	Solid sampling	SS		[158]
Soils	Cr, V	Slurries	SA	Use of DRC for alleviation spectral interferences	[159]
Sediment CRMs	As, Hg, Se, Sn	Slurries	AS	Ir as permanent modifier for analyte trapping	[133]
Silicate-based minerals	Ba, Ce, Cr, Cu, Mg, Mn, Li, Pb, Rb, Sb, Sn, Sr, U, V, Zn	Slurries	SA	W-coil vaporizer	[160]
Geological CRMs	None	Slurries	–	Pre-treatment in the ETV. Removal of silica with HF.	[99]

^a AS: aqueous standards. This term indicates that a calibration curve has been built with aqueous standards.

^b ID: isotope dilution. Enriched spikes are added in aqueous solution unless otherwise indicated.

^c SA: standard addition. This term refers to the situation in which the method of standard additions has been used, adding the spike in aqueous solution form.

^d SS: solid standards. This term indicates that a calibration curve has been built using CRMs in solid form.

of the method to real serum samples was limited by the insufficient sensitivity obtained. Several publications have also appeared reporting on the separation and pre-concentration of different species for different elements in water samples and drinks after liquid–liquid or in-column micro-extractions [164–168]. Labile and non-labile monomeric Al species could be separated after single-

drop micro-extraction with 8-hydroxyquinoline-chloroform [164] or *N*-(2-aminoethyl)-3-aminopropyltrimethoxysilane-silica monolithic capillary micro-extraction [168]; inorganic Se species (Se(IV) and Se(VI)) were separated from one another by hollow fiber liquid phase micro-extraction with ammonium pyrrolidine dithiocarbamate (APDC) on the one hand [165] and cloud point extraction in

Triton X-114 with different chelating agents on the other [166,167]. The same cloud point extraction strategy was used for the separation of inorganic antimony species present in water samples [167]. In all of these cases, the micro-sampling capabilities offered by ETV–ICP–MS were crucial for the successful development of the analytical methods.

Even if the abovementioned hyphenated techniques for elemental speciation with ETV–ICP–MS detection might be of interest, the most interesting feature of the ETV–ICP–MS in this context may be the possibility of performing *direct* elemental speciation based on the different vaporization temperatures of the different chemical species considered. In these instances, speciation may be achieved by gradually raising the temperature of the furnace, a possibility that can be further refined by using a well-suited chemical modifier [14]. Moreover, the ability of the ETV for the direct analysis of all kind of samples with none or minimal sample pre-treatment may be of great interest in these cases, as the original chemical form of the different analyte species in the samples can be preserved better.

This approach has been used in different papers. Gelaude et al. [90] developed a method for the direct Hg speciation in fish tissue samples. The tissue samples were freeze-dried and were then submitted to a multi-step temperature program resulting in the separate vaporization of methylmercury (~150–200 °C) and inorganic Hg (~400–700 °C). The separation was accomplished in 75 s. For the quantification of the two peaks, species-unspecific isotope dilution was used. For this purpose, a stable flow of Ar loaded with gaseous Hg, isotopically enriched in ^{200}Hg , was continuously passed through the ETV while the sample was subjected to the multi-step heating program. Limits of detection in the low ng/g range could be obtained with this method. Guzowsky et al. [169] separated ferrocene from ferrous chloride present in aqueous solutions owing to the different volatilities of both species. They used an ETV coupled to a He-supported GD–TOF–MS in order to be able to detect both the metal and the halide, enabled as a result of the high ionization potential of the discharge gas. Okamoto et al. [170,171] made use of the extremely different vaporization properties of boron compounds to accomplish separation of boric acid and inorganic boron species present in biological and steel samples, after sample dissolution. Volatile boric acid was determined upon vaporization at 800 °C with the use of tetramethylammonium hydroxide as a chemical modifier to avoid analyte losses during the drying and pyrolysis stages. Refractory inorganic boron was determined by subtracting the boric acid content from the total boron concentration. The latter value was obtained after furnace-fusion digestion of the samples with NaOH to unify all boron species, producing the sodium salt of boron that could be vaporized at 1500 °C.

3.4. Overcoming spectral overlap

The ability of ETV for reducing or eliminating the influence of spectral interferences when coupled to ICP–MS systems has been claimed as one of the main advantages of this sample introduction system since it was first introduced by Gray and Date in 1983 [4]. As already discussed in Section 2.3.2, a judicious optimization of the ETV program (including temperature programming and the use of modifiers if necessary) leads, ideally, to a selective vaporization of the target analyte(s) free from solvent or matrix co-vaporization, thus avoiding many spectral interferences from occurring. Moreover, the added temporal dimensionality offered by the ETV and already mentioned before, extends these possibilities even further and can be very useful for effecting the temporal separation of different analytes that otherwise would show mutual (isobaric) interference.

Most of the typical solvent- or matrix-related polyatomic interferences usually hampering the determination of different analytes when PN is used (e.g., ArCl^+ interfering with the determination

of As, or ArO^+ interfering with that of Fe), have been solved by using ETV and were described already in the first years of the technique's life. An illustrative example of these first contributions is the work by Marshall and Franks [172], who reported improved LODs for the determination of P, V and Ti in the presence of HNO_3 , HCl and H_2SO_4 , respectively, when ETV was used for sample introduction. Optimization of the ETV program permitted to remove (or at least reduce) the influence of the different interfering species: $^{14}\text{N}^{16}\text{O}^{1}\text{H}^+$ for $^{31}\text{P}^+$, $^{35}\text{Cl}^{16}\text{O}^+$ for $^{51}\text{V}^+$ and $^{32}\text{S}^{16}\text{O}^+$ for $^{48}\text{Ti}^+$. Many applications making use of similar interference reduction strategies can be found in the recent literature. Turner et al. [173], e.g., reported a method for the highly accurate and sensitive Se determination in water and serum samples with isotope dilution for calibration. Appropriate optimization of the temperature program permitted to overcome $^{40}\text{Ar}^{37}\text{Cl}^+$ spectral interference on $^{77}\text{Se}^+$ and $^{81}\text{Br}^{1}\text{H}^+$ on $^{82}\text{Se}^+$ (which were noteworthy in the serum matrix), thus enabling the use of the isotope dilution calibration strategy. The dry aerosol generated by the ETV also permitted a more energetic plasma resulting in improved ionization efficiency and higher sensitivity for this analyte, which has a rather high ionization potential, to be obtained. Serum analysis for different refractory elements was also reported by Li et al. [174]. Optimization of the temperature program and use of PTFE as fluorinating agent permitted in-situ removal of the sample matrix (containing high concentrations of Na, K, Ca, Mg, Cl, S, P, C, H, O and N) rendering the vaporization of the target analytes (V, Cr, Mo, Ba, La, Ce and W) free from matrix-related spectral interferences. More challenging was the application presented by Yu et al. [112], who optimized an ETV–ICP–MS program for sulfur determination in fossil fuels, the main source of S atmospheric contamination. Both $^{32}\text{S}^+$ and $^{34}\text{S}^+$ signals are subject to severe spectral interferences coming from oxygen-containing molecular ions (e.g., $^{16}\text{O}^{16}\text{O}^+$, $^{16}\text{O}^{18}\text{O}^+$). Moreover, the ionization potential for this analyte is among the higher in the periodic table, leading to poor ionization efficiencies when Ar plasmas are used. In this work, ETV was used for generation of a water-free sample aerosol thus reducing the occurrence of O-based interferences. Non-solvent sources of oxygen were further reduced by addition of nitrogen as an oxygen-scavenger to the plasma. In this way, both $^{32}\text{S}^+$ and $^{34}\text{S}^+$ signals could be detected free from spectral interferences enabling the use of isotope dilution for calibration. Improved ionization efficiencies were also achieved for this challenging analyte owing to the dry sample aerosol generated in the ETV.

Even more interesting than this direct minimization of polyatomic interferences through ETV program optimization would be the ability of ETV–ICP–MS systems to deal with isobaric spectral overlap that would need a mass resolution far beyond the possibilities of most available mass spectrometers. Many applications and fundamental studies in this regard have been reported in the recent literature, some of which are commented on in different sections of this manuscript. Ertas and Holcombe [75] for instance, studied and optimized the factors influencing peak broadening in ETV–ICP–MS as a means to minimize sample peak widths as a way for improving the temporal separation of isobars. Design of the transport tubing (length and inner diameter) was found to be the primary cause for signal broadening, together with the heating rates used for the vaporization stages. Differences in the vaporization characteristics of the elements, optimization of the experimental set-up (transport tube) and that of the ETV program permitted to resolve the isobaric overlaps among Zn and Ni, Se and Ge and Cd, In and Sn. Regarding real-life applications, it is worth stressing that this feature of ETV was proven to be of great value for the analysis of radioactive samples as discussed in Section 3.1. In these instances, mathematical correction for isobaric overlap by means of reference to other isotopes of the interfering element must be treated with extreme caution because the isotopic composition of these elements in this type of samples is in many cases unknown [136]. In this context,

some of the references cited in Section 3.1 are excellent examples illustrating this kind of applications. Song and Probst, e.g., reported the direct determination of ^{99}Tc in presence of up to a 100-fold excess of ^{99}Ru in the sample matrix by an optimized ETV procedure, deploying sodium chlorate and nitric acid as chemical modifiers [132]. A further example developed by the same authors reports the determination of radiocesium (^{135}Cs and ^{137}Cs) in the presence of up to 10 000-fold excess of Ba in the sample matrix with an ETV procedure deploying potassium thiocyanate as modifier [137].

3.5. Extending the capabilities of ETV–ICP–MS: new possibilities deriving from the coupling with modern ICP–MS instruments

3.5.1. Improving the multi-element capabilities of ETV–ICP–MS

As already discussed in Section 2.3.1, when sequential, scanning mass spectrometers (e.g., quadrupole-based instruments) are employed, the multi-element capabilities of ETV–ICP–MS might be considerably compromised due to the short transient signals generated. Several ingenious methodological approaches have been proposed in the literature to extend these multi-element capabilities that are worth being mentioned. Langer and Holcombe [175], for instance, developed a simple set-up to extend the signals produced for the purpose of obtaining a full mass scan from a single ETV firing with a quadrupole-based ICP–MS unit. Their transient extension (TE_x) chamber consisted of a round flask of variable volume (e.g., 100–500 mL) with a mated joint that was placed in-line in between the ETV and the ICP–MS units, allowing the ETV-generated aerosol to enter the chamber in a pulse and exit the TE_x exponentially diluted. Signal extensions from 2 s to 15 s or more (depending on the TE_x volume) could be achieved, permitting to obtain a full mass scan (254 masses) from a single ETV firing with sensitivity losses lower than 20–30% even in the worst cases. The use of the same experimental set-up for the quantitative analysis of natural water samples was reported in a later publication by Ertas and Holcombe [176]. A similar approach was proposed by Venable et al. [83], who placed a single bead string reactor (a short length of tubing packed with 4 mm glass beds) in-line between the ETV and the ICP–MS to obtain the same effect as that observed with the TE_x chamber. By using this set-up, they could quantify $10\ \mu\text{g L}^{-1}$ amounts of 68 elements with acceptable precision from a single ETV firing. A more sophisticated device was proposed later by Balsanek et al. [177] with the same purpose. These workers trapped the transient ETV-generated aerosol into a stainless steel cylinder equipped with a motor-driven piston assembly that could deliver uniform density of an aerosol to the ICP afterwards. The original profile of the ETV signals was in this way transformed into a longer square-wave profile. Signal height could be used instead of integrated signal for quantitative purposes, thus alleviating the requisites for reliable quantification. A minimal decrease (<2–11%) in the integrated signal area was observed with this device.

Even if the abovementioned approaches may help in improving the multi-element capabilities of ETV–ICP–MS with scanning instruments, its use implies an inherent loss in terms of the time-resolved information offered by ETV systems that can be very useful for overcoming spectral overlap as shown in Section 3.4. The only strategy that may actually help further improving the multi-element capabilities of ETV–ICP–MS without any loss of information would be the coupling of the ETV device to an alternative non-scanning mass spectrometer.

ICP–TOF–MS instruments, e.g., which were first presented in 1993 by Myers and Hieftje [178], allow quasi-simultaneous measurement of full mass spectra in short time intervals. In this kind of instrument, the constant ion beam from the ion source is modulated into discrete packages. Each package of ions extracted is then fully analyzed generating complete mass spectra at high rates (typically 20 000–30 000 scans per second). In spite of this high

acquisition rate, some limitations in the data readout apply. Commercially available instruments permit a maximum readout rate of 100 averaged spectra per second, which still results in an excellent time resolution of about 10 ms [179]. Self-evidently, and due to these excellent features, ICP–TOF–MS instruments are superior over scanning quadrupole-based or sector field instrumentation for handling fast transient signals. Several papers have been published reporting the coupling of ETV to ICP–TOF–MS instruments. Mahoney et al. [76] were the first to report such a coupling, demonstrating the ability of ICP–TOF–MS instruments to rapidly record complete elemental spectra throughout the vaporization stage of the ETV temperature cycle. Solutions containing 34 elements were analyzed. LODs of 10–80 fg were calculated for seven elements based upon $10\ \mu\text{L}$ injections. Time-resolved information could be maintained owing to the quasi-simultaneous detection provided by the TOF–MS instrument, and was used for resolving isobaric overlaps among the isotopes of Cd, Sn and In by exploiting differences in the vaporization characteristics of the elements. Bings and Stefánka [180] coupled a tungsten filament ETV with a TOF–MS instrument to determine 17 elements in whole blood and serum samples. LODs in the fg to pg range based upon $10\ \mu\text{L}$ injections were obtained for the elements studied. A phosphate-based matrix-modifier was used and aqueous standards with multiple internal standardization could be deployed for calibration. Lüdke et al. in turn [181], coupled an inductively heated vaporizer (IHV) with an ICP–TOF–MS instrument for the analysis of trace metal contents in size-separated arctic aerosols. The sampling of aerosol particles was performed by impaction on clean graphite filters that were afterwards directly heated up to $2700\ ^\circ\text{C}$ in the IHV. Multi-element analysis in a mass range between ^7Li and ^{209}Bi was carried out. Calibration was accomplished via standard solutions deposited onto a graphite filter. Typical LODs in-between 2 pg and 200 pg were obtained for most of the elements studied.

In spite of the good features for dealing with the fast transient signals generated in the ETV shown by ICP–TOF–MS instruments, and their reasonable price (similar to that for a quadrupole-based instrument), TOF–MS instruments did so far not gain good acceptance in the 10 years since their commercial introduction. This might be mainly due to their lower sensitivity, higher background and poorer abundance sensitivity compared to quadrupole-based systems that so far limit the use of this kind of instruments [179]. The fact that none of the instruments commercially available are (or have been) manufactured by any of the major ICP–MS-producing companies is also often referred to as a potential reason for this lack of commercial success.

Besides ICP–TOF–MS instruments, sector field instruments equipped with multiple detectors to collect (some of) the transmitted ions simultaneously can be also deployed for improving the multi-element capabilities of ETV–ICP–MS. Peschel et al. [145] described the coupling of an ETV to an ICP–MS with a sector field mass spectrometer of Mattauch–Herzog geometry and equipped with an array of detectors for the multi-element analysis of Al_2O_3 ceramic powders introduced in the ETV as slurries. Dynamic ranges were demonstrated to span 3–5 orders of magnitude for Fe, Cu and Ga, and LODs in the low $\mu\text{g g}^{-1}$ for the analysis of $10\ \text{mg mL}^{-1}$ slurries were obtained. This type of instrumentation is to date not commercially available.

3.5.2. Further reduction of spectral overlap

As described in detail in Section 3.4, the use of ETV as a means of sample introduction for ICP–MS can help reducing or eliminating polyatomic and isobaric spectral interferences originating from the solvent and/or the sample matrix. However, the efficiency of interference removal can be limited by factors such as an excessive intensity of the interfering ion with respect to the analyte ion. Moreover, the use of ETV may also lead to an increase in back-

ground signals for carbon-containing ions as a result of carbon being released from the heated graphite furnace, especially when high temperatures must be used for vaporization [23]. In these instances, coupling of the ETV unit to an ICP-MS instrument capable of dealing with spectral interferences may be of help. Two main approaches to deal with spectral interferences can be found nowadays on the ICP-MS market: sector field instruments that can be operated at high mass resolution (offering a maximum resolving power of around 10 000) and quadrupole-based instruments equipped with a collision/reaction cell.

The use of collision/reaction cells with ETV-ICP-MS has been explored for a few applications only. All of the works published to date report the use of instruments equipped with a quadrupole-based cell (termed dynamic reaction cell, or DRC [182], by the manufacturer). The DRC consists of an additional quadrupole in an enclosed cell, situated in-between the ICP and the analyzing quadrupole, which can be pressurized with an adequately chosen gas in order to induce chemical/physical reactions that may help reducing spectral interferences. In this regard, several options are possible: usually, interfering ions can be neutralized via electron transfer or their signal can be shifted to another mass via an atom transfer reaction. Alternately, also the analyte ions can be converted into reaction product ions that can be measured interference-free at another mass-to-charge ratio. Attention must be paid to the fact that also new undesired ions may be formed in the DRC as a result of side-reactions between the introduced gas(es) and some matrix components. This effect can be (partially) counteracted by proper adjustment of the settings for the quadrupole inside the DRC, which, just as the analyzing quadrupole, can act as a band-pass filter.

Most of the papers reporting the use of DRC-ICP-MS in combination with ETV exploit the use of NH_3 as a reaction gas. Ben-Younes et al. [183] presented a comparative study between PN and ETV as introduction systems in order to assess the effectiveness of NH_3 in reducing the influence of carbon-based polyatomic interferences in the determination of three refractory elements (i.e. Cr, Mg, Si) when using ETV. NH_3 was found effective in reducing polyatomic ions interfering with the determination of Cr (interfered by, among others, $^{40}\text{Ar}^{12}\text{C}^+$) and Mg (interfered by, among others, $^{12}\text{C}_2^+$ and $^{12}\text{C}^{14}\text{N}^+$). This approach was not fully successful in the case of Si, although LODs for $^{28}\text{Si}^+$ determination (interfered by, e.g., $^{12}\text{C}^{16}\text{O}^+$ and $^{14}\text{N}_2^+$) and $^{29}\text{Si}^+$ determination (interfered by, e.g., $^{12}\text{C}^{16}\text{OH}^+$ and $^{14}\text{N}_2\text{H}^+$) could be greatly improved over conventional quadrupole-based ICP-MS. Li and Jiang [140] deployed a similar approach for the interference-free direct determination of Cr (together with Cd and Pb) in slurry samples of different plastics. Ho and Jiang in turn [150], reported an ETV-DRC-ICP-MS method to determine Cr and Zn (together with Cd and Pb) in milk powder slurries. The use of ascorbic acid as chemical modifier and the need for high vaporization temperatures for Cr determination, aggravated the already severe problem of C-based interferences affecting Cr and Zn isotopes. The use of NH_3 in the DRC, however, permitted to overcome most of these interferences, e.g., ArC^+ at $m/z=52, 53$ or ArCO^+ at $m/z=68$.

Besides NH_3 , also CH_4 and O_2 have been used as reaction gasses in the DRC for particular applications with ETV-ICP-MS. Tseng et al. on the one hand [148], accomplished the determination of some transition metals (Fe, Co, Ni, Cu and Zn) in slurry samples of plant and animal origin with high amounts of Ca in the matrix (2–4 orders of magnitude higher than the analyte contents). The determination of these analytes in these matrixes is hindered by the occurrence of Ar-based and $\text{CaO}(\text{H})^+$ ions. Even if the sole use of ETV already alleviates the influence of some of these interferences, some further improvement was needed to fully compensate for their influence. Further reduction of the spectral overlap was obtained by using CH_4 as reaction gas in the

DRC. Finally, Grinberg et al. [184] proved the suitability of O_2 as reaction gas in order to reduce the isobaric interferences hampering the ultra-trace determination of the radionuclide ^{90}Sr in environmental samples. ^{90}Sr is a beta-emitting radionuclide, the presence of which in the environment began to be significant after the intensive testing of nuclear weapons in the 1950s and the 1960s. Accurate determination of this radionuclide by means of ICP-MS is hampered by the isobaric overlap with ^{90}Zr and from abundance sensitivity problems due to peak tailing from the ^{89}Y signal. Unfortunately, Zr and Y are usually present at much higher concentrations in environmental samples (e.g., soil samples) and very frequently, cumbersome and time-consuming sample pre-treatments are mandatory for successful determination of ^{90}Sr in this kind of samples. By using O_2 in the DRC, Zr and Y can be selectively oxidized and removed from the m/z region of interest. This effect complements the interference reduction achieved after optimization of the ETV program, such that very low LODs (3.5 pg g^{-1}) could be achieved. Application to real-life samples containing high levels of Fe and Ni, however, was limited by the occurrence of side-reactions in the DRC, creating additional NiO^+ and FeO^+ interferences. This problem was circumvented by implementing a simple chromatographic separation step prior to analysis by ETV-ICP-MS.

In comparison to reaction/collision cell technology, sector field instruments can offer a more universal tool for handling spectral overlap. In fact, the mass resolution offered by this kind of mass spectrometers is much higher than that of quadrupole-based instruments, such that most often the signals from the analyte and the hindering polyatomic ion(s) can be simply resolved from one another [185]. Although being more universally applicable, high resolution instruments are not the final solution for all kind of spectral interferences and, unfortunately, most isobaric interferences are beyond the maximum resolution offered by these instruments. To the best of the author's knowledge, only one paper to date has appeared in the literature reporting the coupling of an ETV unit to a sector field instrument that can be operated at high mass resolution (besides the coupling of ETV to a multicollector (MC)-ICP-MS for precise isotope ratio determination, which will be discussed in Section 3.5.3). In that paper, Resano et al. [186] evaluate the possibilities of such a coupling in terms of multi-elemental capabilities, sensitivity and interference reduction. The direct determination of Cr and Si in solid biological materials is also reported in the paper. The use of medium resolution ($R \approx 4000$) for resolving the analyte peaks from those of carbon-based polyatomic interferences permitted the use of isotope dilution for calibration, with the subsequent improvement in precision and accuracy of the final results.

3.5.3. ETV-ICP-MS beyond quantitative analysis: feasibility for isotope ratio measurements

One of the main advantages of ICP-MS over other analytical techniques is its ability to provide isotopic information. As extensively discussed in Section 2.3.3, this ability has been largely exploited in the field of ETV-ICP-MS for calibration via isotope dilution. Besides this application, however, the capability of ETV-ICP-MS for providing isotopic information can also be exploited in other contexts (e.g., determination of the isotopic composition of selected elements for provenance determination of, e.g., agricultural products or archaeological samples, or for geochronological analysis of geological materials), but this type of work has been explored only seldom. The reasons behind this fact are certainly related with the poor precision attainable for isotope ratio measurements with the quadrupole-based ICP-MS normally used in combination with ETV (limited in most cases to 1–3% relative standard deviation (RSD) [97]), which might be appropriate for isotope dilution calculations, but is often by far insufficient for most other isotope ratio applications.

In spite of this fact, quadrupole-based ETV–ICP–MS has been successfully used in the past for isotope ratio determination in some instances where the 1–3% RSD limit was fit-for-purpose and the other ETV features (e.g., its micro-sampling capabilities or the extremely low LODs attainable) were considered of prime interest. Back in the early 90s, Grégoire determined Os isotope ratios in digested iridosmine samples for geochronological purposes. Temperature programming in the ETV permitted to overcome the Re isobaric interference at a mass-to-charge of 187 without additional sample treatment, and RSD values around 0.5% could be obtained [187]. Quadrupole-based ETV–ICP–MS was also used by the same author for isotope ratio measurements aiming at the evaluation of Cd and Zn metabolic behavior in mammals [188]. For this purpose, a group of sheep was subjected to an infusion experiment with isotopically enriched Cd and Zn. Samples of very limited dimensions (a few mL for body fluids or mg-sized samples for body tissues) with very low concentrations for the target analytes (e.g., below 0.2 ng g^{-1} Cd in blood plasma) could be successfully analyzed for isotope ratio variations with the ETV–ICP–MS method developed. More recently, Chaudhary-Webb et al. used this technique for Pb isotope ratio measurements in complex samples, i.e. blood, pottery and gasoline, as a means to clarify the source for the high levels of Pb in blood observed in the population of a small Mexican village [189]. The use of leaded pottery was eventually identified as the main source of Pb in the blood, as demonstrated by the good correlation of the Pb ratios measured for both samples that were statistically different from those observed for the gasoline samples. Finally, Lee and coworkers performed direct solid sampling analysis of polycarbonate film samples containing a few picogram amounts of Tl, Pb and U particles as a means to assess the feasibility of ETV–ICP–MS for isotopic analysis of swipe samples from nuclear facilities. Sufficiently accurate and precise (<1% RSD) isotope ratio in polycarbonate samples containing 1 pg of the particulate analytes could be obtained [190].

Even if the abovementioned applications might be of considerable interest, it is clear that quadrupole-based ETV–ICP–MS cannot meet the requirements of most isotope ratio applications for which a much better precision is required [191]. Short transient signals are by no means ideal for isotope ratio measurements; however, precision problems can be at least partially alleviated by using ICP–MS instrumentation showing the potential for (quasi) simultaneous ion monitoring like ICP–TOF–MS or MC–ICP–MS. In a recent paper by Rowland et al. [89], the possibilities of these two types of ICP–MS instrumentation for Sr isotope ratio determination in geological samples (NIST SRM 607 potassium feldspar was analyzed) with ETV as the sample introduction system have been evaluated. Careful optimization of the ETV heating program was performed with the ICP–TOF–MS instrument, and permitted to overcome the isobaric interference of ^{87}Rb and ^{87}Sr , thus avoiding the need for time-consuming sample pre-treatment. Final measurements were made using a MC–ICP–MS unit for data collection for best precision values to be obtained. The model age obtained for the feldspar material agreed well with the certified value. However, even if the use of the MC–ICP–MS instrument permitted to achieve a significant improvement in precision (0.3% RSD), it still remained significantly higher than the theoretical limit based on counting statistics, such that also the precision of the age determined needs to be improved further.

Taking all this into account, it is clear that ETV–ICP–MS is not the option of choice for very precise and accurate isotopic analysis, albeit valuable analytical information can be obtained in some challenging situations. The question whether the advantages offered by the ETV sample introduction system offset the loss in precision expected becomes a matter that has to be assessed for every particular situation.

4. Conclusions

After 25 years of evolution, ETV–ICP–MS has certainly reached maturity and is nowadays a well established analytical technique. At this point of the story, however, it is undeniable that ETV has not succeeded in becoming a “standard” introduction technique for ICP–MS, and not many laboratories in the world have an ETV unit at their disposal. The reasons explaining this situation are probably related with the unfortunate lack of interest shown by the main manufacturers of analytical instrumentation towards this technique. Moreover, the extended idea among people not familiar with the field that working with ETV–ICP–MS is an extremely difficult task, together with the lack of clear compilations of well-defined standard conditions for analysis (like, e.g., those existing for GFAAS), further hinders wider acceptance.

Contrary to this belief and as we tried to show in this review, the basic rules guiding the analyst in the work with ETV–ICP–MS can be easily recognized and, although some degree of expertise might indeed be required to fully exploit the wide range of possibilities that this technique can offer, method development should not be regarded as overly difficult. In fact, most of the theoretical aspects related to the work with ETV–ICP–MS have been already addressed by different scientists, and some standard working methodologies can be extracted from the existing literature for successful use of this technique in a great variety of challenging analytical situations.

As a final remark, it is fair to point out that, in spite of its restricted presence in routine laboratories, ETV–ICP–MS has demonstrated capabilities that allow it to play a more important and more widespread role in today’s analytical chemistry. Unfortunately, no significant changes to the present situation can be foreseen in the near future, unless a stronger commitment is made by the instrument-manufacturing companies to provide not only the instrumentation, but also the methodological support (e.g., guides including compilations of working conditions for the most relevant applications, suitable software to deal with transient signals, etc.) that this technique seems to be currently lacking.

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