Review:

Sample introduction systems for the analysis of liquid microsamples by ICP-AES and ICP-MS

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Abstract

There are many fields in which the available sample volume is the limiting factor for an elemental analysis. Over the last ten years, sample introduction systems used in plasma spectrometry (*i.e.*, Inductively Coupled Plasma Atomic Spectrometry, ICP-AES, and Mass Spectrometry, ICP-MS) have evolved in order to expand the field of applicability of these techniques to the analysis of micro and nano samples. A full understanding of the basic processes occurring throughout the sample introduction system is absolutely necessary to improve analytical performance. The first part of the present review deals with fundamental studies concerning the different phenomena taking place from aerosol production to analyte excitation / ionization when the liquid consumption rate does not exceed 100 μl/min. Existing sample introduction systems are currently far from the ideal and a significant effort has been made to develop new and efficient devices. Different approaches for continuously introducing small sample volumes (*i.e.*, microsamples) have been reviewed and compared in the present work. Finally, applications as well as basic guidelines to select the best sample introduction system according to the sample particularities are given at the end of this review.

Keywords: Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES); Inductively Coupled Plasma Mass Spectrometry (ICP-MS); Aerosol transport phenomena; Micro sample analysis; Nebulizer; Spray Chamber; Desolvation System.

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1. Importance of the analysis of microsamples

The analysis of microsamples through Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES) and Mass Spectrometry (ICP-MS) is a subject that has gained great interest over the past years. Several reasons can be argued to try to explain this fact [1,2]:

1. in some fields (*i.e.*, forensic [3], biological [4], clinical analysis, etc.) the sample volume available can be lower than 1 ml;
2. the optimization of new coupling techniques, such as Capillary Electrophoresis (CE) [5] or other chromatographies coupled to ICP-AES (or ICP-MS), involves the use of a low sample consumption system;.
3. the low sample consumption systems improve the analyte transport efficiencies afforded by conventional setups;
4. several interferences caused by the solvent (*i.e.*, polyatomic interferences in ICP-MS) can be reduced by working at very low liquid flow rates;
5. new devices able to provide the concentration of several elements in a cell are required [6];
6. toxic and radioactive wastes should be minimized.

Table 1 shows the amount of sample available in several applications [7]. It can be observed that in some cases the sample volume is below 100 µl. In other instances, the mass of sample available for the analysis is of the order of milligrams. Increasing the sample volume is an obvious solution to this problem, although a dilution is produced that limits seriously the analysis when the analyte concentration is very low. Another way to solve this problem is discrete introduction of the sample. This is an acceptable approach that is not within the scope of the present review and has been

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considered in studies dealing with flow injection analysis methodology [8]. Finally, coupling of chromatographic and non chromatographic separation techniques to ICP spectrometry requires work at extremely low liquid flow rates. As will be mentioned later, this fact presents some important problems.

Usually, when analyzing liquid solutions through ICP-AES and ICP-MS, a nebulizer (*i.e.*, used to transform the liquid solution into an aerosol) is coupled to a spray chamber (*i.e.*, used to remove the aerosol coarsest droplets). The nebulizer is operated at a solution delivery rate on the order of 0.5 - 2 ml/min. Taking into account the time required to carry out a complete signal reading (1 – 5 min, depending on the detection system and the number of elements to be determined), the volume of sample required ranges from roughly 1 to 10 ml. The analysis is therefore difficult when working with sub millilitre samples (*i.e.*, microsamples). The most simple and direct way of performing analyses such as those summarized in Table 1 would be to use a conventional liquid sample introduction system operated at low sample delivery rates.

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Basically, under these conditions, a sharp decrease in the sensitivity is produced with respect to that found at conventional liquid flow rates. Two different reasons can be advanced to account for this fact: *(i)* the mass of analyte introduced into the sample introduction system and, hence, into the plasma is up to 100 times lower and; *(ii)* as will be discussed later, at liquid flow rates on the order of several tens of microliters per minute, the aerosols produced by classical nebulizers are too coarse, thus precluding the transport of solution through the spray chamber. Furthermore, it is also worth mentioning that at these so low liquid flow rates, it is difficult to carry out measurements of the aerosol characteristics and of the mass of solution transported to the plasma with good precision. Hence, an added drawback is the lack of fundamental studies concerning the processes occurring at low liquid flow rates.

It is, therefore, obvious that to perform the analyses included in Table 1, dedicated sample introduction systems are required [2]. These systems must be able to provide good results while lowering as much as possible the sample consumption. It is generally accepted that working at liquid flow rates below 100 – 200 μl/min implies changes in the sample introduction system as well as in the extent of the processes produced during the aerosol generation and its transport towards the plasma. Therefore, a low consumption system could be considered as one being able to work efficiently at liquid flow rates below these values.

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2. Fundamental studies concerning the analysis of microsamples with common micronebulizer-based systems

A micronebulizer is used to generate stable aerosols at liquid flow rates below 100 – 200 μl/min. In comparison to conventional nebulizers operating at delivery rates of the order of a millilitre/min, the design of micronebulizers must be modified to cope with very low delivery rates.

2.1. Aerosol generation

Several micronebulizers have been developed and they have demonstrated better performance (*i.e.*, finer aerosols, higher ICP sensitivities and lower limits of detection) at low liquid flow rates than conventional nebulizers. Table 2 compares the critical dimensions for a set of pneumatic nebulizers and micronebulizers. It can be noted that, in general terms, concentric micronebulizers (Figure 1.a) have lower capillary inner diameters and wall thickness than conventional ones. Furthermore, for some concentric

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micronebulizers, the gas exit cross sectional area is also reduced. The modifications in these dimensions have several important implications. They can be highlighted by taking as reference some of the calculations included in the thorough review published in 1988 by Sharp on fundamentals of pneumatic aerosol generation [9]:

(i) Once the sample emerges through the nebulizer capillary, the liquid stream core remains unaltered over approximately five times the capillary diameter [9]. Taking into account the data in Table 2, for a conventional pneumatic concentric nebulizer, this distance takes a value of 2000 μm, whereas in the case of a High Efficiency Nebulizer (HEN), the liquid vein remains unaffected by the gas stream only for a length of 400 – 500 μm. Therefore, for the HEN the aerosol generation is produced closer to the gas exit (*i.e.*, where the gas has a high kinetic energy) than for a conventional nebulizer.

(ii) For micronebulizers, the distance (L) outside the nebulizer along which the gas stream remains able to generate droplets changes with respect to conventional devices. Therefore, the area of the interaction region between the liquid and the high velocity gas is modified. For conventional pneumatic concentric nebulizers, we can calculate the interaction area by taking into account that the annulus width is typically 20 – 30 μm [9], hence L is 100 – 150 μm. As the perimeter of the sample capillary is 1.63 mm, the interaction area is about 0.16 – 0.25 mm^2. A similar calculation yields L values for micronebulizers (such as the HEN, MCN and MMN) included within the 90 to 110 μm range, which, for 0.31 to 0.63 mm capillary perimeters, indicates that the gas range of action goes from 0.03 to 0.07 mm^2. In conclusion, it can be indicated that at a given liquid and gas flow rates, the liquid – gas contact area is significantly lower for micronebulizers than for conventional ones. This is detrimental from the point of view of generation of fine droplets.

(iii) In pneumatic concentric nebulizers, the liquid emerges from the centred capillary and, due to the action of the gas stream, it moves towards the gas exit. This effect causes the thickness of the liquid stream moving outwards from the nebulizer capillary to decrease [9]. This process is called prefilming. At a given liquid flow rate, the thickness of the solution on the front walls of the sample capillary slipping towards the gas stream is higher for thin capillaries (*i.e.*, like those used in the case of micronebulizers) than for coarser ones. Therefore, from this point of view, the liquid and gas interaction is expected to be less efficient in the case of micronebulizers.

(iv) At a given volumetric gas flow rate, the energy available to produce aerosol depends on the nebulizer gas exit cross-sectional area. Therefore, irrespective of the pneumatic nebulizer used, the lower the value of this dimension, the higher the kinetic energy of the gas stream as it expands at the nozzle [9]. As can be seen from Table 2, for some micronebulizers the gas exit area is lower than for conventional devices. As a result, finer aerosols should be produced for the formers.

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(v) Tip blockage can be more severe if the dimensions of the nebulizer capillary are reduced. When working with high salt content solutions, pneumatic concentric nebulizers become blocked due to the solution re – nebulization. In this case, some droplets are deposited on the nebulizer tip walls, from which they are drawn towards the gas exit where they are nebulized again. If salty solutions are analyzed, the dry gas evaporates a fraction of the solvent high enough to cause crystal formation at the gas annulus [9]. As soon as the annulus blocks, even partially, nebulization stops. Obviously, this effect would be more severe for nebulizers having a low gas exit cross-sectional area than for those with high values of this critical dimension. Among the different options tested to reduce the significance of the blockage problems, the best one appears to be recessing the liquid capillary with respect to the nebulizer nozzle.

(vi) Finally, an implication of using micronebulizers is the reduction in memory effects found for a given spray chamber and liquid flow rate as compared with conventional nebulizers.. This is mainly due to the fact that capillaries with reduced dimensions are used with these devices (Table 2).

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For conventional pneumatic nebulizers, the dimensions of liquid capillaries (*i.e.*, wall thickness and inner diameter) are not appropriate to generate fine aerosols at low flow rates. It has been claimed that it is difficult to generate stable aerosols with conventional nebulizers at liquid flow rates below 300 µl/min [10]. Nonetheless, conventional pneumatic nebulizers are able to produce 'stable' though not 'fine' aerosols at liquid flows as low as 30 µl/min. It is generally accepted that glass concentric nebulizers afford their best analytical figures of merit when the liquid flow rate is settled at a value close to the free uptake rate. This fact has also been confirmed for micronebulizers [11]. Figure 2 shows the variation of the primary aerosol surface mean diameter ($D_{3,2}$) versus the delivery liquid flow rate (Q_l) for two different classical glass-made pneumatic concentric nebulizers and a micronebulizer. The data presented in this figure confirm the assessments made earlier. For the conventional nebulizers, a decrease in the liquid flow rate initially leads to a slight drop in $D_{3,2}$ (*i.e.*, aerosols become finer), then this parameter rises as Q_l goes down. The decrease in the mean diameter can be accounted for by an increase in the gas- to-liquid volume ratio, thus favouring the production of small droplets. However, at liquid flow rates below 100 µl/min, the $D_{3,2}$ increases as Q_l is decreased. The trend found for a micronebulizer (MMN) is far different, because the $D_{3,2}$ decreases as Q_l is lowered down to 60 µl/min. Below this liquid flow rate, the $D_{3,2}$ appears to slightly increase. In fact, Sharp has explained this increase in $D_{3,2}$ with Q_l according to the following mechanism [9]: as the liquid stream emerges from the nebulizer liquid delivery capillary, it trends to move

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outward until it reaches the nebulizer annulus and then it is fractionated into droplets. In order for this mechanism to take place in a regular stable way, the liquid stream thickness must not be much lower than the gas action length (L), otherwise coarse droplets are generated. At low liquid flow rates, therefore, the dimensions of the liquid stream are too small to produce a stable aerosol with a conventional pneumatic concentric nebulizer. Presumably, the liquid flow rate below which coarse aerosols are produced will be lower for micronebulizers (Figure 2) because of the reduced dimensions of the capillary.

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Additionally, it should be indicated that, once the aerosol has been generated, at low liquid flow rates, the solvent evaporation produced along the sizer measurement zone is more significant at low than at high liquid flow rates and for small than for big droplets. Therefore, a higher fraction of finest droplets disappears at low than at high liquid flow rates. As a result the proportion of coarse droplets is higher at low flow rates thus giving rise to the increase in the aerosol mean drop size shown in Figure 2.

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Another reason can be given to explain the data in Figure 2 for the MMN; provided that below a given Q_l the aerosol liquid volume is very low and taking into account that a system based on the Fraunhofer diffraction of a laser beam has been used to take the data in Figure 2, it can be said that the total diffracted light energy is low. Under these conditions, small changes in the background can seriously affect the results finally obtained by increasing the energy apparently scattered by coarse droplets. A shift of the results towards aerosols coarser than the actual ones is produced. Furthermore, the precision of the measurements is degraded.

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The effect of the nebulizer gas flow rate (Q_g) on the characteristics of the aerosols also depends on the liquid uptake rate (Q_l) [12]. Thus, for a HEN at low Q_l values (*c.a.*, 85 µl/min) an increase in Q_g did not modify in a significant way the

characteristics of the primary aerosols. Note that at conventional liquid flow rates (*c.a.*, 1-2 ml/min) the higher the Q_g, the finer the aerosols produced by a pneumatic nebulizer. Therefore, when the solution mass to be nebulized increases, the mass of gas required to efficiently produce the aerosol also rises [9,12].

2.2. Aerosol transport

When working at liquid flow rates below approximately 100 μl/min, the relative extent of the processes occurring inside the spray chamber changes with respect to the situation found at conventional liquid flow rates. On the one hand, solvent evaporation is enhanced and, on the other hand, droplet coalescence is dampened in the former situation.

2.2.1. Solvent evaporation

A theoretical study can be performed in order to evaluate the extent of solvent evaporation and the evolution of the aerosol characteristics as the sample is nebulized at low liquid flow rates [13].

The variation of the diameter of a droplet with time as a result of solvent evaporation can be described according to the following equation [14,15]:

$$d^3 = d_0^3 - E\,t \qquad (1)$$

where d is the drop diameter at a given time t, d_0 is the initial drop diameter and E is the so-called evaporation factor, which is given by:

$$E = \frac{48 D_v \sigma p_s M^2}{(\rho R T)^2} \qquad (2)$$

where D_v is the diffusion coefficient for solvent vapour, σ is the solvent surface tension, p_s is the saturated vapour pressure, M is the molecular mass of the solvent, ρ is the solvent density, R is the gas constant, and T is the absolute temperature. Equations (1) and (2) have several simplifying assumptions, the most important being that the aerosol inside the chamber is under isothermal conditions and its flow regime is laminar [14]. It is also assumed that the liquid and vapour phases of the solvent are in equilibrium and the electric charge has a negligible effect on the vapour pressure. It is interesting to mention that equations (1) and (2) are valid for droplets with diameters higher than 0.1 μm and that the drop in the temperature produced as the solvent evaporates does not have any significant effect on the droplet evaporation rate [16,17].

The sizer used to obtain the data required to carry out the theoretical study (*i.e.*, based on the Fraunhofer diffraction of a laser beam) was equipped with a 31 ring detector. In this way, the complete drop size distribution was classified into 31 different fractions corresponding to 31 different size ranges. The basis of this theoretical simulation was to plot in frequency the volume drop size distribution of the aerosol generated by the nebulizer. A total of 31 bars was then obtained. Equation (1) was then applied to each drop size range such that the evolution of the size ranges with time was calculated. For a given drop size range (i), the aerosol liquid volume of the droplets was calculated as a function of time according to:

$$V_i = \frac{4}{3}\pi R_i^3$$

$$V_i = \frac{1}{6}\pi \left[(d_0)_i^3 - E\,t \right] \qquad (3)$$

where R_i and $(d_0)_i$ are the mean radius and diameter for each drop size range, respectively. For each initial diameter, $(d_0)_i$, the volume was calculated at different

times (equation 3). The fraction of solvent not evaporated (NE) for each size range was obtained by dividing each one of these volumes by the initial aerosol liquid volume:

$$NE = \frac{V_i}{(V_0)_i} \qquad (4)$$

Finally, by multiplying NE by the percentage of liquid volume in the band (obtained from the measured drop size distribution) and by the liquid flow rate, the aerosol liquid volume flow rate (AL) contained in each size range at a given time is obtained:

$$AL = 30 NE\ (\%\ in\ band)$$

$$AL = 30\left[1 - \frac{Et}{(d_0)_i^3}\right](\%\ in\ band) \qquad (5)$$

Figure 3 shows the complete absolute drop size distribution curves at three different times for water at a 30 μl/min (Figure 3a) and 1000 μl/min (Figure 3b) liquid flow rate, and for a 2 mol/l nitric acid solution at a 30 μl/min liquid uptake rate (Figure 3). By integrating these curves at different times, the solvent volume evaporated can be calculated as a function of time [13]. At 25ºC, the theoretical data indicated that the maximum amount of water that could evaporate to saturate the argon stream was 20 – 30 mg/(l of argon) [18,19]. The time at which the argon stream was saturated depended on the Q_l value and the sample matrix. Thus, at 30 μl/min, 6 s after the aerosol generation, the argon stream was considered to be saturated with water. This time was shortened down to 2 s at 1000 μl/min. In other words, longer residence times inside the spray chamber would not promote further solvent evaporation. It is interesting to note that, as has been suggested [20], a significant fraction of the solvent could evaporate from the solution deposited on the inner walls of the chamber.

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The simulated drop size distributions are considered at three different times: 0 s, which corresponds to the primary aerosols (*i.e.*, the aerosols generated by the nebulizer); 1 s, which is roughly the aerosol residence time in a low inner volume spray chamber (*i.e.*, ranging from 10 to 20 cm^3) and 6 s at 30 µl/min and 2 s at 1000 µl/min, which corresponds to the time required to saturate the argon stream. Note that all the calculations were performed at a 0.7 l/min nebulizer gas flow rate.

When plain water solutions were nebulized (Figure 3,a), theoretical calculations indicated that, 1 s after the aerosol generation, all droplets with diameters lower than about 2 µm were completely evaporated. Droplets with diameters higher than about 9 µm, in turn, did not modify their diameters in an appreciable way. This expected trend confirmed that the small droplets evaporated faster than the bigger ones. By considering the time required to saturate the argon stream (grey lines in Figure 3,a) it could be concluded that the change in the drop size distribution produced by solvent evaporation became remarkable. Thus, for example, the aerosol liquid volume contained in droplets with diameters of about 6.7 µm is approximately two times lower 6 s after the aerosol generation than 1 s after the nebulization is produced. Furthermore, according to the calculations, droplets with diameters lower than 3.4 µm are completely evaporated. The implication of these results is quite interesting because, in order to enhance the solvent evaporation thus increasing the transport of solution towards the plasma at low liquid flow rates, it is very important to use nebulizers able to generate droplets with diameters lower than 2 µm.

Figure 4 shows the accumulated volume drop size distribution curves for several pneumatic micronebulizers. The percentages of aerosol liquid volumes contained in droplets with diameters below 2 µm were 10.4, 21.6 and 31.6% for the MMN, PFAN, and HEN, respectively. From these data, we can conclude that, if low inner volume

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spray chambers are going to be used, the most appropriate micronebulizer designs would be the HEN or the PFAN. As noted previously, under these circumstances, droplets with diameters lower than 3.4 μm would disappear. The aerosol liquid volume percentages contained in droplets with diameters below 3.4 μm (*i.e.*, those that would evaporate completely) are 15.4, 30.4 and 40.2% for the MMN, PFAN and HEN, respectively.

As the liquid flow rate is increased from 30 to 1000 μl/min, the proportion of water evaporated to saturate the 0.7 l/min argon stream shifts to lower values. In fact, the respective values of this shift are 70% and 2% of the total water mass nebulized, respectively. As a result, the time required to saturate the argon stream decreased as Q_l went up and, consequently, the change in the aerosol characteristics caused by solvent evaporation was less significant. These trends can be observed in Figure 3b. It can be seen that, unlike at low liquid flow rates, the aerosol liquid volume contained in droplets with diameters close to 6 μm was similar 1 s after the aerosol generation and 2 s after the nebulization (both volumes were just a 7% different).

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The solvent evaporation rate also depends on the solution matrix. For a common matrix encountered with ICP techniques such as nitric acid, solvent evaporation is dampened mainly as a result of the low vapour pressure and the moderate density of this solution. These characteristics lead to a reduction in the value of the evaporation factor (equation 2). In fact, the corresponding evaporation factors were 1.5×10^{-2} and 1×10^{-2} $\mu m^3/ms$ for distilled water and 2 mol/l nitric acid, respectively. The drop size distribution changes for nitric acid solutions (Figure 3c) were less significant than for distilled water. Thus, 1 and 10 s after the generation of the aerosol, droplets with diameters lower than 1.4 and 2.75 μm were completely evaporated. Remember that for water, the calculations indicated that the respective diameters were 2 and 3.4 μm.

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The consequence of solvent evaporation is the disappearance of fine droplets (i.e., generation of coarse aerosols) until the coarsest droplets start to significantly decrease their diameters (i.e., the aerosols become finer) [21]. The median of the simulated volume drop size distribution (D_{50}) can be calculated from the data generated through the procedure mentioned above. For a 10 s residence time, the calculated D_{50} values are about 6 and 11 μm for water and 2 mol/l nitric acid, respectively. As regards the experimental data, measured D_{50} values for the aerosols leaving a double pass spray chamber are 3.5 and 1.5 μm for distilled water and 2 mol/l nitric, respectively. Therefore, it can be concluded that evaporation is not the most important process leading to a change in the characteristics of the aerosols leaving the spray chamber (*i.e.*, tertiary aerosols) as a function of the matrix. Other factors, such as removal of coarse droplets through impacts against the chamber walls and droplet fission by electrical repulsion, may play a key role in terms of matrix effects [22]. Besides, it is important to bear in mind that the simulation performed in the present study had some inherent approximations [14,15].

From all the above taken considerations, it can be concluded that in order to promote complete aerosol solvent evaporation inside the spray chamber, thus favouring the transport of solution towards the plasma, two factors should be born in mind: first, the mass rate of water nebulized must be lower than 20-30 mg for a 1 l/min argon stream and; second, the aerosols produced by the nebulizer must be fine enough. There are several evidences of complete solvent evaporation inside the spray chamber when very low liquid sample flow rates are used. Thus, for example, Aeschliman *et al.* [23] found that when a 2000 mg/l yttrium solution was introduced into the plasma at 20 μl/min, the initial radiation zone (IRZ) at the plasma base was located at positions far upstream with respect to the observation made at 100 μl/min. Furthermore, high speed

videos demonstrated that at 100 μl/min there were occasional distortions of the IRZ tip as a large red droplet clouds were formed. A second evidence derives from the fact that there is not solution drain when working under these circumstances.

2.2.2. Droplet coalescence

Another phenomenon taking place inside the spray chamber is droplet coagulation. Droplet recombination can occur according to three different mechanisms [21]. The existence of velocity gradients at the exit of the nebulizer, mixing of small particles entrained in the turbulent eddies, or different aerosol drop diameters, and differences in droplet acceleration, cause an intensification of droplet recombination once the aerosol is generated. Coagulation caused by differences in droplet velocity is significant mainly near the nebulizer nozzle. Note that in this area differences in droplet velocities are highly significant. According to the work performed by Liu and Montaser with a Phase Doppler Particle Sizer [12], it was shown that at 1.5 cm from the nebulizer exit the droplet velocity distributions were broader than at 11.5 cm from the nebulizer. Thus, at 1.5 cm, droplets had velocities from 10 to 65 m/s, whereas at 11.5 cm the velocities were included within the approximately 1 to 11 m/s range.

It has been claimed that, at low liquid flow rates, the transport of solution is favoured with respect to that obtained at conventional values of this parameter, because coalescence is less frequently produced than if the liquid flow rate rises [21,24,25]. According to the calculations made by Sharp [21], for a pneumatic nebulizer and at a 1.5 ml/min liquid flow rate, the number of collisions between droplets at the exit of the nebulizer (*i.e.*, in a cylinder whose diameter and length are 100 μm and 0.1 mm, respectively) is about $10^{20} s^{-1} m^{-3}$, which indicates the enormous significance of the

coalescence process. If the calculations made by Sharp are performed at liquid flow rates close to 50 μl/min, and the following data are considered: aerosol volume swept out, 7.85 x 10^{-13} m^3, time required by the droplets to go through a 0.1 mm distance from the nebulizer tip: 5 x 10^{-6} s, and droplet size: 10 μm, we find that the number of particles passing through the swept volume is *ca.* 9 and the aerosol droplet density is about 10^{13} particles/m^3. Note that the number density for a 1.5 ml/min liquid flow rate is 3 x 10^{14} particles/m^3 [21]. The number of collisions can be calculated in a different way, depending on the coagulation mechanism considered. If the coagulation is mainly produced by the existence of velocity gradients in the aerosol jet boundary, the number of collisions (N) is given by:

$$N = \frac{32}{3} n^2 \Gamma a^3 \qquad (6)$$

where *n* is the number of droplets per volume unit, Γ is the velocity gradient and *a* is the particle radius. Equation (6) indicates that the number of collisions between droplets varies with the square of the aerosol droplet density. This is also accomplished for the other two droplet coagulation mechanisms [21]. If, according to Sharp, at 1.5 ml/min the number of collisions for 10 μm droplets is 4 x 10^{19}, by lowering the liquid flow rate down to 50 μl/min, N will be approximately three orders of magnitude lower (*i.e.*, 4.4 x 10^{16}).

Coalescence has a direct effect on droplet diameters. In fact, drop size increases as a result of this phenomenon. For monodisperse aerosols, the variation of diameter with time d(t) is given by [26]:

$$d(t) = d_0 (1 + N_0 K t)^{1/3} \qquad (7)$$

where d_0 is the initial diameter, N_0 is the initial particle number density and K is the coagulation coefficient.

Equation 7 can be applied to determine the change in drop diameter with time. The results are presented in Figure 5. Two different liquid flow rates were considered: 30 μl/min (Figure 5.a) and 1 ml/min (Figure 5.b). The drop diameter was calculated by assuming that the aerosol was monodisperse within each drop size range supplied by the sizer (a system based on the Fraunhofer diffraction of a laser beam). For most cases, and as equation 7 indicates, the drop diameter increased with time as a result of droplet coagulation. The x axis scale was extended up to 10 s, which was the estimated aerosol residence time in a double pass spray chamber.

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At 30 μl/min, droplets with diameters higher than 1.9 μm did not change their diameters in a noticeable way (Figure 6.a), whereas at 1 ml/min the increase of drop size for this diameter was quite important. At this high liquid flow rate, the calculations indicated that the increase in diameter with time was noticeable even for droplets with diameters close to 5 μm. This fact was undoubtedly due to the higher initial droplet number density (N_0 in equation 7) at high rather than at low liquid flow rates.

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The above mentioned trends can be made even more obvious by taking into account the drop size variations in relative terms. Figure 6 shows the relative change in drop diameter as a function of time. The influence of coalescence was more significant for small droplets than for coarse ones. The reason for this behaviour seemed to be the higher droplet number density (N_0) for the finest droplets. The influence of the liquid flow rate can also be highlighted in this figure. For 1.41 μm droplets and at 30 μl/min, the diameter increased by a factor of just 10% with respect to the initial one (Figure 6.a). Meanwhile, for the same drop size, at 1 ml/min (Figure 6.b) coalescence resulted in an increase in the drop diameter by a factor as high as 57 % (*i.e.*, from 1.41 to 2.21 μm). To illustrate the importance of coalescence, it may be noted that a conventional pneumatic concentric nebulizer operated at 1 ml/min generates 5 times as much primary

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aerosol volume contained in droplets with diameters lower than 5 μm than a micronebulizer operated at 50 μl/min. However, the analyte transport rate is just two times higher for the former device than for the latter one. Because of the much higher aerosol droplet density at 1 ml/min, fine droplets grow through coalescence and they are removed from the aerosol stream inside the spray chamber.

The points raised above are useful for deciding whether to use a large or a small spray chamber if high sensitivities (or analyte transport efficiencies) are sought. On the one hand, solvent evaporation is more significant if the aerosol residence time inside the spray chamber is long enough. Nevertheless, on the other hand, as has been illustrated, coalescence becomes more significant as the aerosol spends more time in the chamber. What these calculations clearly demonstrate is that working at low liquid flow rates can be considered as a good approach to improve the analyte transport efficiency. These calculations can also help provide an understanding as to why decreasing the liquid flow rate by a given factor does not result in a corresponding proportional decrease in the emission signal. For example, one of the earlier studies carried out with the HEN by Olesik *et al.* [27] claimed that the HEN operated at a 50 μl/min liquid flow rate afforded limits of detection similar to those measured for a conventional pneumatic concentric nebulizer operated at a 1 ml/min sample flow rate. Further measurements of the efficiency of the analyte transport towards the plasma (ε_n) indicated that for the HEN this parameter took a value close to 60% at 10 μl/min, whereas it dropped down to 8% at 120 μl/min [28,29]. At low liquid flow rates (*c.a.*, 2 μl/min) aerosol transport efficiencies close to 90% were reported [25].

A problem that can be observed when working at low liquid flow rates derives from the poor precision and discrepancies found when measuring the aerosol transport parameters. Thus, for a MCN coupled to a cyclonic spray chamber, the solvent transport

efficiency, ε_s, at a 100 μl/min delivery liquid flow rate and a 1 l/min gas flow rate generated values close to 85% [30]. This result was different from the about 20% encountered in a different report at a 0.7 l/min gas flow rate [28]. Several reasons could be argued in order to try to explain this inconsistency. First, whereas in reference [30] an indirect method [31] was employed to measure the mass of solvent leaving the spray chamber, reference [28] used a direct method for this purpose [32]. Second, a cyclonic spray chamber was used in reference 30, whereas in reference 28 the chamber used was a double pass one. Third, provided that very low liquid flow rates are used, a change in the temperature at which these experiments were carried out strongly affects the results obtained.

2.2.3.- Signal production, plasma thermal characteristics and matrix effects

Olesik *et al*. [27] observed that the thermal conditions of the plasma were not deteriorated as the liquid flow rate decreased. Indeed, the plasma had a higher excitation capability when operating at low liquid flow rates with a HEN than in the case of a conventional pneumatic concentric nebulizer operated at conventional flow rates. This conclusion was reached after measuring the magnesium net ionic emission intensity to net atomic emission intensity ratio (MgII/MgI) [33]. An increase in this ratio indicates that the plasma increases in robustness. For the HEN operated at 50 μl/min, the MgII/MgI ratio was 7.8, whereas in the case of the pneumatic concentric nebulizer, the magnesium ratio was 4.8 at 1 ml/min. Accordingly, the argon emission intensity was also higher at low rather than at high liquid flow rates [27]. This trend cannot be considered as a rule, because if the solvent mass reaching the plasma is too low, its

thermal conductivity decreases, thus leading to a poor energy transfer to the sample and, therefore, to a deterioration of the thermal characteristics of the plasma [34].

Considerations of solvent evaporation, droplet coagulation and thermal effects of the plasma made in the preceding section can be useful to provide insight into the experimental changes in the analytical results as a function of the liquid flow rate. Thus, Ackley *et al.* [35] found that, for a MCN, the ICP-MS signal increased with liquid flow rate up to 150 μl/min and then decreased significantly beyond this liquid flow rate. These results agreed quite well with those obtained in ICP-AES, in which the signal-to-background ratio at 80 μl/min was similar to that at 160 μl/min. Similar trends have been observed for the MMN and HEN. The signals for a conventional pneumatic concentric nebulizer steeply increased with Q_l in the range 10 – 30 μl/min [28,35]. Thus, these results can be explained on the basis that, on the one hand, the aerosols generated by the micronebulizers become coarser as Q_l is increased, thus slowing down solvent evaporation and, on the other hand, because the drop number density is higher at high liquid flows, drop coalescence plays a very important role. Both effects make an increase in the liquid flow rate by a given factor to lead to a variation in the signal by a lower factor.

When working at liquid flow rates below about 100 μl/min, interferences caused by organic and inorganic concomitants have an impact different from that observed if this variable is close to 1 ml/min. Two groups can be distinguished: *(i)* inorganic matrices, comprising acids and salts, and; *(ii)* organic matrices, such as alcohols and some carboxylic acids.

For the first group of matrices, the magnitude of the matrix effect is higher at lower than conventional Q_l values [22,36]. In order to assess the extent of the non

spectroscopic interferences, the so-called relative signal (I_{rel}) can be calculated according to:

$$I_{rel} = \frac{I}{I_0} \qquad (8)$$

where I is the net emission intensity found in the presence of a given matrix and I_0 is the analytical signal measured in its absence. A value of unity in I_{rel} means that the matrix effect can be neglected.

In the case of inorganic acids, such as nitric or sulphuric acid, it has been found that at room temperature and with double pass or cyclonic spray chambers, the interferences become more severe as the liquid flow rate goes down [36,37]. Thus, for example, for a 0.9 mol/l nitric solution the ICP-AES emission intensities were 17 and 47% lower than for a plain water solution at 0.6 ml/min and 30 μl/min, respectively. These data were obtained with a MCN coupled to a double pass spray chamber. Similar results were obtained with a conventional nebulizer. Therefore, apparently the nebulizer design did not play a relevant role in terms of interferences at low liquid flow rates. The two possible sources of the interferences caused by inorganic acids in ICP-AES are the modification in the aerosol generation and/or transport processes, and the change in the thermal characteristics of the plasma [38]. The second factor can be ignored, because previous reports claim [27] the MgII/MgI ratio remains unchanged or increases as Q_l drops. Instead, the aerosol production and its transport towards the plasma appear to be responsible for the intensification of matrix effects at low Q_l. Because the primary aerosol characteristics are modified neither for nitric acid nor for sulphuric acid solutions, aerosol transport seems to be the process leading to the observed interferences [36].

When inorganic salts are a major component of the sample solution, similar trends as for inorganic acids are found [39,40]. For a double pass spray chamber and a

HEN operated at 20 μl/min, the signal in the presence of 5000 mg/l sodium was about 50% lower than the intensity obtained for a plain water solution. In contrast, when Q_l rose up to 200 μl/min, the drop in the signal caused by the presence of sodium was only of 20%. I_{rel} did not change substantially with Q_l above this value [22]. Qualitatively speaking, the signal drop factors fitted well with those for the analyte mass transported to the plasma.

A direct consequence of the results found for inorganic matrices is that when the available sample volume is the limiting factor to perform an analysis, procedures such as matrix matching, internal standardization or standard additions should be more carefully taken into account than at liquid flow rates on the order of ml/min.

Theoretically, the extent of interferences could be eliminated by favouring the aerosol transport to the plasma so as the mass of analyte delivered to it would be the same irrespectively of the sample matrix. One way to reach this goal is to heat the aerosol. This has two beneficial consequences: *(i)* the mass of solvent that can be evaporated before saturating the gas stream increases; and, *(ii)* the drop size decreases and, hence, the evaporation takes place quickly. This is partially the reason why some matrix effects can be avoided by using a desolvation system.

The matrix effects described so far are known as steady-state effects and cause a modification in the analytical signal with respect to aqueous solutions. In addition, the presence of inorganic matrices (mainly acids) leads to a change in the signal stabilization time when switching between solutions of different matrix composition. These are the so-called equilibration effects [41] or transient effects [42]. Accordingly, on switching from different concentrated nitric acid solutions, the ICP-AES and ICP-MS signals suffered from either an undershoot or an overshoot, depending on the relative change in acid concentration. Then, after a given period of time, the signals

reached steady-state values. For example, at a liquid flow rate of 40 μl/min, the time elapsed for analytical signal stabilization when switching from a 1 mol/l to a 4 mol/l nitric acid concentration was as long as 20 min [37]. The equilibration time was about 4-5 min when the liquid flow rate increased up to 0.6 ml/min. For inorganic salts, transient effects were much less pronounced than for acids. Thus, when introducing 5000 mg/l sodium matrices after running the system with distilled water, the time for signal stabilization was just 20 s longer at 50 μl/min than at 200 μl/min [22].

Unlike inorganic concomitants, when organic matrices are present in the solution the aerosol generation process is severely modified with respect to plain water solutions. For pneumatic nebulizers, the physical properties influencing the aerosol characteristics are mainly surface tension and viscosity [9]. Note that organic solvents have lower surface tension and, in some instances, lower viscosities than water [43]. As a result, finer primary aerosols are produced in the case of organic matrices [44,45]. Furthermore, the solvent evaporation inside the spray chamber is much more significant than for inorganic acids because either the organic solvent is more volatile than inorganic matrices [43] and/or finer droplets are generated for organic compounds [46]. Consequently, when an organic solvent is present in the sample, the analyte mass leaving the spray chamber per unit of time increases when compared with aqueous solutions [47] and, if the thermal characteristics of the plasma are not significantly deteriorated, higher sensitivities are obtained in ICP-AES [48].

In contrast to the situation described for inorganic species, at low liquid flow rates the extent of the interferences caused by organic solvents can be less pronounced than at conventional values of this parameter [49,50]. For a given sample introduction assembly, if the operating conditions are appropriate to allow the complete evaporation of an aqueous solution, it will also be possible to completely evaporate more volatile

samples (*e.g.*, alcoholic solutions, carboxylic acid solutions). Hence, the mass of analyte transported towards the plasma is expected to be similar, irrespective of the volatility of the solution and the characteristics of the primary aerosols. There are two factors that should be considered in order to completely evaporate an aerosol: first, the aerosol generated by the nebulizer must be fine enough and second, the liquid-to-gas volume ratio must be sufficiently low.

The former factor is very important since, as previously mentioned, only small droplets evaporate completely before exiting the spray chamber. According to the data shown in Figure 3a, for a plain water solution and a 6 s aerosol residence time inside the spray chamber, droplets with diameters lower than 3.4 μm will completely evaporate. If the nebulizer is operated at low liquid flow rates (*i.e.*, below 20 μl/min) and it generates primary aerosols with maximum diameters below 3.4 μm, the total solution will evaporate and will be transported to the plasma for both water and volatile solutions. As a result, the interference induced by a volatile organic solvent in terms of aerosol transport rate disappears.

Eliminado: Figure 3

Because the mass of solvent (or matrix) transported to the plasma is low, oxide levels in ICP-MS are much lower at low liquid flow rates than at higher ones [51], thus giving rise to higher ionization efficiencies [52,53]. ICP-MS matrix effects caused by the presence of ethanol in the solution are also mitigated at low liquid flow rates. Thus, for the analysis of undiluted wines in ICP-MS, Augagneur *et al.* [50] found that at 1 ml/min the signal for the wine sample decreased by a factor of 2 – 5 with respect to that for a plain water standard, while at 30 μl/min, the signal suppression effect disappeared. At 10 μl/min, several organic solvents and petroleum may be analyzed directly through ICP-MS with the DIHEN [54], not feasible at 50 μl/min [55].

3.- Devices used for the introduction of liquid microsamples in ICP techniques

Generally speaking, sample introduction systems used for the analysis of low liquid sample volumes in which the analytical signal is continuously registered can be classified into three different groups:

(i) a nebulizer coupled to a spray chamber;

(ii) a nebulizer coupled to a desolvation system;

(iii) a direct injection nebulizer.

The present section describes these three different possibilities.

3.1.- Micronebulizers coupled to spray chambers

Several micronebulizers have been developed to perform the analysis of microsamples (Table 2). The suitability of pneumatic concentric micronebulizers for the analysis of microsamples has been demonstrated in ICP-AES as well as in ICP-MS [53, 56,57]. Among pneumatic concentric micronebulizers we can find the MicroConcentric Nebulizer (MCN) [58] and the aforementioned HEN [27], MMN, and PFAN.

Con formato: Fuente: Sin Negrita

Eliminado: Table 2

3.1.1. High Efficiency Nebulizer (HEN)

Originally introduced in 1992 [59], the HEN is made entirely of glass (Figure 7c). Its design is similar to a Meinhard® A type pneumatic concentric nebulizer, but it has reduced critical dimensions [5660]. This fact has three important implications: first, because of the reduced inner diameter of the capillary, even clean aqueous solutions must be filtered to avoid tip blockage caused by the presence of fibres or small particles;

Eliminado: Figure 7

second, because of the low cross-sectional area of the gas exit, the gas pressure should be rather high (Table 2). This latter factor makes it necessary to use an external additional gas cylinder with the consequent requirement for using special high pressure adapters and lines for the gas stream [60]; and third, the HEN is a rather fragile device [10]. In fact the capillary of this nebulizer can be easily broken when cleaning the HEN if it is not carefully used.

Con formato: Fuente: Sin Negrita

Eliminado: Table 2

Figure 7c shows a magnified picture of the nebulizer tip whereas a top view is shown in Figure 7d. In the latter figure, it can be observed that the nebulizer capillary is not perfectly centred with respect to the nebulizer orifice. This fact could lead to problems associated with unstable aerosol generation. However, as one of the referees of the present review verified experimentally, this situation is only found when the gas is not flowing through the nebulizer. When a gas stream is introduced, the capillary is centred by the action of the argon flow.

Eliminado: Figure 7

Eliminado: Figure 7

The aerosols obtained at the exit of the spray chamber (tertiary aerosols) with the HEN are finer than those found for a conventional pneumatic concentric nebulizer. The Sauter mean diameter ($D_{3,2}$) is approximately 2 – 3 times lower for Q_l included within the 10 to 1200 μl/min range [12]. In fact, 90-95% of the aerosol volume consists of droplets finer than 8 μm [29], which are efficiently vaporized in an Ar ICP [61]. Tertiary aerosols for a HEN and a conventional pneumatic nebulizer travel at nearly the same velocity although, as for primary aerosols, the droplet velocity distribution is significantly narrower for the micronebulizer [12]. As a result, the ICP-MS and ICP-AES short-term signal precision is better for the HEN than for a conventional pneumatic concentric nebulizer [27,29,51]. A further advantage of the HEN is that, at low liquid flow rates, the tertiary aerosol droplet number density is much higher for this nebulizer than for a conventional concentric one. Thus, at 10 – 20 μl/min, this parameter is up to

about 30-fold higher for the HEN, while it is just a 25% lower than the number density for tertiary aerosols obtained with a conventional nebulizer operated at 1.2 ml/min [12]. The combination of the primary aerosol size and velocity distributions is likely the reason for this result.

As for other pneumatic nebulizers, for the HEN there is a variability of the results from one nebulizer for another. Thus, at 50 µl/min liquid flow rate and 0.7 l/min gas flow rate, the median of the primary aerosol volume drop size distribution were 2.8 and 3.9 µm for two similar HEN designs.

3.1.2. Microconcentric Nebulizer (MCN)

The MCN can be easily adapted to either double pass or cyclonic spray chambers by means of special end caps. Figure 7a shows a schematic of the MCN body and a picture of its nozzle. It consists of a polyamide narrow capillary (see Table 2) adapted to a tee shaped plastic body. The gas exit cross-sectional area is reduced at the exit of the nebulizer by means of a sapphire adapter. As can be observed from the picture shown in Figure 7a, the liquid capillary ends outside the nebulizer. This can be considered as a drawback because the aerosol is generated at the exit of the nebulizer where the gas stream has lost a fraction of its kinetic energy. Additionally, the capillary tip can become long term deteriorated and, consequently, aerosol production is degraded. In addition, the position of the polyamide capillary with respect to the nebulizer nozzle is a critical variable and small changes in it can lead to noticeable modifications in the nebulizer performance [62]. Therefore, the MCN can be considered as a rather fragile nebulizer.

Eliminado: Figure 7

Con formato: Fuente: Sin Negrita

Eliminado: Table 2

Eliminado: Figure 7

In ICP-AES, the MCN gives rise to limits of detection similar to or slightly higher than those calculated for conventional nebulizers operated at liquid flow rates more than ten times higher [63]. This nebulizer provides higher ICP-MS sensitivities than conventional pneumatic nebulizers operated at nearly the same rates. Thus, at 50 μl/min, the intensities for ion lines with the MCN are about 3 times higher than those obtained with a cross-flow nebulizer. If the delivery rates take values below 30 μl/min, the MCN still gives stable signals while the standard cross-flow does not generate any analytical signal [53]. In agreement with these results, at a given liquid and nebulizer gas flow rate, the MCN leads to higher oxide ratios (UO^+:U^+) than the cross-flow. These results owe to the higher mass of solution transported to the plasma in the case of the micronebulizer.

The MCN appears to show a high tolerance to high dissolved solids [52,53]. Thus, for samples having a salinity up to 3.5%, no blockage problems were observed [64]. However, other reports [62] indicated that the MCN became blocked when buffer solutions containing 50 mM of tris were nebulized. Because it is entirely made of rugged polymeric materials, the MCN shows high tolerance to HF. In this case, the ICP-MS signal did not change in a significant way when the acid concentration was increased from about 1% to 20% [65].

In contrast, the MCN is in some sense more sensitive to changes in the sample salt concentration than a conventional pneumatic concentric device. De Wit and Blust [64] determined the signal stability, taken as the standard deviation from a set of 10 consecutive signal replicates, for solutions containing different salt concentrations. In the case of water samples, both nebulizers provided similar stabilities. Nonetheless, even for diluted salt solutions the signal stability was significantly poorer (*i.e.*, higher standard deviations) for the MCN operated at 100 μl/min than for a conventional

pneumatic nebulizer at 1.6 ml/min. Another problem encountered when working with the MCN is the different behaviour found between two different MCNs. Thus, according to some authors, the precision [62] as well as the matrix effects [66] depend to some extent on the MCN used.

3.1.3. MicroMist nebulizer (MMN)

The MMN is a modified glass conventional concentric nebulizer [67]. The most important difference with respect to other micronebulizers, such as the MCN and the HEN, is that for the MMN the liquid capillary is recessed with respect to the nebulizer tip (Figure 7e). This fact confers to the MMN the ability to work with high salt content solutions without suffering from nebulizer tip blockage. Furthermore, the outer wall of the inner capillary is a tapered, ground glass piece. This may reduce the variability of the results found for two similar MMNs.

Eliminado: Figure 7

A problem that has been found with the MMN derives from the nebulizer to nebulizer dimensional irreproducibility. This point has been illustrated by characterizing the free liquid uptake rate for three different MMNs. Thus, according to Yanes and Miller-Ihli [68], whereas for one MMN an increase in the gas flow rate led to an initial increase and then to a drop in the free liquid uptake rate, for a second one the uptake rate did not vary significantly with Q_g. For a third MMN, a decrease in the liquid flow rate was registered as the gas flow rate increased. Not only the trends with Q_g, but also the absolute values of the liquid free uptake rate were different, depending on the MMN used. Thus, for three nominally identical nebulizers and at Q_g = 1.05 l/min, the liquid flow rates were roughly 20, 140 and 180 μl/min.

3.1.4. PFA micronebulizer (PFAN)

The PFA (tetrafluoroethylene–per-fluoroalkyl vinyl ether copolymer) micronebulizer is an HF resistant, all-Teflon concentric nebulizer design. It is also useful for the analysis of samples containing high concentrations of organic solvents and dissolved solids [69,70].

Apparently, this nebulizer is identical to a pneumatic concentric nebulizer. However, from a close inspection of the nebulizer tip, it can be observed that the liquid capillary ends inside the nebulizer (Figure 7f). The PFAN sample tubing is much more recessed than in the case of the MMN (*i.e.*, 6 mm and about 1 mm, respectively). Therefore, the aerosol generation mechanism is somewhat different from that for other concentric micronebulizers. The liquid stream emerges through this capillary and is deposited on the inner walls of the nebulizer. Simultaneously, the gas stream is accelerated as it goes along the nozzle. Therefore, the liquid and gas interaction takes place inside the nebulizer. As a result, the thickness of the liquid vein attached to the inner walls of the nebulizer decreases. This process, known as liquid prefilming, leads to a close interaction between the gas and liquid streams and promotes the production of fine droplets [71,72]. The prefilming is also produced in conventional pneumatic nebulizers although in this case the process takes place at the exit of the nebulizer [9].

Eliminado: Figure 7

The PFA nebulizer has been extensively used under free aspiration mode [23,73]. This allows the analysis of extremely diluted samples without contamination from pump tubing and, at the same time, reduces the signal noise. Unfortunately, changes in the solution viscosity can modify the liquid flow rate, thus degrading the accuracy of the results.

3.1.5. Demountable concentric nebulizers

One of the problems found with concentric micronebulizers is tip blockage that may occur when high salt content solutions, slurries or non-filtered solutions are analyzed. A remedy proposed to mitigate this problem is to use a demountable pneumatic micronebulizer. In this way, only the damaged component (*i.e.*, generally the sample capillary) instead of the entire nebulizer, needs replacement.

The Concentric Capillary Nebulizer (CCN) [74] is a demountable pneumatic concentric micronebulizer that has a stainless steel body used to adapt a PEEK tube containing the sample capillary (Figure 8). A second body is used to adapt the nebulizer to a conventional spray chamber. Finally, the system is sealed by means of a Teflon ferrule to avoid gas leakage.

Eliminado: Figure 8

Characterization of the aerosols reveals that the drop size distribution curves are multi modal (*i.e.*, several maxima are found in the distribution represented in band). According to Wang *et al.* [74], most of the droplets produced by the CCN had diameters below 10 μm. However aerosol surface mean diameters ($D_{3,2}$) included within the 7.5 to 54.9 μm range were obtained. $D_{3,2}$ values for concentric and cross flow nebulizer were about 9 and 16 μm, respectively. Under optimum conditions, tertiary aerosols for the CCN were finer and less dispersed than those found for conventional pneumatic nebulizers. Thus, for a cyclonic spray chamber CCN tertiary $D_{3,2}$ values ranged from 2.8 to 4.1 μm whereas they were 5.8 μm for a pneumatic concentric conventional nebulizer. Note that in these experiments the CCN and concentric nebulizer were operated at liquid flow rates of 50-500 μl/min and 1 ml/min, respectively. As regards the aerosol size dispersion, the CCN span took lower values than unity while for the concentric

nebulizer it was >100. The reported solvent transport efficiency for the CCN was close to 60% at 50 μl/min liquid flow rate delivery.

Another demountable concentric nebulizer (DCN) has been recently characterized [75]. The nozzle of the DCN is made from a 100 μl surgical pipette and the solution is driven to it by means of fused-silica tubing having 95 or 190 μm inner diameters. This assembly is fitted by means of a brass tee. According to O'Brien *et al.* [75], a decrease in the sample capillary inner diameter gave rise to finer primary aerosols. Thus, for the DCN equipped with a 95 μm capillary id, at a gas flow rate of 1 l/min and a liquid flow rate of 0.5 ml/min, 70% of the aerosol mass was contained in droplets with diameters less than 10 μm. The good performance of the DCN at low liquid flow rates was demonstrated by the fact that with this nebulizer operated at 85 μl/min, the ICP-MS limits of detection were from 2 to 20 times lower than those for a conventional cross-flow nebulizer obtained in a different study by the same authors [76].

3.1.6. High efficiency cross-flow micronebulizer (HECFMN)

The above mentioned micronebulizers are of the concentric type. They have several common characteristics and/or drawbacks that should be considered: *(i)* in some cases, the tolerance to dissolved solids is low, thus giving rise to irreversible tip blockage; *(ii)* some of them are fragile; *(iii)* all of them have a suction created in the sample uptake tubing that degrades the separation efficiency in techniques such as capillary electrophoresis or μ-HPLC. A cross-flow nebulizer has been adapted to work in ICP-MS at liquid flow rates in the range of 5 to 120 μl/min to overcome the drawbacks mentioned above [77]. The nebulizer body is made of PTFE whereas a

fussed silica sample capillary is used for the sample and a PEEK nozzle is employed for the argon stream (Figure 9 a). This nebulizer was made in such a way that the sample uptake capillary could be easily replaced. Furthermore, by means of a U-shaped cut performed at the end of the gas exit capillary, it was easy to achieve alignment of the capillaries in a reproducible way. Table 2 shows a comparison between the critical dimensions of the HECFMN and a conventional cross-flow nebulizer. Again, the micronebulizer had capillaries with lower inner diameters than the conventional one. The dimensions of the sample capillary have an important effect on the ICP-MS signal. Thus, it has been observed that for a given outer diameter (*i.e.*, 375 μm) lowering the inner diameter from 150 to 75 μm led to an increase in the signal by a factor of up to 2. Conversely, for an identical inner diameter, both signal and precision were slightly improved (*i.e.*, by a factor lower than 1.3) using capillaries with higher outer diameters. Capillaries having 375 μm od and 75 μm id provided the best results in terms of both sensitivity and signal RSD.

Eliminado: Figure 9

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In a comparison study, Li *et al.* [77] estimated that the HECFMN provided finer and more uniform primary aerosols than a conventional cross-flow nebulizer. This study was carried out by exposing several bands of pH paper to the aerosols produced with a diluted nitric acid solution and further observing the marks caused by the droplets. As a result, the mass of analyte delivered to the plasma per unit of time was higher (*i.e.*, HECFMN analyte transport efficiencies ranged from 23 to 100% as the liquid flow rate was varied between 100 and 5 μl/min). By comparison of the ICP-MS limits of detection for the HECFMN at 50 μl/min with those obtained for a conventional nebulizer operated at 1 ml/min, it was found that they were similar for some elements although for others they were up to 4 times lower for the former nebulizer.

3.1.7. Parallel Path Micronebulizer (PPMN)

The parallel path microcronebulizer (MiraMist®) has been used for the introduction of liquid samples in plasma spectrometry [78,79]. In this particular design, the liquid and gas streams are aligned to each other. Figure 9.b shows a scheme of the nebulizer nozzle and a picture of the PPMN. The liquid passes through the conduction channel (Figure 9.b.1) until it reaches its end. As it emerges through the sample orifice the liquid bulk remains unaltered due to surface tension until it enters into contact with the gas exit. At this moment, the gas stream transfers a fraction of its initial kinetic energy, the liquid is deformed and some droplets are produced (Figure 9.b.2).

Eliminado: Figure 9

Eliminado: Figure 9

Eliminado: Figure 9

The PPMN is made completely of Teflon and has a relatively large conduit for the sample that permits the fitting of a 350 μm od glass capillary to work at liquid flow rates on the order of several microliters per minute in CE or microLC applications. As it can be seen in Table 2, the gas back pressure is higher than that available in most plasma instruments. Therefore, it is necessary to use an extra gas line when this nebulizer is being operated. There is another parallel path micronebulizer available to work at liquid flow rates higher than 50 μl/min [78]. Due to the fact that the liquid and gas outlets are separated, this nebulizer has no suction [80]. For that reason, it is compatible with CE – ICP coupling. According to the manufacturer, the PPMN does not suffer from blockage when working with high salt content solutions or slurries.

Con formato: Fuente: Sin Negrita

Eliminado: Table 2

For the PPN, the liquid passes across a “trench” between the sample tube and the gas orifice and then to a spout that sticks out into the middle of the gas orifice. This last component is hand made. Although the trench should have an influence on the nebulization process, we did not find any published work dealing with this parameter.

A recent study reported that the position of the gas outlet on the nebulizer plays a very important role in terms of sensitivity. Thus, Yanes and Miller-Ihli [81] found that a change in the orientation of the nebulizer inside the spray chamber led to up to a two-fold increase in the ICP-MS signal. This was due to the better orientation of the aerosol cone inside the spray chamber that made the solution transport more likely. Comparison of different PPMNs provided relative signal changes as high as 100%. Therefore, not only the nebulizer orientation but also the distance between the gas and the liquid exits significantly affected the performance of the system.

3.1.8. Sonic Spray Nebulizer (SSN)

The Sonic Spray Nebulizer (SSN) [82] is a modified version of the Sonic Spray Ionization device initially used for ionizing organic compounds in LC/MS [83]. As can be seen in Figure 9c, the SSN consists of a cavity with a final orifice. The end of a 150 μm od 50 μm id silica capillary is placed in the middle of this orifice. A gas stream is introduced into the nebulizer cavity and it is accelerated as it goes through the orifice. Simultaneously, the solution is delivered to the nebulizer and reaches the end of the capillary, thus giving rise to the aerosol. At 1.0 l/min nebulizer gas flow rate and 50 μl/min delivery flow rate, the SSN is able to provide ICP-AES sensitivities from 0.5 to 1 times those obtained for a conventional concentric nebulizer operated at 800 μl/min. This fact means that with the SSN, absolute sensitivities for ICP-AES are more than five-fold improved with respect to conventional pneumatic nebulizers [84]. According to Huang *et al.* [84], this improvement was due to an increase in the nebulization efficiency.

Eliminado: Figure 9

3.1.9. Multi Micro Spray Nebulizer (MMSN)

The Multimicrospray Nebulizer (MMSN) [85] presents a way to enhance the interaction efficiency between the gas and liquid streams. This device is an improved version of the SSN. In this case, the sample solution is divided into three streams (Figure 9,d). Each one of the three capillaries employed is centred with three respective gas exit orifices. There are thus three aerosol generation points (*i.e.*, 'nebulization units') behaving like three micronebulizers. As a result, the gas energy is more efficiently employed in the aerosol generation. Indeed, it has been demonstrated that the analyte transport efficiencies and sensitivities reached by the MMSN were higher than those provided by a conventional pneumatic concentric nebulizer and a SSN. Furthermore, the sensitivities provided by the MMSN operated at liquid flow rates below 200 μl/min were higher than those reported for a conventional pneumatic concentric nebulizer operated at liquid flow rates included within the 0.5-1.5 ml/min range. The improvement factor was close to two for most of the elements tested.

Eliminado: Figure 9

3.1.10. Oscillating Capillary Nebulizer (OCN)

Strictly speaking, the Oscillating Capillary Nebulizer (OCN) [86,87] cannot be considered as a 'pure' pneumatic micronebulizer. It consists of two coaxially mounted silica capillaries. Samples travel along the central capillary (40-50 μm id, 105-150 μm od) whereas gas flows through the area left between this capillary and an external one (250 μm id, 350-510 μm od) [87]. The gas stream induces liquid capillary oscillations. A longitudinal standing wave appears along the liquid capillary, which is partially responsible for the aerosol generation. Droplets are also produced as a result of the

liquid and high velocity gas stream interaction. This device is also demountable and if damage is produced on any component, it can be easily replaced.

The OCN generates fine aerosols and it is able to work properly at liquid flow rates as low as 1 μl/min with analyte transport efficiencies approaching 100%. In an optimization study, Hoang *et al.* [87] observed that, in order to obtain fine primary aerosols, sample tubes with lower inner diameters and wall thickness were required. Interestingly, and unlike conventional nebulizers, with the OCN, aerosols leaving a single pass spray chamber were coarser than primary aerosols. According to these authors this was due to the enhanced coalescence found in the case of the OCN compared to conventional pneumatic nebulizers. The reason for this behaviour could be based on the low efficiency in removing coarse droplets presented by the spray chamber used (*i.e.*, a single pass spray design) and on the high droplet number density of the aerosols generated by the OCN.

In addition to the nebulizers described so far, there are other devices that have been used for the introduction of liquid microsamples in ICP techniques, such as the Babington, Glass Frit, Micro-ultrasonic nebulizers, the Monodisperse Dried Microparticulate Injector and the Electrospray Nebulizer. Over the last years, these nebulizers have not been subject to any important developments. The principles of operation and the results reached by these additional micronebulizers can be found in the literature [88].

3.2. Comparison of micronebulizers

As a result of their critical dimensions (Table 2), the liquid and gas interaction takes place more efficiently and finer primary aerosols are generated for the micronebulizers than for the conventional ones [28]. By examining some pneumatic concentric micronebulizers, it can be concluded that, in general, the gas back pressure follows the decreasing order: HEN>MMN>PFAN. The kinetic energy available for aerosol generation is higher for the HEN than for the remaining micronebulizers, leading to finer primary aerosols. Recalling Figure 4, it can be observed that, for given gas and liquid flow rates, the HEN generated the finest primary aerosols among the devices tested (*i.e.*, the drop size distribution curves were shifted towards the left with respect to the remaining nebulizers). Approximately 89% of the aerosol liquid volume generated by the HEN is contained in droplets with diameters less than 10 μm. This result was in full agreement with the data reported by Olesik *et al.* [27] and Liu *et al.* [29]. For the data in Figure 4, the percentage of aerosol liquid contained in droplets with diameters less than 10 μm was 93%.

The results found for the PFAN were highly interesting. It can be seen that the gas back pressure is lower than for the MMN. Therefore, the amount of kinetic energy required to produce the aerosol is higher for MMN. Nonetheless, coarser primary aerosols were reported for the MMN than for the PFAN. This result was explained by taking into account the aforementioned liquid prefilming [71,72]. The data obtained with ICP-MS are quite similar to those just discussed for ICP-AES, i.e., the sensitivities are up to four times higher for the HEN than for the remaining micronebulizers.

As regards the free liquid uptake rate (Table 3), for a 0.75 l/min gas flow rate, this parameter is 40, 290 and 160 μl/min for the HEN, MMN and PFAN micronebulizer, respectively [72]. If we compare the data for the HEN with those for the MMN or PFAN, it emerges that the narrower the nebulizer capillary, the lower the free

Con formato: Fuente: Sin Negrita

Eliminado: Table 2

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Eliminado: Figure 4

liquid uptake rate. Finally, the results for the MMN and PFAN are likely due to both the higher backpressure required for the MMN and the capillary recess in the case of the PFAN [72]. The nebulizer type also affects the value of the uptake rate (Table 3). Thus, it can be observed that the use of a cross-flow design with reduced sample capillary dimensions gives rise to a drop in the free uptake rate of liquid with respect to the remaining systems.

Comparison between the MMN and the MCN led to the conclusion that the former generates coarser droplets with subsequent loss of sensitivity. Thus, Kuczewski *et al.* [89] found that the ^{103}Rh signal for the MCN was 1.25 to 2 times higher than that obtained for the MMN. In concordance with this study Becker *et al.* [90] reported ^{230}Th limits of detection about 3 times lower for the former nebulizer than for the MMN. For other isotopes (*e.g.*, ^{237}Np, ^{238}U) similar limits of detection were obtained for both nebulizers. Interestingly, as Table 4 shows, the MO^+/M^+ values found in the literature for the different micronebulizers tested are similar irrespective of the ICP-MS instrument, liquid and gas flow rates used.

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When dealing with LC-ICP-MS coupling, the mobile phase and the liquid flow rate preclude the selection of the best micronebulizer. Thus, for example, for a mobile phase consisting of 70% (*v/v*) methanol and 29% (*v/v*) water, the MCN provided at Q_l = 200 μl/min higher limits of detection than both a MMN and a conventional pneumatic concentric nebulizer [35]. In contrast, if the mobile phase was 10% (*v/v*) methanol, the ICP-MS signal for the MCN at 100 μl/min was slightly lower than that for the MMN and about 9-fold higher than that for the conventional nebulizer. These results were accompanied by an increase in the mass of solvent (both in liquid and vapour form) transported to the plasma in the case of micronebulizers with respect to the conventional

one. According to these results, the benefits of low flow nebulizers were only achieved when low liquid flow rates (*i.e.*, below 100 µl/min) were used.

For Capillary Electrophoresis (CE), generally a small sample volume is analyzed. Therefore, the challenge for coupling CE to ICP techniques is to develop an efficient interface [91]. Several micronebulizers have been extensively used for this purpose [92,93,94].

Despite the fact that the HEN affords better analytical figures of merit, the MMN is better suited for CZE-ICP-MS coupling because, unlike the HEN, a make – up gas flow (*ca*, 0.5 l/min) in the spray chamber is not necessary [95]. Note that in this study, the HEN was directly connected to the spectrometer gas line. The MMN has also been recommended for CE-ICP-MS coupling over the MCN because of simplicity of operation and transport efficiency [96,97]. In addition, unlike the MCN, because the MMN is made entirely of glass, it is easy to detect the presence of bubbles. Finally, the MCN is more vulnerable to tip blockage caused by the crystallization of the buffer salt [96].

Additionally, the results obtained by Polec *et al.* [98] with a MCN equipped with a reduced inner diameter capillary were better in terms of analytical figures of merit (*i.e.*, lower limits of detection and higher sensitivities) than those for a conventional MCN [99] or a MMN [100]. Thus, for example, Cd ICP-MS limits of detection were 10 [98] and 180 ng/ml [99] for the modified and conventional MCN, respectively. As regards speciation of mercury, the MCN led to limits of detection similar to other CE-ICP-MS interfaces [101]. However, the long term stability exhibited by the MCN is poorer than that achievable with other nebulizers such as the MMN [**¡Error! Marcador no definido.**].

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The majority of the nebulizers used as interfaces between CZE-ICP techniques are self-aspirating systems and the separation can be degraded. Even though the MCN provides higher sensitivities and lower limits of detection, a cross-flow nebulizer affords better CZE-ICP-MS separation efficiencies for metallothioneins [62]. This arises because of the higher dead volume for the former (*c.a.*, 640 nl) than for the cross-flow nebulizer (essentially zero).

The Oscillating Capillary Nebulizer (OCN) works satisfactorily as an interface between HPLC and ICP-MS [86]. With a home made OCN equipped with a gas capillary having 250 μm id and 360 μm od, B'Hymer *et al.* [102] found that it afforded higher limits of detection than the HEN for the speciation of four organo-arsenic compounds. This was attributed to the lower sensitivity and the higher background noise showed by the former device. Nonetheless, the peak efficiencies, defined as the number of theoretical plates, were virtually the same for the two devices tested. Meanwhile, the precisions reported for the OCN were acceptable for arsenic species both in terms of peak height and area.

The results found by the OCN can be improved by modifying the dimensions of the gas capillary. With a 255 μm id and 510 μm od capillary this nebulizer provides ICP-MS sensitivities 2.5 to 3 times superior than those measured for a HEN [87]. This arises because of the improved analyte transport efficiency.

3.3. Selected Applications of pneumatic micronebulizers

Pneumatic concentric micronebulizers have been successfully applied to the determination of samples of different nature. The MCN has been used for the analysis of hair, biological samples and peptides by ICP-MS. Multielement analyses have been

performed on only 100 μl of sample with recoveries close to 100% [103]. For analysis of Certified Reference Materials of biological origin, such as bovine liver, mussel tissue and powder milk, satisfactory results were obtained using ICP-AES, although the analytical performance was degraded for elements present at levels close to the detection limit [64]. Undiluted wine samples have been analyzed by ICP-MS employing a MCN with a reduction in the matrix effects and a consequent increase in the sensitivity [50]. A method based on the coupling of a flow injection system to a High Resolution ICP-MS with the MCN acting as an interface has been particularly efficient for the analysis of geological microsamples [104]. A 10 mg silicate sample containing less than 10 μg/ml was efficiently analyzed. In some instances, the nebulizer is operated under its free aspiration mode. This is done in order to reduce to a minimum both the signal fluctuations and the likelihood of contamination of the sample by the pump Tygon tubing. Both factors are particularly needed when conducting environmental analysis on low sample volumes (*c.a.*, 1 ml) such as those obtained when dealing with Alpine snow and ice [105,106]. In ICP-MS, Barbante *et al.* [105] reported a 3-fold increase in sensitivity for the MCN operated at 40 – 80 μl/min with respect to a pneumatic concentric nebulizer at 800 μl/min.

The HEN has been used as an interface between microscale flow injection (μFI) – HPLC and ICP-MS showing the following features [107]: *(i)* limits of detection on the femtogram range; *(ii)* less sample matrix is introduced into the plasma than in continuous mode; *(iii)* its coupling to a conventional spray chamber is simple because its external dimensions are equal to those for conventional pneumatic concentric nebulizers. These facts, together with the advantages offered by μFI systems (*i.e.*, low matrix effects, reduction in the sample and carrier volume and increased sample throughput) made this coupling very interesting for speciation studies.

Other applications of the HEN include its coupling to a desolvation system for the analysis of corrosive samples [108]. At a 200 μl/min delivery flow rate, the reported analyte transport efficiency for this kind of samples is close to 50%. This value is slightly higher than that found for an Ultrasonic nebulizer (*i.e.*, 40%). The use of the HEN for the analysis of biological samples has also been reported [29,109].

Liquid Chromatography columns with internal diameters from 0.5 to 2 mm (microbore columns) have several important advantages in chromatographic applications, such as reduced consumption of mobile phase and their suitability for the analysis of microsamples. Note that the sample volume consumed when coupling to ICP-MS has been even lower than 1 μl [107]. One of the problems that can be found with microbore columns is that the analytical signal is too low, because of the poor efficiency of the sample introduction systems. This problem can be overcome by using micronebulizers. Additionally, due to their low dead volume, they contribute to achieving narrow peaks. The MCN has been used as an interface between liquid chromatography and ICP spectrometry. When coupled to an ion exchange column, the MCN can be efficiently employed to perform the determination of bromate and bromide in waters through ICP-MS [110] or to speciation studies [52,111]. Porous graphitic columns have also been used in conjunction with a MCN for the determination of boron in urine and blood plasma through ICP-AES and ICP-MS [112]. Because of the low sample consumption rates when working with micronebulizers, it is possible to work with reversed phase liquid chromatography with carbon containing mobile phases. However, this advantage can be partially hampered by the higher solvent transport efficiency exhibited by low flow nebulizers. A PFAN has been adapted to a Peltier cooled spray chamber and has been successfully used for the chiral speciation of selenium compounds [113]. The MMN has been used as an interface between HPLC

and ICP-SFMS for arsenic speciation. In order to accommodate the liquid flow through the column (*i.e.*, 1.5 ml/min) to the sample uptake of the MMN (*i.e.*, 0.2 ml/min), a solvent split at a 1 : 7.5 was used. Even under these conditions, limits of detection for the MMN were two-fold lower than those provided with a conventional pneumatic nebulizer without liquid flow splitting [114].

The Parallel Path Micronebulizer is an attractive alternative for coupling μHPLC or CE to ICP techniques [80]. Thus, with this system, Yanes and Miller-Ihli [115] successfully separated five cobalt species through μHPLC-ICP-MS. Figure 9.b shows a schematic of the manifold used by these authors. Because this is a non self-aspirating nebulizer, it can be potentially used in CE applications. As for other systems, a make-up liquid stream is still required in order to provide electrical connection.

Eliminado: Figure 9

An ideal capillary electrophoresis ICP-MS interface should fulfil three main requirements: *(i)* it must provide electrical contact for electrophoretic separations; *(ii)* it must adapt the electroosmotic flow to the flow through the nebulizer capillary; *(iii)* any laminar flow inside the CE capillary should be avoided. The suction observed for pneumatic concentric micronebulizers causes the appearance of a laminar flow through the capillary, giving rise to a loss of separation efficiency. In order to mitigate this, a make-up flow is often employed. Another solution consists of the application of a negative pressure to the inlet vial [99]. The suction effect has been further mitigated by reduction of the capillary inner diameter of the nebulizer [92,116]. CZE-ICP-MS was studied by Olesik *et al.* [117]. In their work, the CZE capillary was directly inserted into the nebulizer capillary, while grounding was accomplished by coating a portion of the nebulizer liquid conduction with silver paint. A sheathing electrolyte flow was able to eliminate the laminar flow in the electrophoresis capillary. In other work, Lu *et al.* [118] used an interface in which the nebulizer CZE capillary position could be varied and the

electrical connection was achieved with an electrolyte solution. They also improved the separation by applying a negative pressure at the sample inlet to compensate for the nebulizer suction effect. The magnitude and direction of the laminar flow can also be modified by means of a sheath electrolyte stream [119] or by using sol-gel frits placed inside the CE capillary [120,121].

The MMN has proven to be very efficient for CE-ICP-MS coupling and it has been applied to the separation of different oxidation states of long-lived actinides [**¡Error! Marcador no definido.**] and speciation of arsenic in soils [122]. With a method based on large volume sample stacking, Álvarez-Llamas *et al*. [123] speciated metallothioneins through CE-ICP-MS and observed that the use of a HEN as an interface provided limits of detection for ^{114}Cd about four times lower than when a Babington nebulizer was used.

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The MCN has been employed as an interface between separation and plasma techniques [124,125]. In CE-ICP-AES, sensitivities for the separation and determination of $Cr_2O_7^{2-}$ and Cr^{3+} and Cu^{2+} and $Cu(EDTA)^{2-}$ are higher for the MCN in comparison to a conventional pneumatic concentric nebulizer due to the higher analyte transport efficiency [126]. Furthermore, provided that the suction action of the MCN is less pronounced than that for the conventional nebulizer, the separation becomes more efficient in the first case. Note that the sample flow rate used in this study was close to 4 μl/min, and that for the make up solution about 13 and 34 μl/min for the MCN and conventional nebulizer, respectively. In general terms, the limits of detection are lower for the former nebulizer. With a modified MCN [98], the pressure in the system was regulated by the self-aspirating flow of the make up liquid. Another means used to reduce the suction effect consists of the use of a High Efficiency Cross-Flow Micronebulizer (HECFMN). Due to the configuration of this device, the suction effect

is mitigated with respect to the aforementioned micronebulizers, thus supplying good separation efficiencies [127].

A modified version of the OCN has been used as a CE-ICP-MS interface [128]. In this case, three concentric tubes, instead of two, were used. The innermost capillary drove the solution towards the nebulizer nozzle whereas the buffer solution was pumped through the space left between this capillary and the intermediate one. Finally, the nebulizer gas circulated between the outermost capillary and the intermediate one.

With pneumatic concentric micronebulizers, interferences caused by the presence of other elements can be eliminated by using capillaries with a strong cation exchanger retained on their inner surfaces. These capillaries are easily regenerated by running a concentrated acid solution through the nebulizer, the interfering cations being exchanged by protons. Thus, Riepe *et al.* [129] used a modified MCN for the determination of ^{103}Rh in the presence of interfering species. In order to achieve this study, the MCN was equipped with a silica capillary. After activation of this capillary with NaOH, the cation exchanger was fixed to the capillary. The interfering elements were retained in the capillary and just the analyte was driven towards the spectrometer. With this method, no significant differences were found between the calibration lines obtained in the presence and in the absence of the interferents.

3.4.- Low inner volume spray chambers

The design of the spray chamber has a crucial effect on the analytical performance of ICP spectrometers. According to Schaldach *et al.* [130], the spray chamber geometry is important mainly when working at low liquid flow rates. Despite its importance, relatively few reports dealing with the development of new spray

chambers useful for working at liquid flow rates, on the order of several microliters per minute, have been published. Basically, efforts have been concentrated on the reduction of the inner volume of already existing spray chamber designs so as to shorten the wash-out times [131,132,133]. The most commonly used spray chambers are depicted in Figure 10. The double pass spray chamber (Figure 10.a) is often the design taken for reference. Typically, this chamber has an inner volume of about 100 cm^3. In this case, the aerosol goes through a tube and then it is forced to modify its trajectory by 180º. When working at low liquid flow rates with this chamber, the wash-out times are too long, with subsequent drop in analytical throughput. Non-spectroscopic interferences, in turn, are severe, thus loosing in terms of analysis accuracy.

Eliminado: Figure 10

Eliminado: Figure 10

Basically, two categories of spray chambers have been proposed in order to efficiently analyze liquid microsamples: the cyclonic spray chambers (Figure 11.b) and the single pass ones (Figure 11.c). Chambers of this kind with inner volumes lower than 5 – 20 cm^3 are recommended.

Eliminado: Figure 11

Eliminado: Figure 11

3.4.1. Low inner volume cyclonic spray chamber

More than ten years ago, Hieftje *et al.* presented a low inner volume rotary spray chamber similar to the cyclonic devices [134,135]. More recently, a commercially available mini cyclonic spray chamber (called Cinnabar, Figure 11.a) has been used in conjunction with a micronebulizer [136]. This chamber typically has a 20 cm^3 inner volume instead of the approximately 40 cm^3 characterizing conventional cyclonic designs [67]. The Cinnabar is made of either glass or polyethylene. As Schaldach *et al.* concluded from the simulations performed using computational fluid dynamics [137], 'the cyclone spray chamber acts primarily like an impact chamber with regard to the

Eliminado: Figure 11

deposition behaviour of aerosol droplets, and not as a typical cyclone used in technical areas'. Therefore, in this design, the primary aerosol is tangentially introduced into the chamber. A fraction of the aerosol is then lost as it impacts the chamber walls and the remaining droplets emerge through the upper exit of the chamber.

The Cinnabar is an efficient design for removing coarse droplets. Thus, aerosols leaving the Cinnabar have similar characteristics to those obtained after using a double pass spray chamber [136]. Furthermore, the mass of analyte delivered to the plasma and, hence, the ICP-AES sensitivities and limits of detection, are also similar for both devices. Moreover, the Cinnabar exhibits important advantages over the double pass spray chamber. On the one hand, the wash out times at low liquid flow rates are about two times shorter. Thus, at 20 μl/min, this parameter was 34 s and 78 s for the Cinnabar and double pass spray chamber, respectively. On the other hand, matrix effects caused by mineral acids are less severe for the former design, thus leading to recoveries close to 100% for certified solid reference materials [22]. Unlike other cyclonic spray chambers, the position of the nebulizer inside the Cinnabar spray chamber has no significant effect on the ICP-AES analytical figures of merit.

For ICP-MS, the signals are just slightly enhanced with respect to a double pass spray chamber and the wash out times found with the Cinnabar are significantly shortened [138]. Due to its simplicity and the small dispersion arising with this spray chamber, it has been successfully applied as a CE-ICP-MS interface [139].

3.4.2. Single pass spray chambers

A system based on the use of a single pass spray chamber is the commercially available self aspirating interface developed by Prange and Schaummloffel for CE and

ICP-MS coupling [140,141]. In their studies, a modified MCN with a narrower capillary is used in order to avoid any laminar flow inside the CE capillary. Furthermore, the optimization of the nebulization and the CE is carried out independently because the interface is divided into two parts: the CE capillary and the nebulizer capillary. A make up liquid is used to provide electrical contact and to adapt the nebulizer flow rate to the electroosmotic flow. The inner volume of the single pass spray chamber is about 5 – 8 cm^3 [142,143] and, because the liquid flow rate is very low (*i.e.*, 2 – 12 μl/min), the solvent totally evaporates inside the spray chamber. As a result, this interface is considered as a total sample consumption system and there is no need for an exit drain. In a recent modification, the inner volume of the spray chamber has been decreased to 4 cm^3 and the nebulizer capillary inner diameter has been reduced [144]. At low flow rates (*ca* 0.1 μl/min) the modified interface has given rise to higher sensitivity than the older one. With this new interface, it has also been demonstrated that the signal does not change under gradient conditions. In other words, the sensitivity is not modified as the sample matrix changes, which is due to the fact that both the full sample is introduced into the plasma and the liquid flow rates used are very low.

Excellent separation efficiencies have been obtained for arsenic, selenium, tellurium and antimony [140]. In addition, this interface has been efficiently applied to the separation of metallothioneins in samples having very different matrices [145]. The application of this concept to selenopeptide mapping by capillary HPLC (*i.e.*, using columns with 300 μm id) coupled to ICP-MS has demonstrated a performance superior to the interfaces existing so far in terms of chromatographic resolution and detection limits [146]. An octopole reaction cell has been used to permit the determination of sulphur [147] and phosphorous [148] in biological samples through a CE-ICP-MS system equipped with the above mentioned interface. By using xenon or helium,

respectively as collision gases, the interferences caused at the sulphur and phosphorous masses have been mitigated.

Low inner volume single pass spray chambers provide a simplified means to transport primary aerosols towards the plasma. These designs are perfect for working at low liquid flow rates. Figure 11b shows a picture of a low inner volume (*i.e.*, 8 cm^3) single pass spray chamber. This device is operated vertically when the torch is also vertical and the nebulizer is adapted to the chamber base. The aerosol follows a direct path until it reaches the chamber exit.

Eliminado: Figure 11

If the primary aerosol is fine enough and the liquid-to-mass volume ratio is low enough, the totality of the solvent contained in the aerosol will evaporate before the droplets reach the walls of the chamber. The chamber acts, therefore, as an interface to promote solvent evaporation before the aerosol enters the plasma, instead of being used as a drop size selection system. Single pass spray chambers have been used in ICP-AES at low liquid flow rates [149]. Compared to double pass and conventional cyclonic spray chambers, single pass designs with inner volumes included within the 8 to 20 cm^3 range provide about two times higher emission intensities. This is likely due to the fact that the aerosol path inside the chamber is very simple and the inertial droplet losses are less significant, thus favouring the transport of solution towards the plasma. In contrast, single pass spray chambers can degrade the signal stability, since coarse droplets can be introduced into the plasma. The simplicity of the aerosol trajectory inside the chamber also leads to a shortening of the wash-out times. If sample throughput must be increased, the inner volume of the spray chamber can be further lowered. Nevertheless, the use of smaller spray chamber with an inner volume of *c.a.* 4 cm^3 can lead to a severe drop in the analytical signal [149,150,151]. This fact is mainly due to the aerosol losses of produced by impacts against the front chamber inner walls.

It is recognized that the spray chamber is an important source of matrix effects in ICP techniques [152]. Inorganic acids [153] and dissolved salts [154] can cause a signal depression with respect to a plain water standard. The extent of the interferences caused by these inorganic species is strongly dependent on the design of the spray chamber. Thus, for a Cinnabar spray chamber, the signal drop induced by either sulphuric or nitric acid solutions was less significant than for a double pass spray chamber. The single pass spray chambers, in turn, were able to mitigate, or even to eliminate the interferences caused by these acids [149].

The simplicity of the spray chamber and the torch configuration has made it possible to integrate both components into the so-called Torch Integrated Sample Introduction System (TISIS) [155]. Figure 12 shows a schematic of the TISIS. As can be seen in Figure 12a, two Teflon pieces are used: one to adapt the nebulizer to the base of the torch and another employed to fit the injector torch. The TISIS can be operated either in a vertical or horizontal position. The nebulizer produces the mist at low liquid flow rates inside the cavity left between the two Teflon adapters. Because the liquid-to-gas volume ratio is very low, the chamber acts as an evaporation cavity instead of working as a drop size selection device. In fact, it has been visually observed that at liquid flow rates below 20 – 30 μl/min, the spray chamber walls remain dry. Under these circumstances, there is no need for a drain. At liquid flow rates above this value, the spray chamber walls become wet and it is necessary to draw out the accumulated waste solution.

Eliminado: Figure 12

Eliminado: Figure 12

The versatility of the system allows easy modification of the inner volume of the spray chamber in order to optimize the analytical figures of merit [156]. This is achieved by adapting an easy-to-adjust polyethylene cylindrical body at the torch base. Large cavities (*c.a.*, 20 cm^3 inner volume) are preferred to obtain high sensitivities

whereas small ones (*c.a.*, 5 cm^3) provide short wash-out times. Compared to a double pass spray chamber and a Cinnabar, the TISIS ICP-AES emission intensities are enhanced up to five times [156,157]. With a low inner volume cavity, memory effects for the TISIS are less severe than those for a Cinnabar spray chamber [156,157]. Moreover, the steady-state and transient matrix effects caused by organic as well as inorganic concomitants are less severe for the TISIS than for Cinnabar and double pass spray chambers. The recoveries obtained for certified reference materials with calibration with plain water standards are close to 100% for the TISIS both in continuous [156] and discontinuous mode [158].

A modification of the TISIS has been tested for use in ICP-MS by Cairns *et al.* [159]. In their report, a make-up gas line has been adapted to the base of the TISIS cavity. In summary, the new system afforded the following advantages over a conventional sample introduction system: *(i)* a 30-fold shortening of wash out time; *(ii)* a three-fold lower signal depression caused by seawater matrices; and *(iii)* higher absolute sensitivities. A further advantage of the TISIS over other systems, such as direct injection nebulizers or direct injection high efficiency nebulizers, is the lower oxide ratios.

3.5. Desolvation systems

The main goals of a desolvation system are to decrease the plasma solvent load, on the one hand, and to increase the analyte transport efficiency on the other. In order to do this, the aerosol can be first heated (Figure 13,a), either by a conduction mechanism or a radiation one [160]. As a result, the aerosol solvent is evaporated. Then a second step can be used to remove the solvent initially evaporated from the aerosol stream.

Eliminado: Figure 13

Aerosol desolvation improves the performance of ICP spectrometers. At low liquid flow rates, Nam *et al.* [51] found that the ICP-MS limits of detection were generally lower for a desolvation system placed after a double pass spray chamber than for the spray chamber alone. This analytical parameter was not affected by the liquid flow rate in the 10 to 1200 μl/min range.

Porous [161,162] as well as non-porous [163,164] membranes have been used in ICP-AES and ICP-MS for solvent elimination. In the case of porous membranes, the solvent evaporated in the first step of the desolvation system is removed as it diffuses through the membrane pores, whereas analyte and residual droplets remain in the carrier stream. The non-porous membranes eliminate the vapour solvent as a result of their affinity for it. The solvent moves through the membrane as a consequence of the established concentration gradient across the membrane. Both membrane types require an additional dry sweep gas stream to maintain large concentration gradients.

At liquid flow rates below 100 μl/min, desolvation systems equipped with membranes provide excellent performance in ICP-AES and ICP-MS. In the so-called High Efficiency Sample Introduction System (HESIS) [165,166], a pneumatic micronebulizer is coupled to a heated single pass spray chamber. A hot argon stream is introduced longitudinally to the spray chamber. As a consequence, aerosol solvent evaporation is enhanced and analyte transport efficiencies close to 100% are obtained. A membrane dryer is finally used to remove the solvent vapour.

Two commercially available modifications of the HESIS have appeared [65]. In the so-called Aridus™ (Figure 13,b) a fluoropolymer micronebulizer is adapted to a plastic single pass spray chamber heated at about 75ºC. This chamber has an exit drain that enables the system to work at liquid flow rates up to 100 μl/min. A heated (160ºC) fluoropolymer membrane is set up at the chamber exit. A sweep argon stream is

Eliminado: Figure 13

introduced to remove the solvent vapour. Finally, a nitrogen stream can be added to the aerosol in order to enhance the energy transfer inside the plasma, thus increasing the sensitivity. However, it has been observed that this signal enhancement is due to dynamic flow effects originating in the membrane [167]. In addition, even though the use of a nitrogen make-up stream reduces oxide production, it can generate new spectral interferences. The other membrane based desolvation system is the MCN6000. It is similar to the Aridus^{TM} but it does not have an exit drain in the spray chamber. Unlike the Aridus^{TM}, the spray chamber of the MCN6000 is vertically adapted to about a 2-m desolvating microporous Teflon membrane.

With these desolvation systems, ICP-MS limits of detection are enhanced by more than one order of magnitude with respect to those indicated in the already existing ICP-MS based methods [168,169]. Under certain conditions, the Aridus^{TM} provides limits of detection even lower than an ultrasonic nebulizer equipped with a membrane desolvation system [170]. However, it has been suggested that, due to the large surface areas of the system (note that this system has an about 400 cm^3 inner volume) the memory effects should be more severe for the MCN6000 than for conventional sample introduction systems [168]. Unexpectedly, according to Ma *et al.* [171], lower wash-in and wash-out times are reported for the former systems. ICP-MS interferences caused by oxide formation are minimized by using these devices. The reported CeO^+/Ce^+ ratios for a conventional liquid sample introduction system and the Aridus^{TM} were about 3% and 0.05%, respectively [65]. Meanwhile, and with a guard electrode placed at the torch top, both systems provided similar sensitivities. Therefore, according to the work by Prohaska *et al.* [167], the only interest in using an MCN6000 was the fact that polyatomic interferences were reduced in ICP-MS with respect to a MCN. In fact, this device provided lower hydride [172] and oxide [168] formation yields than other

sample introduction systems. This feature made it possible to use the MCN6000 for such determinations as Pu isotopes in seawater [173] or arsenic in steels [174] with good precisions. As regards the long term stability of the ICP-MS signal, the MCN6000 was able to provide only a 10-15% drift over a three day period of operation [175]. The determination of ^{239}Pu and the $^{240}Pu/^{239}Pu$ isotopic ratio are problematic due to the interference caused by $^{238}UH^{+}$ and the tailing of the uranium peak. By using an Aridus^{TM}, this kind of analysis can be efficiently performed in urine samples without suffering from the problem of hydride generation [176,177]. In fact, the degree of formation of this hydride was reduced by a factor of ten with respect to a conventional liquid sample introduction system [170]. Non-spectroscopic interferences caused by the presence of organic compounds (*e.g.*, methanol) are also mitigated when using a membrane based desolvation system. This point is highly interesting for HPLC ICP-MS coupling, particularly when the mobile phase composition changes with time. This situation is often found when working with gradient elution [178].

A problem that can be observed when using membrane based desolvation systems emerges when high salt content or highly viscous solutions are introduced [179]. These analyses can cause membrane blockage and, in order to prevent it, the membrane should be rinsed after every 10 samples. Despite this, Field *et al.* [180] used the MCN6000 for the analysis of very low seawater volumes. These authors claimed that one of the advantages of this desolvation assembly was that, if the nebulizer becomes blocked, it can be removed from the system and cleaned without shutting down the plasma. Note that the MCN6000 has proven to be efficient for the analysis of samples containing suspended solid particles [168].

Apart from this drawback, when working with porous membranes and with the analyte present as a volatile species, a fraction of it may be not transported towards the

plasma and is lost as it diffuses through the membrane pores. Results supporting this phenomenon have been presented for elements such as copper [181] and selenium [178]. In the case of organo – chlorine, -bromine, or –iodine compounds, it has been observed that they are also partially lost in the membrane [11]. A potential problem of these membranes is that if the sample solution concentration is very low, the particle that remains after the solvent evaporates may be small enough to also potentially pass through the pores and be lost.

Another reported shortcoming of the MCN6000 is the appearance of signal spikes caused by the droplet formation at the nebulizer tip. In order to overcome this, the original nebulizer and spray chamber have been replaced by PFAN systems [175]. In this way, it is possible to increase the aerosol heating temperature from 75ºC to 105ºC, thus enhancing droplet evaporation. This allowed working properly at liquid flow rates on the order of 100 μl/min, whereas at higher rates (*i.e.*, 150 μl/min) signal spikes were found. From all these observations, Field and Sherrell [175] concluded that the MCN6000 worked most efficiently when the delivery liquid flow rate matched the desolvator capability. By working in this way and cleaning the system with appropriate acid solutions, the blanks and limits of detection were reduced. In fact, these authors were able to analyze up to 60 Lake Superior water samples per day containing analyte concentrations in the ppq – ppt range. Note that the wash-out times were also shortened when switching from Teflon to PFA. Thus, Regelous *et al.* [182] found that to achieve an accurate determination of protactinium, the wash solution (*i.e.*, 0.6 mol/l HCl and 0.02 mol/l HF) had to be aspirated between samples for 20 and 30 min when PFA and Teflon chambers were used, respectively.

An interesting application of the Aridus^{TM} is the determination of ultra – low traces of Ir and Pt in polar ice through ICP-SF-MS. Working under clean conditions,

Gabrielli *et al.* [183] were able to determine sub ppq concentrations of these metals in ice. This was possible because of the high sensitivity of the instrument, the low instrumental background, the low sample consumption (*i.e.*, the liquid flow rate being < 100 μl/min) and the reduction of spectral interferences. With this desolvation system, Regelous *et al.* [182] analyzed silicate rock samples with a multicollector ICP-MS and reported limits of detection for protactinium close to 200 ag/ml. Only 6 ng of Th were required to achieve a precise isotopic thorium analysis on silicate rock samples with an Aridus^{TM} followed by a multicollector ICP-MS [184]. By a precise uranium isotopic analysis, Christensen *et al.* [185] were able to find the source of uranium contamination in an area used to store high level radioactive wastes. This assembly was also applied to conduct quantitative analysis with laser ablation. The sample was ablated with the laser beam, whereas standards were introduced *via* either the Aridus^{TM} [181] or the MCN6000 [186]. By working in this way, the thermal characteristics of plasma were matched for these sample introduction methods because in both cases dry plasma conditions were achieved.

More recently, a new desolvation system has been used for the analysis of liquid samples with ICP techniques. This system, commercially available as the Apex [187,188], is based on the use of a heated cyclonic spray chamber coupled to a multiple step condensation unit. The cyclonic spray chamber is heated to a temperature ranging from 120 to 140ºC whereas the Peltier-cooled multipass condenser is set either at 5ºC or at -2ºC. A N_2 stream is added so the sensitivity is increased [189]. This system can also be equipped with a Nafion membrane to remove the solvent vapour [190]. Compared with a conventional sample introduction system with a micronebulizer operated at liquid flow rates from 50 to 70 μl/min, the APEX generated ICP-MS signals for Fe which were 4 to 6 times higher [191]. In other studies, it was claimed that the ^{226}Ra ionic

intensity improvement factor was as high as 12 [192]. Unlike other desolvation systems, no signal spikes were found when the APEX was operated long term. Wash out times were rather short (*i.e.*, about 80 seconds were required to reduce the ^{56}Fe signal to background levels) [191]. This desolvation system is recommended for applications in which HF is used such as geochemistry and semiconductor analysis [188].

A double membrane desolvation system has also been used with ICP-AES and ICP-MS. In this system, a heated (*i.e.*, 80 ºC) double pass spray chamber with a MCN is coupled to a two PTFE concentric membrane tubes having a 3.5 μm maximum pore size (70% porosity). The membranes were placed in such a way that the solvent elimination took place using two countercurrent argon flows. The solvent vapour diffused through the membrane pores and a dry aerosol was introduced into the plasma. A characterization of this assembly was done by Sung and Lim using ICP techniques for the analysis of isopropyl alcohol [193]. An increase in the sweep gas flow gave rise to a drop in the ICP emission intensity for all the elements tested, thus indicating that the analytes were likely retained on the membrane. Simultaneously, it was observed that the carbon emission decreased sharply with this gas flow rate, thus demonstrating the efficiency of the membranes to remove organic solvents.

Finally, it is worth mentioning that the use of membrane based desolvation systems are beneficial for mitigating non-spectral interferences in ICP-AES caused by inorganic acids [66,194]. Al low liquid flow rates, for matrices containing acids like hydrochloric and nitric the interferences are eliminated even for concentrated solutions. Sulphuric acid solutions show a more conspicuous matrix effect, although with this kind of desolvation system, the extent of the interference is less significant than in the case of a conventional sample introduction system [66].

3.6. Aerosol Direct Injection

The use of an aerosol transport system to interface the nebulizer with the torch has been considered as a source of problems. This is because spray chambers or desolvation systems suffer from the following drawbacks: *(i)* appearance of memory effects; *(ii)* intensification of steady-state as well as transient matrix effects; *(iii)* signal noise; *(iv)* removal of a high proportion of the analyte nebulized with subsequent loss of sensitivity, mainly when working at liquid flow rates above 20 µl/min; *(v)* waste generation and *(vi)* post-column broadening effects when separation methods are coupled to ICP techniques. Furthermore, these components represent an added complexity to the sample introduction system.

An obvious way of reducing these problems would be the removal of the aerosol transport system and the direct introduction of the primary aerosol inside the plasma. This solution was first tried by Greendfiled *et al.* in the 1960s [2] and by Fassel and co-workers twenty years ago [195,196]. These authors introduced the so–called direct injection nebulizer (DIN). The load that can be accepted by the plasma with the operating conditions currently used (*i.e.*, a power less than 1.5 kW) is usually in the range of 20 to 40 mg/min. Therefore, aerosol direct injection is perfectly adapted to work at low liquid flow rates. As a result of the introduction of primary aerosols at the plasma base, the analyte transport efficiency is virtually 100%. This fact leads to the advantage of improved absolute sensitivity with respect to conventional nebulizer – spray chamber combinations. Nonetheless, there are several constraints, such as the requirement of generating a fine enough primary aerosol and the need for a robust system in order to reduce signal noise and matrix effects.

3.6.1. Direct Injection Nebulizer (DIN)

The DIN has been extensively used in ICP-AES and ICP-MS [2]. An external ceramic/stainless tube is adapted into the torch and a narrow (*i.e.*, about 120 μm od, 60 μm id) [66] sample capillary is inserted into this ceramic body. The gas flows through the annulus left between both tubes (*i.e.*, typically 15 μm wide). In a study concerning the dimensions of the external tube, Tangen *et al.* [197] observed that, with a 0.7 mm id tube, a noisy signal was obtained, whereas the signal was stable for a 0.5 mm id one. According to these authors, the sample capillary had a tendency to vibrate when the wide tube was used, thus disturbing the nebulization process. The aerosol production can be optimized by modifying the position of the capillary end. According to Wiederin *et al.* [198] the best mist was produced when the capillary extended about 100 μm beyond the nebulizer body. The sample solution is injected into the line through a computer controlled six-port valve and delivered to the nebulizer by a gas displacement pump. The operation of this pumping system requires high pressures (*ca*, 40 - 50 bar) to reach liquid flow rates ranging from 50 to 100 μl/min. In this way, excellent signal stabilities are obtained. The gas is supplied by means of a cylinder. Due to the low gas flow rates used with this nebulizer (*ca*, 0.2-0.5 l/min) an additional ~ 0.3 l/min argon stream is introduced in order to efficiently inject the aerosol into the plasma central channel. Therefore, the total gas flow inside the plasma channel can be optimized independently of the nebulizer gas flow.

An important variable is the distance between the nebulizer and the plasma base. The DIN tip is normally placed about 1 mm below the torch central tube to produce a nebulizer nozzle – initial plasma radiation zone gap close to 4 mm. Shum *et al.* [199] studied the change in mean drop diameter versus the aerosol cone axial position. They

found that at 4 mm from the nebulizer nozzle, the aerosols produced by the DIN were generally finer than those measured just at the exit of the nebulizer.

Because of its characteristics, the DIN provides finer primary aerosols and a narrower drop size distribution than conventional pneumatic concentric nebulizers. Thus, at 0.5 l/min nebulizer gas flow rate, the Sauter mean diameters ($D_{3,2}$) were 7.1 and 12.0 μm for the DIN and the conventional nebulizer, respectively. The reason given was that because the sample capillary inner diameter and wall thickness were lower for the DIN, the liquid and gas interaction was closer, thus producing fine droplets [200]. In contrast, if a double pass spray chamber was used in conjunction with the classical nebulizer, the $D_{3,2}$ decreased down to 4.1 μm. These findings revealed that the aerosols introduced into the plasma with a DIN were coarser than those leaving a spray chamber. Spatially speaking, as for other pneumatic concentric nebulizers, for the DIN the coarsest droplets were preferentially found at the aerosol cone edges, whereas the finest ones were located at the cone centre [201].

As mentioned earlier, the DIN is a system that should be operated at low liquid flow rates. As regards the effect of this variable, Wiederin *et al.* [198] noticed that the ICP-MS signal increased linearly with Q_l and it peaked at about 120 μl/min. A dramatic decrease in the sensitivity was found above this rate, which was attributed to the increase in solvent loading or in the mean drop size. A similar trend was found in ICP-AES but the signal peaked at 160 μl/min [195].

Due to the blockage problems encountered with the DIN, several modifications were proposed, such as an increase in the sheathing gas flow rate, a decrease in the injector tube inner diameter and extension of the sample capillary 0.5 mm past the end of the metal nebulizer tip [202]. The nebulization process was degraded if the DIN was

overheated. This problem was observed by Powell *et al.* [203] when the RF power was increased above 1.3 kW.

As expected, the wash-out times with the DIN were markedly shorter than those for conventional sample introduction systems. Because the inner volume can be even lower than 1 μl [**¡Error! Marcador no definido.**], the wash-out times for mercury solutions were as short as 15 s. Note that for a classical system, this parameter extended to more than 10 min [198]. The DIN has also been used with reduced memory effects for the determination of analytes such as boron [204]. The very low dead volume of the DIN makes it suitable for flow injection analysis [202]. This feature allows steady signals to be obtained even when injecting less than 100 μl sample volumes [202,205].

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Considering matrix effects with the DIN, it has been found that because there is no spray chamber, interferences related to the aerosol transport are eliminated and, by carefully controlling the plasma thermal characteristics, the signal could be the same irrespective of the sample matrix. Indeed, experiments carried out with ICP-AES demonstrated that interferences caused by mineral acids such as hydrochloric, nitric or sulphuric were less severe for the DIN than for a MCN coupled to a double pass spray chamber [66]. This was mainly true at low liquid flow rates (*i.e.*, 5 – 10 μl/min). However, for concentrated nitric and diluted sulphuric acid solutions, there was a residual interference. The reason for this was found to be the pumping system. Note that the pressure, instead of the liquid flow, was controlled with the gas displacement pump. Therefore, an increase in the solution viscosity led to a drop in the effective liquid flow rate. As a result, the actual value of this parameter in the case of concentrated nitric acid and diluted sulphuric acid solutions was lower than that for water, which caused a signal drop. MIP-MS signals obtained with the DIN dropped when concentrated sodium solutions were analyzed [206]. Nonetheless, no nebulizer clogging was observed.

An interesting modification of the DIN developed to eliminate the mass interferences caused by YO^+ and $ArCu^+$ when determining ^{105}Pd has been reported by García *et al.* [207]. In this modified version of the direct injection nebulizer, a strong cation modifier was covalently bonded to the inner surface of a silica capillary that was finally adapted to the DIN. The sample went through the capillary with the interfering elements (*i.e.*, Cu and Y) being initially retained, permitting the Pd signal to be registered free of these interferents. The retained elements were finally eluted with a hydrochloric acid solution. Good recoveries were obtained for the analysis of car exhausts and road dust. The use of these activated silica capillaries in combination with the DIN also mitigated the interferences caused by HfO^+ for the determination of Pt [208]. With a similar approach, García-Sánchez *et al.* [209] carried out speciation of lead in rainwater samples. With a capillary containing a strong anion exchanger, the interferences caused by ClO^+ ions on ^{51}V were virtually eliminated, and two vanadium oxidation states (*i.e.*, V(IV) and V(V)) were separated [210]. This methodology presents advantages over other methods for correcting this kind of interference, such as simplicity, reduction in consumed reagents, improved precision and automation.

The hyphenation between HPLC and ICP-MS has been carried out by means of a laboratory-constructed DIN [211]. Provided the low dead volume and the absence of a spray chamber, post-column band broadening was minimized. However, the DIN could only be efficiently used under isocratic conditions, because if a gradient was applied, the signal changed as a function of the mobile phase composition [11]. The use of organic solvent solutions (*e.g.*, methanol) as mobile phases made the optimum operating conditions different with respect to those for the analysis of plain water samples. Thus, it was found that for 30% methanol – water mixtures, the optimum nebulizer gas flow

rate was 0.15 l/min and the RF power was 1.5 kW instead of 0.2 l/min and 1.3 kW for aqueous solutions [212].

Because it does not show any significant suction, the DIN is also suitable for CE – ICP coupling [213,214]. In order to accomplish this, the CE capillary was placed inside the fused silica nebulizer capillary. The make up liquid stream used to establish the continuous electrical contact was pumped through the nebulizer capillary. By doing so, the nebulization and the separation processes could be optimized separately. At liquid flow rates below 10-15 μl/min, the signal started to pulse [213,215]. Therefore, a laboratory made DIN with a lower gas exit cross-sectional area was developed [215]. It was found that by recessing the sample capillary about 1 mm with respect to the nebulizer body, the system was able to work properly within the desired liquid flow rate range. In fact, the signal increased linearly from 1 to 7 μl/min. By extending the liquid capillary 1 mm beyond the nebulizer tip, the system was suitable for work at liquid flow rates ranging from 9 to 15 μl/min.

Figure 14a shows a comparison between the ICP-AES emission intensities found for several elements with the DIN and MCN6000. The results are compared against those measured for a MCN coupled to a double pass spray chamber. The MCN provided lower intensities than the DIN, thus indicating that a fraction of the analyte was lost either in the aerosol heating chamber or in the membrane. The signal improvement factor was included within the 2.8 to 3.7 range. This result was undoubtedly due to the higher analyte transport efficiency in the case of the DIN. In fact, at the liquid flow rate tested, this parameter was about 3 times lower for the MCN than for the DIN (*i.e.*, 30% and 100%, respectively). As a result, limits of detection, calculated as 3 times the standard deviation of ten consecutive blank readings, were

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lower for the DIN than for the other two sample introduction systems evaluated (Figure 14 b).

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3.6.2. Direct Injection High Efficiency Nebulizer (DIHEN)

The use of the DIN has been restricted by both its fragility and its high cost. Furthermore, it is complicated to use and a high pressure auxiliary gas line and gas displacement pump are required. In order to mitigate these problems, a relatively low cost version of the DIN was introduced by Montaser and coworkers: the so-called Direct Injection High Efficiency Nebulizer (DIHEN) [**¡Error! Marcador no definido.**]. The DIHEN is commercially available [60] and it is entirely made of glass or quartz (Q-DIHEN). This nebulizer is similar to a HEN, but it is longer (200 mm instead of the 75 mm for the HEN) in order to be easily fitted into the torch (Figure 15 a). Generally, this nebulizer is placed 3 mm upstream of the torch central tube, at about 5 mm from the plasma base. DIHEN critical dimensions are slightly larger than those for the HEN (see Table 2). A support tube is used for the sample capillary in order to reduce the capillary damage caused by the oscillations induced by the gas stream, thus enhancing the nebulizer robustness. These oscillations were highlighted when the aerosol drop size distributions were measured, because multimodal curves were obtained. The oscillations were more obvious at low than at high gas flow rates [**¡Error! Marcador no definido.**]. Unlike the DIN, the DIHEN does not require a high pressure pumping system and for moderate liquid flow rates (*ca*, 80 µl/min) a peristaltic pump can be used. Nonetheless, this can cause severe variations in the signal with time due to the pulses [216,217], and a syringe pump is advisable when the spray chamber is removed from the sample introduction system [226]. The dead volume of the DIHEN (*i.e.*, 55 µl) is much larger

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than that for the DIN (below 1 μl). Nonetheless, by inserting a PTFE tube, the inner volume can be reduced down to 10 – 15 μl [218,219]. The early studies performed using ICP-MS with the DIHEN revealed that the optimum signals were obtained at high RF power values (*i.e.*, 1.4 - 1.5 kW) and low nebulizer gas flow rates (*i.e.*, 0.16 - 0.25 l/min). In fact, it was found that the signal increased steeply by either increasing the former variable or decreasing the latter one [**¡Error! Marcador no definido.**]. The drop in sensitivity with the nebulizer gas flow rate was attributed to the fact that the axial and radial drop size distributions became wider as Q_g went up. As a result the aerosol was more confined within the plasma central channel at low than at high liquid flow rates. Another variable influencing the performance of the DIHEN is the RF frequency. Thus, with an inductively coupled plasma time-of-flight mass spectrometer (ICP-TOFMS), the sensitivity doubled as the frequency decreased from 40 to 27 MHz [218]. The increase in the secondary discharge observed with the DIHEN at the lower frequency was also responsible for the higher background values with respect to a conventional liquid sample introduction system.

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As for conventional pneumatic nebulizers, different results were reported when two different DIHENs were compared [220]. Thus the optimum signal values were 40% (for ^{226}Ra) and 30% (for ^{238}U) different, depending on the particular DIHEN used. Not only the sensitivities, but also the optimum nebulizer gas flow rate slightly differed (*i.e.*, 0.16 and 0.18 l/min) for two DIHENs. Minnich and Montaser [221] also recognized this fact and for two DIHENs the optimum gas flow rates were 0.14 and 0.2 l/min. These differences arose due to slight changes in the sample capillary dimensions and in the gas annulus area. Langlois *et al.* [222] used four different DIHENs and found that the gas backpressures were significantly different. Thus, in order to reach a 0.3 l/min gas flow

rate, this variable took values ranging from 3.4 to 4.4 bars, depending on the particular nebulizer used.

The aerosols produced by the DIHEN are coarser than the tertiary aerosols leaving a spray chamber [223]. In fact, it has been shown that only 45% of the aerosol volume produced by the DIHEN is contained in droplets whose diameters are lower than 10 μm [224]. Studies of the measurement of the spatial distribution of aerosols generated by this nebulizer demonstrated that droplets with diameters as high as 30 μm were located at the outermost aerosol cone regions [225]. Note that these very coarse droplets are introduced into the plasma when the DIHEN is used. As a consequence, signal deteriorates and noise and matrix effects are intensified. In the aerosol cone edges, satellite droplets or aggregates were projected, which were likely produced because of the rotational movement of the aerosol [226]. Furthermore, it has been recently shown that, with this nebulizer, the radial motion of droplets leads to a dispersion of the aerosol across the torch [227]. These could be the reasons why the analytical performance was not as good as expected. In fact, only 30% of the aerosol generated by the DIHEN was introduced into the plasma central channel and hence, contributed efficiently to the analytical signal. The aerosol spread has been attributed to the large cone of the DIHEN aerosol. At 50 mm from the nebulizer tip, the aerosol cone diameter was around 30 mm [226]. Due to differences in aerosol drop size and velocity, the number of surviving droplets after the plasma observation zone was much higher for the DIHEN than for a nebulizer-spray chamber combination [227]. In fact, according to the simulation study performed by Benson *et al.* [228], a large fraction of the aerosol liquid volume (*i.e.*, that consisting of coarse droplets) persisted in the plasma at distances higher than 4 mm. This, and the presence of gas flows with velocities higher

than 50 m/s in the central channel, which accelerated the aerosol droplets, hampered the aerosol desolvation.

At a given liquid flow rate (85 μl/min), the ICP-MS limits of detection obtained with a DIHEN were similar to those encountered for a HEN coupled to a double pass spray chamber. According to McLean *et al.* [**¡Error! Marcador no definido.**], this fact demonstrated that the detrimental solvent effects did not have an appreciable influence on the plasma thermal characteristics. Becker *et al*. [220] demonstrated that the DIHEN afforded ICP-QMS sensitivities 3 to 5 times higher than those measured for a MMN coupled to a Cinnabar spray chamber. Thus, it was possible to carry out determinations of long-lived radionuclides in aqueous solutions at ng/l levels while working at liquid flow rates as low as 1 μl/min. The same authors used the DIHEN for uranium isotope ratio measurements and found the precisions of the ratios were better than those obtained with the MMN. The short term precision exhibited by the DIHEN was generally better than that found for conventional sample introduction systems using a spray chamber. This fact derived from the elimination of noise sources associated with the aerosol transport system [220]. Similar conclusions could be drawn from the studies carried out using ICP-TOF-MS by Westphal *et al.* [218]. In this case, the absolute limits of detection were found to be one order of magnitude lower than those for a conventional pneumatic concentric nebulizer coupled with a cyclonic spray chamber. With an ICP-MS equipped with a hexapole collision cell, the DIHEN provided sensitivities 2 to 9 times higher than the MMN coupled to a Cinnabar chamber, although the limits of detection were similar for both assemblies [219]. In this study, it was reported that the use of a shielded torch improved more significantly the sensitivities for the DIHEN than for the MMN. Shielding was more important when a double-focusing sector field ICP-MS was used. Thus, whereas for a MMN the shield caused an increase

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in the signal, for the DIHEN the sensitivity was lower with than without a shield [229]. The reason argued to try to explain this result was the higher solvent plasma load observed in the case of the DIHEN caused a drop in plasma temperature and electron number density. Therefore, it was concluded that the main advantage of the DIHEN was the lower sample mass consumed. Despite this, it was found that the DIHEN provided higher absolute sensitivities than either an Aridus^{TM} or a MMN coupled to a Cinnabar for two different instruments: an ICP-QMS and an ICP-SF-MS [230]. In the case of the SF-MS spectrometer equipped with a torch shield, the DIHEN provided absolute sensitivities about 7-fold higher than a PFAN [231]. The guard electrode design was further modified by McLean *et al.* [232]. In this case, the electrode was always positioned between the load coil and the torch and it was electronically switched on and off. The sensitivity found for the DIHEN with the new configuration was six-fold higher than that for the initial design. This was achieved at RF power values lower (*i.e.*, 1.1 kW) than those required in other studies (*i.e.*, 1.5 kW). In ICP-AES, the DIHEN proved to be superior to a HEN when coupled to a cyclonic spray chamber in terms of sensitivity, limits of detection and precision [223].

Because the totality of the nebulized solvent is introduced into the plasma, with the DIHEN the molecular ion intensities are significantly higher as compared with those provided by systems based on the use of a spray chamber. This is especially true for oxide ions, for which the intensities are 2 – 3 times higher for the DIHEN (see Table 4). Within the direct injection nebulizer category, the DIHEN provides higher oxide ion ratios than the DIN (Table 4). In general terms, for the DIHEN [220], the oxide ratio increased at low RF power values (*i.e.*, < 1.3 kW) and low (*i.e.*, < 0.14 l/min) and high (*i.e.*, > 0.16 l/min) gas flow rates. Under cool plasma conditions, achieved by decreasing the RF power [221], the $^{38}ArH^{+}$, $^{40}Ar^{+}$ and $^{40}Ar^{16}O^{+}$ ionization was so poor that the most

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abundant isotopes of K, Ca and Fe were successfully measured with the DIHEN [218]. However, for strong oxides (*e.g.*, CeO^+ with 8.8 eV bond strength), a huge increase in the oxide-to-ion ratio was noticed under cool plasma conditions (*i.e.*, at 0.8 kW RF power). Thus, the CeO^+/Ce^+ ratio was 4200, meaning that 99.9% of Ce was present in the oxide form [218]. In this case, and others such as V, Y, La, Tb, Ho, Th and U, the measurement should be taken either by measuring the elemental ion intensities under normal plasma conditions or by registering the oxide signals if cool plasma conditions are selected [221]. With a double focusing ICP-MS, the DIHEN afforded higher oxide ratios than a MMN (Table 4) [233]. The ThO^+/Th^+ ratio was about two times higher for the former device. The use of collision/reaction cells appears very interesting, particularly in the case of direct injection nebulizers. Thus, the oxide ratio found for CeO^+/Ce^+ with the DIHEN decreased (see Table 4) when instruments fitted with a collision cell [219] were used. For oxides with lower bond strengths (*e.g.*, YbO^+ with 3.8 eV) the respective oxide ratios were 3 and 0.4% without and with a collision cell, respectively. Compared with an Aridus^{TM}, the DIHEN provided hydride ratios (*i.e.*, UH^+/U^+) about one order of magnitude higher.

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Non-spectroscopic interferences have been found with the DIHEN when inorganic as well as organic matrices are introduced. Thus, for instance, Björn and Frech [234] reported a drop in the ICP-MS signal when sulphuric instead of nitric acid solutions were analyzed. The presence of methanol in the sample also induced a drop in the sensitivity for elements with low as well as high ionization potentials (IP). These authors underlined the importance of spatial effects. Thus, in the case of elements with low IP, for nitric acid an enhancement in the signal was found on plasma axis, whereas a drop was produced off the plasma axis with respect to plain water solutions. However, provided that finer and less dense droplets were introduced into the plasma for methanol

when compared to water, the aerosol was spread over a larger volume. Concomitantly, an on-axis signal suppression and an off-axis signal enhancement was produced as compared with water. Of course, this trend was gas flow rate dependent and, at high gas flow rates (*i.e.*, 0.5 l/min) the magnitude of the interference was less dependent on the plasma sampling zone. According to Björn and Frech, the matrix induced spatial aerosol redistribution effects were more likely for the DIHEN than for systems based on the use of a spray chamber. In fact, for a nitric acid solution, these authors encountered ICP-MS matrix effects more severe in the case of the DIHEN than for the MCN matched to a cyclonic spray chamber. In ICP-AES, it has been pointed out that for the DIHEN, attention should be paid to the thermal characteristics of the plasma. In fact, the MgII/MgI ratio for the DIHEN was lower than that for a sample introduction system that used a spray chamber [223,235]. This fact indicated that the plasma was less robust when the aerosol was directly introduced *via* the DIHEN than when a conventional liquid sample introduction system was used. This trend was confirmed in both axially and radially observed plasmas [237]. Thus, at liquid flow rates below 20-30 μl/min, satisfactory performance was observed for the DIHEN and matrix effects were mitigated with respect to the situation found at higher Q_l values [223]. This behaviour was later confirmed by O'Brien *et al.* [237]. Clearly, the interferences for the DIHEN arose from deterioration of the plasma. Under some circumstances, non-spectroscopic interferences were more remarkable for this nebulizer than for a HEN coupled to a cyclonic spray chamber. In order to increase the plasma robustness when the DIHEN was used, a small fraction of oxygen and helium was added to the outer plasma gas stream. In this way, Chirinos *et al.* found that the MgII/MgI ratios were insensitive to changes in the matrix composition [235] and, consequently, matrix effects caused by sodium were mitigated [237]. To the contrary, the addition of a molecular gas to the

plasma led to a downward shift in its position, which made nebulizer tip damage more likely.

The low nebulizer dead volumes and the absence of a spray chamber led to short wash-out times for the DIHEN, which makes it perfectly amenable for achieving fast transient analysis [218]. Compared with a double pass spray chamber, it was observed that the wash out times for mercury, boron and iodide solutions were respectively 8, 4 and 100 times shorter for the DIHEN. For example, in the case of mercury the wash-out times were 6 and 48 s for the DIHEN and for a nebulizer - spray chamber combination, respectively [236]. As transient matrix effects originate in the spray chamber, they were much less significant for the DIHEN than for a conventional system. Björn and Frech [234] reported that the time required for signal equilibration when switched from a 0.22 mol/l to a 2.22 mol/l nitric acid solution was 3.5 and 0.3 minutes for a MCN coupled to a cyclonic spray chamber and the DIHEN, respectively. This fact is also very important when attempting to increase sample throughput.

An additional theoretical advantage of the DIHEN is that volatile analytes are not preferentially transported to the plasma. In a study of the effect of the chemical form of iodine on sensitivity with an ICP-SF-MS, Langlois *et al.* [222] concluded that, if a Cinnabar spray chamber was used, the signal found when this element was present as iodomethane was 4 – 6 times higher than that measured when iodide was present as iodine. For the DIHEN, the signal was expected to be the same irrespective of the chemical form of the iodine. Nonetheless, the signal for CH_3I was from a 20 to 40% lower than that for I^-. Further experiments were conducted to verify that this problem was not due to changes in the analyte spatial distribution within the plasma, depending on its chemical form. Similar results have been obtained with different selenium species for a laboratory made direct injection nebulizer. This system has proved to be less

sensitive to changes in the selenium species volatility than others based on the use of a spray chamber or desolvation assembly [178].

As regards the drawbacks of the DIHEN, it is important to indicate that, depending on the nebulization conditions, droplets with diameters higher than 10 - 20 μm can be introduced into the plasma [223]. Moreover, the interferences caused by inorganic acids may be similar to or even more severe than those for a micronebulizer coupled to a spray chamber [234]. Due to the somewhat coarse aerosols and the high solvent plasma load, the RF power must be high (*i.e.*, about 1.5 kW) to obtain optimum analytical performance [**¡Error! Marcador no definido.**]. Furthermore, the DIHEN is costly and care should be taken in order to prevent the nebulizer tip melting, which can be easily produced due to the proximity of the nebulizer tip to the plasma [218,236] and/or the very low gas flow rate used that reduces the gas cooling action [223]. A recommendation to protect the nebulizer tip from excessive heating is to increase the intermediate gas flow up to 1.2 l/min [235]. The tip melting can be more problematic during the plasma ignition step. Therefore, it is also recommended to use high values of both the coolant and the auxiliary gas streams (*i.e.*, 20 and 4 l/min, respectively) and, once the plasma has been ignited, to decrease these variables to the values used for the signal measurement (*i.e.*, 15 and 2 l/min, respectively) [237]. All these are probably the reasons why this nebulizer is not widely used for routine analysis despite its advantages.

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Another drawback of the DIHEN is that it is prone to tip blockage because of the narrow capillary used [218]. Thus, Chirinos *et al.* [235] indicated that the DIHEN tip became clogged when a 1% sodium chloride solution was analyzed. If some organic solvents such as ethanol were nebulized at liquid flow rates from 25 to 100 μl/min, a carbon deposit was observed at the nebulizer tip [55]. This produced an asymmetric aerosol with a subsequent loss in sensitivity. This was a serious problem because the

treatment required to clean the nebulizer tip was too aggressive and after three repeated blockages and cleaning procedures, the nebulizer was virtually broken. For that reason, a new version of the DIHEN has been developed; the so – called Large Bore Direct Injection Nebulizer (LB-DIHEN) [224]. In this new design, the sample capillary and the gas annulus area have been enlarged with respect to the initial DIHEN version. As regards the effect of the nebulization conditions on the ICP-MS sensitivities, it has been found that the signal peaked at higher gas flow rates for the LB-DIHEN (*i.e.*, ~ 0.35 l/min) than for its precursor (*i.e.*, ~ 0.15 - 0.25 l/min). A similar comment can be made concerning the liquid flow rate, because the optimum value of this parameter was about 110 μl/min. Due to its dimensions, the LB-DIHEN provides coarser aerosols than the DIHEN. Thus the respective percentages of aerosol liquid volume contained in droplets smaller than 8 μm were 3 and 35%. In contrast, aerosols generated by the LB-DIHEN had lower average velocities than those produced by the DIHEN, thus increasing the analyte residence time in the plasma. In general, it can be said that the former device provided lower ICP-MS sensitivities [249] and more severe matrix effects [234] than the latter one. Furthermore, the precision reached with the LB-DIHEN was worse than that afforded by a pneumatic nebulizer coupled to a spray chamber [224]. The LB-DIHEN is suitable for the analysis of high salt content solutions [238] and slurries, and for this reason it has been applied to the analysis of biological samples [239] having a high concentration in cell agglomerations with diameters ranging from 16 to 18 μm. In order to improve the liquid and gas generation while preventing the nebulizer tip blockage, the inner diameter of the sample capillary has been reduced from 320 to 205 μm [238]. With this modification of the LB-DIHEN, good precisions and accuracies were obtained when U was determined in synthetic urine samples.

The DIHEN is a good interface between separation techniques and ICP spectrochemistry. Acon *et al.* [240] employed connections with reduced dead volume to couple the DIHEN as an interface between microbore HPLC and ICP-MS. The total dead volume of the interface was just 13 μl. With this setup, naturally occurring cobalamines were successfully separated. With the introduction of a 20 μm id and 90 μm od capillary inside the DIHEN, it has been used for micro and nano HPLC-ICP-MS coupling. Wind *et al.* [241] found that, although the sensitivities were similar for a DIHEN and a PFAN coupled to a low inner volume spray chamber, the peak resolution was much better for the former. This allowed the separation of peaks of phosphopeptide compounds which otherwise appeared together when the spray chamber was used. Furthermore, low dead volume DIHEN was demonstrated to provide better precision and to be less sensitive to changes in the mobile phase composition than the conventional sample introduction system and did not require the use of a make-up liquid stream.

Due to its characteristics, the DIHEN has also been used as a CE-ICP-MS interface. The main advantages against an interface consisting of a cross-flow nebulizer coupled to a double pass spray chamber are [242]: *(i)* the peaks are sharper and more symmetrical; and, *(ii)* provided that the amount of buffer is lower, lower background levels are obtained. An interesting application combined anodic stripping voltammetry (ASV) with ICP-MS wherein the DIHEN served as an efficient interface [243]. The ASV-ICP-MS hyphenation was very interesting for the determination of metals at sub-ppt levels with a reduction in the memory and matrix effects and an improvement in the analytical figures of merit with respect to the MCN.

The DIHEN has been applied to the direct analysis of biological samples [244]. Samples containing organic solvents have also been analyzed with this nebulizer. The

introduction of the totality of the solution nebulized into the plasma led to a deterioration of the thermal characteristics of the plasma, especially when organic solvents were present [55]. A microemulsion with Triton X-100 was prepared to carry out the analysis of gasoline samples by ID-ICP-MS in conjunction with a DIHEN [245]. This method was more appropriate and faster than the classical sample microwave-assisted digestion and subsequent analysis. Nonetheless, the inhomogeneities of the micro-emulsions were responsible for the degradation in the method precision. Finally, four times higher limits of detection were found with the DIHEN as compared with a PFAN coupled with a double pass spray chamber but operated at a liquid flow rate eight times higher (*i.e.*, 25 and 200 μl/min for the DIHEN and PFAN, respectively). Petroleum samples dissolved in xylene were also analyzed using the DIHEN by means of a segmented injection methodology [**¡Error! Marcador no definido.**]. Factorial design indicated that the optimum operating conditions for the analysis of organic solvents were different from those for the analysis of aqueous specimens. In order to reduce the problems potentially caused by the solvent plasma load and deposition of carbon at the nebulizer tip, the liquid flow rate was very low (*i.e.*, 10 μl/min). Because of the easy-to-rinse system, a signal approaching steady-state one was obtained by injecting just 20 – 50 μl sample volumes. Limits of detection were higher for organic samples than for aqueous ones, although they were comparable to those found for a DIN. With this methodology, recoveries close to 100% were obtained for spiked samples.

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Because of the fragility of the DIHEN and in order to reduce its cost, a demountable Direct Injection Nebulizer has been developed. Figure 15.b shows a schematic of the demountable direct injection high efficiency nebulizer initially used by Bendahl *et al.* [246]. The sample capillary and the nebulizer shield are adjusted by

Eliminado: Figure 15

means of a PEEK piece. In this way, if the nebulizer is melted, it is easy to replace the damaged part. Because it has mobile parts, the nebulization process can be optimized by adjusting the position of the sample capillary. The aerosol was fine and centred with the external torch tube when the capillary extended 0.1-0.2 mm beyond the nozzle surface [246,247,248]. Under these circumstances, better ICP-MS analytical figures of merit were obtained compared to the conventional DIHEN [246]. The reasons given for these results were the reduced dimensions of the demountable direct injection nebulizer with respect to the classical one (see Table 2). With the latter device, a decrease in the nebulizer flow rate yielded a rise in the ICP-MS sensitivity. However, if this variable was too low (*i.e.*, < 0.17 l/min) a drop in the signal was observed that was attributed to the generation of coarse droplets [247]. More recently, an adjustment vernier has been used in order to precisely modify the position of the liquid capillary [249]. In this case, the nebulizer dead volume is just 11 μl and it is not necessary to use any special capillary to further lower it. Comparative studies have demonstrated that the demountable DIHEN generates aerosols slightly finer than a conventional DIHEN. Since both nebulizers have similar critical dimensions, different aerosols are produced because the liquid and gas interaction takes place more efficiently with the former design. Thus, according to the work by Westphal and coworkers [249], 49% of the aerosol liquid volume was contained in droplets with diameters lower than 8 μm for the demountable DIHEN, whereas for the conventional one the corresponding percentage was 35%. Due to its optimized design, ICP-MS sensitivities obtained under optimum conditions were about 2.4 times higher for the demountable DIHEN than for the classical one. At liquid flow rates below 10 μl/min, the magnitude of the improvement in analytical figures of merit was even higher. The demountable DIHEN provided lower

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oxide ratios than the conventional one, likely due to the fineness of the aerosols produced, (see Table 4).

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The demountable DIHEN was first used as a CE-ICP-MS interface for speciation of selenium [246]. Wang and Hansen used a demountable DIN with a 1.2 µl dead volume as an interface between sequential injection preconcentration and ICP-MS [247,248]. By means of a cation exchanger bead suspension, ICP-MS interferences caused by alkaline earth and alkaline metals were virtually eliminated. In a different approach, a sequential injection scheme was designed to carry out metal determinations at ultratrace levels after preconcentration following a solvent extraction back extraction procedure [250]

3.6.3. Vulkan Direct Injection Nebulizer

A new version of direct injection nebulizer is commercially available [67] and has been recently characterized for use in ICP-AES [251]. This nebulizer is similar to the DIHEN in the sense that it is fitted to the torch by means of a special adapter and its tip it positioned at 2 – 3 mm from the plasma base. Two principal differences can be found between these direct injection nebulizer: *(i)* unlike for the DIHEN, in the case of the Vulkan DIN, the sample capillary ends 0.7 – 0.8 mm behind the nebulizer nozzle; and, *(ii)* the sample capillary is thicker for the latter design. These two modifications confer to the Vulkan DIN a higher robustness than for the DIHEN.

When operated the Vulkan DIN at a 90 µl/min delivery flow rate it has been observed that the ICP-AES signal enhances 2-3 times with respect to that found in the case of a MCN coupled to a cyclonic spray chamber. This was found for lines having E_{sum} values (*i.e.*, sum of ionization and excitation potentials) lower than 3 eV. On the

contrary, when the E_{sum} of the lines increased, the sensitivities found for the MCN were 1 to 4 times higher than those measured for the Vulkan DIN. Further studies led to the conclusion that in the case of the Vulkan the energy transfer efficiency from the induction region to the species was poor. This fact was in agreement with the observation that the plasma ionization temperature was 300 – 1100 K lower for the Vulkan DIN than for a MCN coupled to a cyclonic spray chamber. Ion number density and MgII/MgI ratios were lower for the former nebulizer. This facts led to the existence of non spectroscopic matrix effects for this direct injection nebulizer [251].

3.6.4. Reduced length torch

The two general approaches described above for the direct introduction of aerosol into the plasma pose several problems due to their high cost and fragility. A novel alternative for directly introducing very low liquid sample volumes into the plasma has been recently suggested [252,253,254,255,256,257,258,259]. This new approach consists of the modification of the torch design. Instead of using a conventional torch and an extended micronebulizer such as the DIHEN, it is possible to reduce the length of the torch so as to replace the DIHEN by a commercially available micronebulizer by simply using a PTFE adapter. In the reduced length torch, the critical dimensions (*i.e.*, the intermediate to external tube gap, the distance between the coolant gas inlet and the end of the intermediate tube and the overall torch diameter) are similar to those of a conventional design. In contrast, its length has been shortened. With this setup, the position of the nebulizer can be easily modified by moving it up or down. The new torch has, therefore, three main advantages: *(i)* a low cost conventional micronebulizer can be used to introduce the sample into the plasma; *(ii)* a nebulizer

more resistant to the work at high temperatures and less prone to tip blockage than the DIHEN can be used; and, *(iii)* a single torch can be operated for working with a spray chamber or in a direct injection mode.

Figure 15 c shows a picture of the reduced length torch and a conventional one. The distance between the external and intermediate tubes should be at least ten times the space between the two tubes in order to achieve a laminar flow. This space is usually in the range 0.7-1.0 mm, which means that a useful length of 10 mm is then sufficient. The overall torch diameter was equal to that for a conventional torch (*i.e.*, 18 mm).

So far, this system has been used in conjunction with a MMN [**¡Error! Marcador no definido.**] and it has proven to be suitable for the analysis of microsamples. Nonetheless, due to the fact that the aerosols generated by the micronebulizer used were too coarse, the sensitivities obtained were similar to those found for a micronebulizer coupled to a double pass spray chamber. Further benefits of the reduced length were the reduced ICP-AES non- spectroscopic matrix effects compared to conventional systems.

4.- Applications of microsample introduction systems

The above described systems have been applied to the analysis of samples of diverse nature. Table 6 summarizes a representative list with more than eighty applications of low sample consumption systems. The comments made at the beginning of the present review can be verified with this table. Thus the micronebulizers have been extensively used for elemental determinations in samples in which the sample size is an important factor due to several reasons (sample availability, toxicity,…). It can be verified that the sample volume consumed can be as low as several tens of nanoliters,

Eliminado: Figure 15

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but, in general terms, in most of the cases this variable is typically in the 0.1-1 ml range. In order to achieve this, either the sample is injected *via* a valve or stable pumping devices (*i.e.*, HPLC, gas displacement pumps and syringe pumps) are used. Liquid flows as low as 0.5 μl/min can be achieved.

From the list in Table 6, four large groups of samples can be found: *(i)* environmental; *(ii)* biological; *(iii)* foods; and *(iv)* radioactive analytes. Among them, the two former groups appear to have received more attention than the latter two (65% of the studies are related with these two application groups). Only a 10% of the reports deal with radioactive samples. This fact is likely due to the lack of availability of these specimens. In any case, the usefulness of a low sample consumption system for the analysis of radioactive wastes is more than justified. Note that with such a device, it is possible to carry out precise analyses requiring just 1 ml or several milligrams of sample. The situation found for foods (*i.e.*, just 11% of the studies) is due to the fact that the amount of sample is not a limiting factor.

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According to the literature, micronebulizers have been widely applied for the analysis of biological samples. It is worth mentioning that of the biological samples, those of human origin have been the subject of many studies. Almost 50% of biological samples analysed involved determinations of human fluids (mainly urine). In some instances, a low sample consumption system is used because the available sample volume or mass is very low. Nonetheless, in other cases, the analysis must be performed through the use of separation techniques (*e.g.*, capillary electrophoresis) requiring work at very low liquid flow rates to enhance analyte separation or matrix removal. Therefore, in these cases, it is compulsory to use a system able to operate efficiently at liquid flow rates on the order of several microliters per minute. Similar comments can be made in order to try to explain the high number of reports dealing with the analysis

of environmental samples using a micronebulizer with or without an additional aerosol transport device.

5.- Summary and future developments

The application of ICP-AES and ICP-MS to the analysis of small sample volumes has required the modification of the liquid sample introduction system, since several new analytical problems have to be solved.

Nebulizers aimed at working at low liquid flow rates (*i.e.*, micronebulizers) such as the HEN and PFAN are very promising and they provide better results than other systems (MCN and MMN). The results found for the former two are similar, in spite of the fact that for a given gas flow rate, the pressure applied to the argon stream is about 3 times lower. This fact could be accounted for by considering that liquid sample prefilming produced at the tip of the nebulizer promotes an enhancement in the liquid and gas interaction. An advantage of the PFAN is that it can be adapted to the spectrometer gas line, whereas a high pressure gas line should be used for the HEN. The use of some pneumatic micronebulizers is not restricted to low liquid flow rates, but also to conventional values, making it possible to apply them to routine analysis.

The incorporation of the prefilming effect into the aerosol generation mechanism is beneficial in order to achieve a closer and more efficient gas – liquid interaction. The prefilming leads to a decrease in the liquid vein thickness. Hence, it is possible to increase the nebulizer liquid capillary inner diameter without disturbing the aerosol generation process. Of course, it should be taken into account that if the capillary of the nebulizer has too large an inner diameter, memory effects will increase. Nevertheless, a

compromise id can be used, thus avoiding capillary tip blockage without increasing the severity of memory effects.

The best nebulizer characteristics also depend on the particular application. Thus, in the case of capillary electrophoresis, besides the analytical figures of merit, the suction effect is an important issue. Apart from using other devices, such as the highly efficient cross-flow micronebulizer or the parallel path micronebulizer, the suction can be mitigated by lowering the velocity of the gas stream at the liquid – gas interaction point. In this way, the pressure drop responsible for solution aspiration would decrease. This could be achieved by recessing the nebulizer sample capillary. In the case of the PFAN nebulizer, the end of the liquid capillary is located 7 mm from the nebulizer tip. Apparently, this recess is not sufficient to eliminate the solution suction effect (Table 3).

In general terms, low inner volume spray chambers provide better analytical figures of merit than conventional devices. With a spray chamber, several aspects can be improved: *(i)* the sensitivities; *(ii)* the memory effects; *(iii)* matrix effects. In this field, the operating conditions together with simple chamber designs facilitate solvent evaporation. Therefore, the chamber role switches from a droplet selection device to an evaporation cavity, allowing the transfer of the totality of the analyte to the plasma. Single pass spray chambers are a good example of the evolution of the aerosol transport device towards evaporation cavities. With this kind of device, it is possible to analyze several tens of nanoliters of radioactive samples with good analytical figures of merit [260].

The use of a desolvation system improves the sensitivity and can reduce the extent of the matrix effect with respect to a conventional sample introduction apparatus, although in general terms memory effects are enhanced. Indeed, according to studies found in the literature, these devices are used when extremely low limits of detection

are required for elements suffering from serious ICP-MS polyatomic interferences caused by the solvent.

In the authors' opinion, there is a current trend towards total consumption systems that do not use any aerosol transport device [261]. The latest studies performed with a demountable DIHEN have been very promising. Better results are expected to be obtained with a nebulizer having reduced dimensions and liquid flow rates on the order of several nl/min [249]. In fact, theoretically, a device close to the ideal one would be a robust direct injection nebulizer able to provide micrometric or sub-micrometric droplets.

After exposing all the points treated in the present review a question still remains: what would be the ideal low sample consumption introduction system? The answer to this question is not obvious. However, it is possible to make a selection of the best micronebulizer and aerosol transport device for a given application. In order to try to illustrate this, a couple of schemes have been included in Figure 16. According to these two flow charts, the points that should be considered to select the nebulization device are whether the sample contains suspended or dissolved solids or if it contains hydrofluoric acid. The presence of organic solvents, in turn, would preclude the selection of the aerosol transport device.

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Table 1. Available sample volumes for various metal determinations.*

Types of analysis	Available sample volume, mass or flow rate	Analytes
Cells	20 μl	Na, Mg, K, Fe, Cu, Zn, Cd, Se
Suspended nanoparticles	100 μl	Fe
Brain	1 mg	Fe, Ca, K
Metalloproteins	50 μl	Fe, Cu, Zn
Dust	5 mg	B, Mg, Si, Mn, Sr, Zn
CE Speciation	nl/min	As, Se, Fe, Cr

* Taken from ref. [7]

Table 2

Dimensions of pneumatic nebulizers used for working with low (below 100 – 200 μl/min range) liquid flow rates. Comparison with conventional nebulizers.

Nebulizer	Gas exit cross-sectional area (mm^2)	Liquid capillary inner diameter (μm)	Liquid capillary wall thickness (μm)	Gas back pressure at 1 l/min argon (psig)	Nebulizer dead volume (μl)
Conventional nebulizers (optimum for liquid flow rates ~ 0.5 – 1.0 ml/min)					
Concentric nebulizer	~ 0.028	400	60	30-40	~100
Cross-flow nebulizer	0.02	500	200	30-40	
Parallel path nebulizer (conventional flow rates)	0.03	425	-----	30-40	
Micronebulizers (suitable for liquid flor rates < 100 – 200 μl/min)					
High Efficiency Nebulizer (HEN) [12]	0.007 - 0.008	80 - 100	30	150	
MicroMist (MMN) [28]	0.018	140	50	50	
PFA Nebulizer [72] (PFAN)	0.021	270		40	
Microconcentric Nebulizer (MCN) [28]	0.017	100	30	50	0.64
Parallel path micronebulizer (low flows) [78]	~0.015	75	--	90-110	
Sonic Spray Nebulizer [82]	0.019	150	50	72	
Oscillating Capillary Nebulizer [102]	------	50	50	120-200	
Demountable concentric nebulizer DCN [75]	0.032	95	50		
Direct Injection Nebulizer (DIN) [65]		60	30	45/70*	<1, 2 pl [107]
Direct Injection High Efficiency	0.0094	104	20	155	10-55

Nebulizer (DIHEN) [**¡Error! Marcador no definido.**]					
Large Bore Direct Injection High Efficiency Nebulizer [224] (LB-DIHEN)	0.0371	318	16	36	
Demountable DIHEN [246]	0.005	40	5-10	70[#]	1.2
Demountable DIHEN [249]	0.008	100	21	20[#]	11

*Pressures required to reach 0.25 and 0.6 l/min gas flow rates, respectively.

[#] Gas flow rate 0.2 l/min.

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Table 3

Values of the free aspiration uptake rate for different nebulizers.*

Nebulizer	Free aspiration uptake rate (μl/min) / Gas flow rate (l/min) [Reference]
HEN	40/0.75[72]
MMN	290/0.75[72]
	150/0.75[68] 230/0.75[68]
MMN	290/0.75[72]
	150/0.75[68] 230/0.75[68]
MCN	28/0.8[62]
PFAN	160/0.75[72]
HECFMN	8.9/1.0[77]
Mira Mist	0/1.0[78]
OCN	5/0.7[121]
Laboratory made DIN	10/0.2 [246]
Conventional concentric	1100/0.75[72]
Conventional cross flow	1930/1.0[77]

* Elestroosmotic flow in CE is on the order of 1 μl/min

Table 4

Comparison between the oxide ion ratio (MO^+/M^+) obtained for several micronebulizers with ICP-MS.*

Nebulizer	Q_l (μl/min)	Q_g (l/min)	Oxide ion ratio (%)		
			CeO^+/Ce^+	BaO^+/Ba^+	UO^+/U^+
HEN/double pass spray chamber [51]	85	1	1.3	0.06	
HECFMN/double pass spray chamber [77]	70	0.9	3.3	0.8	
MCN/double pass spray chamber [53]	50	0.9			0.016
MCN/double pass spray chamber [99]	100	0.9	0.7		
MMN/Cinnabar spray chamber [220]				3.1	
Conventional Cross-flow nebulizer / double pass spray chamber [99,220]	700	0.9	0.9		2.7
MCN6000 [168]	100	0.93	0.01	0.0008	
MCN and double membrane desolvator [193]	110	1.5	0.05		
DIN [202]	75	1	8		
DIHEN [**¡Error! Marcador no definido.**,220]	85	0.25	48	1.1	5.1
DIHEN with hexapole collision cell [219]	60	0.18	20		
DIHEN [249]	85	0.18	7.6		
DIHEN DF-ICP-MS [233]	85	0.18			No torch shielding: 10.4 Torch shielding: 28.3
Micromist DF-ICP-MS [233]	85	1.067			No torch shielding: 4.0 Torch shielding:

MMN DF-ICP-MS [233]	85	1.067		15.0 No torch shielding: 4.0 Torch shielding: 15.0
Demountable DIHEN [249]	85	0.16	3.8	

*Unless otherwise stated, the results are obtained with an ICP quadrupole MS with neither collision nor reaction cell.

Table 5

Limits of detection obtained in CE-ICP-MS using different nebulizers as interfaces.

Reference	Nebulizer used for the interface	Element	Limit of detection (ng/ml)
[101]	MCN	Hg(II)	170
		CH_3-Hg	80
		C_2H_5-Hg	100
[118]	Concentric	^{57}Fe	2500
		^{114}Cd	55
[99]	MCN	^{114}Cd	110
		^{66}Zn	470
[262]	Concentric nebulizer	^{114}Cd	2360
	Cross-flow nebulizer	^{114}Cd	210
[263]	Ultrasonic nebulizer	As(III)	84
		DMA	158
		As(V)	95
		Se(IV)	606
		Se(VI)	2080
[96]	MCN & MicroMist	As(III)	2.1
		MMA	1.6
		DMA	1.7
		As(V)	1.3
[213]	Direct Injection Nebulizer	As(III)	0.1
		As(V)	0.02
		Se(IV)	0.3
		Se(VI)	0.1
		Cd^{2+}	0.06
[125]	MCN &	CH_3-Hg	13.6
		Hg^{2+}	6.0
	Cross-flow	CH_3-Hg	149
		Hg^{2+}	112
[123]	HEN	^{114}Cd	454
	Babington	^{114}Cd	104
[147]	Modified MCN coupled to a single pass spray chamber (ICP-MS with octopole reaction cell)	^{32}S	3.2
		^{34}S	1.3
		^{56}Fe	0.4
		^{114}Cd	0.4

Table 6

Some applications of widely employed low sample consumption systems.

Sample introduction system	Application/Technique	Comments	Reference
MCN + Single pass spray chamber	Selenium speciation in selenized yeast / size exclusion chromatography and capillary zone electrophoresis – ICP-QMS	Five selenium compounds were baseline separated with LODs within the 7 to 18 ng/l range with a 20 nl injection.	[143]
MCN + double pass spray chamber	Rh in particulate car exhaust fumes / ICP-QMS	The injected volume was 2.5 μl and the nebulizer was operated at 50 μL/min.	[129]
MCN + double pass spray chamber	Mercury speciation in contact lenses solutions / CE – ICP-MS		[101]
MCN + cyclonic spray chamber	Mercury speciation in biological certified materials / CZE – ICP-QMS	170 nl of solution was injected into the system yielding LODs of 13.6 and 6.0 ng/ml for CH_3Hg^+ and Hg^{2+}, respectively	[125]
MCN	Main matrix elements and trace elements in plant reference samples / ICP-AES		[63]
MCN + double pass spray chamber	Rare earth elements in wine / ICP-MS	Multielement determinations were carried out by consuming just 100 μl of sample at a liquid flow rate of 30 μL/min	[50]
MCN + double pass spray chamber	Rh, Pd and Pt in snow and ice / ICP-DFMS	The LODs were 0.02, 0.08 and 0.008 pg/g for Rh, Pd and Pt, respectively whereas the sample consumption volume was only 40 – 80 μl/min.	[105]
MCN + double pass spray chamber	Trace elements in snow and ice / ICP-DFMS	All the procedures had to be carried out under ultra clean conditions	[106]
MCN	Total sulphur in soils, sediments, waters and a meteorite / ID ICP-SFMS	Sulphur is oxidized to sulphate. The determined concentrations were from 5.25 μg/g to 2% and the	[104]

		required sample size was just 13-40 mg.	
MCN + double pass spray chamber	Metals in milk powder (BCR CRM 63), bovine liver (BCR CRM 185) and mussel tissue (BCR CRM 278) / ICP-AES	At 100 μl/min liquid flow rate, the LODs were within the 0.13 to 174 μg/l range.	[64]
MCN + double pass spray chamber	Metals in polymers / ICP-QMS	The polymer samples were received as methanol solutions and the analysis was possible with the consumption of just 90 μl of sample.	[264]
MCN	Cd and Zn in mouse and rabbit liver proteins / CZE – ICP-QMS	The number of peaks appeared on the electropherogram depended on the Cd:Zn concentration ratio	[265]
MCN + double pass spray chamber	Multi-element analysis in hair (NIES No. 5) and peptides	Analyses were carried out continuously with a sample consumption always lower than 100 μl.	[103]
MCN / MMN + Cinnabar spray chamber	Thorium and Uranium isotope ratio measurement in radioactive wastes / ICP-QMS	For a concentration close to 1 μg/l, the precision of isotope ratio measurement was even lower than 1%. The time required for an analysis was just 3 min and the consumed sample volume was about 0.3 ml.	[**¡Error! Marcador no definido.**]
MCN	Bromate in drinking waters / Flow Injection ICP-QMS	With an anion exchanger and at 140 μl/min the LOD was 0.13 μg/l (injected volume: 500 μl) the sample throughput was high (6 h^{-1}) and the precision was good (RSD < 2%).	[110]
MCN + double pass spray chamber	Simultaneous speciation of two selenium and arsenic species in spiked groundwater / IC – ICP-QMS	At a liquid flow rate of 100 μl/min, the LODs were 1 and 4 ng/ml for As and Se, respectively.	[52]
MMN + Cinnabar spray chamber	Separation of plutonium oxidation states in natural groundwater samples / CE – ICP-QMS	Pu (VI) concentrations as low as 10^{-5} mol/l were easily detected	[**¡Error! Marcador no definido.**]
HEN	Cd, Cu and Zn speciation metallothioneins in eel liver cytosols / CE – ICP-QMS		[123]
HEN + double pass spray chamber	Trace elements in oyster tissue (NIST SRM 1566) bovine liver (NIST SRM 1577a) and		[29] ICP-AES

	orchard leaves (NIST SRM 1571) / ICP-AES and ICP-QMS		[109] ICP-QMS
HEN + double pass spray chamber	Ni, Zn, V, Ba and Pb in certified ground water (NIST SRM 1643 c) / ICP-QMS	At a 85 μl/min liquid flow rate good concordance between measured and certified concentrations were found	[51]
MMN + cyclonic spray chamber	Arsenic speciation in soils / CE- ICP-SFMS and High Performance ionic chromatography (HPIC) – ICP-SFMS	HPIC and CE allowed for the separation of 5 and 6 arsenic species, respectively. For HPIC, LODs were in the 0.04-0.08 ng/g range, whereas for CE they were 100 times higher.	[122]
PFAN + Peltier cooled spray chamber	Absolute configuration of selenomethionine in Antarctic krill / Reversed phase HPLC-ICP- QMS	The enantiomers of selenomethionine were derivatized into diastereomeric isoindole compounds. The achieved LOD for Se was 4 μg/l.	[113]
PFAN + Double pass spray chamber	Phosphorous in yeast lipid extracts / HPLC ICP-QMS	Spray chamber cooling was used for removal of interference. The absolute LODs for the different compounds ranged from 0.21 to 1.2 ng. The injected sample volume was 2 μl and seven different compounds were baseline resolved.	[266]
PFAN + Teflon spray chamber	Phosphorylation degree of α and β-caseins / ICP-QMS with dynamic reaction cell	The method can be used for determinations in the 10 to 1000 fmol/μl concentration range.	[73]
MM + Cinnabar	Iodide in food samples / ID ICP-MS	The short wash out times allow for the determination of I in food samples without the need for adding oxidizing agents. The isotope dilution technique was applied by measuring the ^{129}I intensity.	[138]
MM / HEN + double pass spray chamber	Cadmium and zinc speciation in rabbit liver metallothioneins / CE – ICP-QMS and CE – ICP-DFMS	For the MM, the LOD obtained for each Cd isoform was 2 pg.	[95]
DCN + double pass or cyclonic spray chamber	Trace elements in water (NIST SRM 1643c) and spinach (NIST SRM 1570) / ICP-QMS	Recoveries close to 100% were found for all the elements tested except for Zn	[75]
Single pass spray	Sulphur in metalloproteins from bream liver /	Limits of detection were 1.3 μg/l and 3.2 μg/l for ^{32}S	[147]

chamber	CE – ICP-QMS with an octopole reaction cell	and ^{34}S, respectively.	
Single pass spray chamber	Phosphorous in enzymatically digested calf thymus DNA / CE and HPLC - ICP-QMS with an octopole reaction cell	The four monophosphorylated deoxynucleotides present in the DNA chain were successfully resolved. Absolute limits of detection for P were 0.6 pg and 0.03 ng with CE and HPLC, respectively.	[148]
Single pass spray chamber	Determination of the $^{235}U/^{238}U$ ratio in urine and ^{242}Pu in water / nano-flow injection – ICP-SFMS	At a 7 μl/min liquid flow rate 54 nl samples were analyzed. Plutonium was determined at the sub-femtomolar level.	[260]
Single pass spray chamber	Selenopeptide mapping in a selenium containing protein / Reversed-Phase HPLC – ICP-QMS with and without collision cell	The liquid flow rate ranged from 0.5 to 7.5 μl/min and just 200 nl of sample was injected. LODs were about 200 fg Se. Resolution was sharply increased with respect to conventional HPLC-ICP-MS	[146]
Single pass spray chamber	Metallothioneins in human brain cytosols / CZE – ICP-SFMS		[145]
MCN6000	Rear earth elements in marine particulate matter / ICP-SFMS	Detection limits were 1-40 ppq which, when combined with the low liquid flow rate (100 μl/min) yielded 1-20 fg absolute LODs.	[168]
MCN6000	Arsenic in steel / ICP-QMS	The background equivalent concentration was 25 times lower than for a conventional sample introduction system. At 60 μl/min the limit of quantification was 0.12 μg/g.	[174]
MCN6000	P, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Y, Mo, Cd, Re, Tl and Pb in lake waters / ICP-SFMS	Elements were detected at levels below 1 ppb or ppt (Re).	[175]
MCN6000	^{239}Pu and ^{240}Pu in seawater / Sequential injection ICP-SFMS	3-10 l of sample were preconcentrated to 7 ml thus affording LODs of 0.64 and 0.19 fg/ml for ^{239}Pu and ^{240}Pu, respectively.	[173]
MCN6000	V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Cd and Pb in seawater samples	This analysis was carried out using only 50 μl of sample without suffering from the interferences usually present in this kind of sample	[180]

MCN6000 / MCN	Al, Sc, Ti, V, Cr, Mn, Fe, Ni, Co, Cu, As, Ag, Pt, Au, Pb in human milk / ICP-SFMS		[167]
MCN6000	Isotopic analysis of uranium in tree bark / ICP-QMS	Very low ^{238}U limits of detection (0.004 ng/l) and good $^{235}U/^{238}U$ precisions (0.4-3.1% RSD) were achieved by operating the system at 80 µl/min	[171]
Aridus^{TM}	Protactinium in silicate rock / Multicollector ICP-MS	A few tens of femtograms of Pa are sufficient to yield good precisions and accuracies	[182]
Aridus^{TM} / MMN	Anionic and cationic arsenic compounds in freshwater fish / HPLC ICP-SFMS	Conventional HPLC (1.5 ml/min) was coupled to a micronebulizer system by applying a 1:7.5 splitting factor. 100 µl of sample was injected.	[114]
Aridus^{TM}	Determination of uranium isotope ratios in groundwater samples / Multicollector ICP-MS	The radioactive contamination sources are unequivocally detected	[185]
Aridus^{TM}	Ir and Pt / preconcentration ICP-SFMS	Limits of detection achieved were 0.02 ppg and 0.08 ppq for Ir and Pt, respectively.	[183]
Aridus^{TM}	Mo isotope composition / Multicollector ICP-MS	Mo isotope variations can be determined to a precision of 0.2 ‰	[267]
Aridus^{TM}	Fe isotopic composition / Multicollector ICP-MS	The isotopic composition of Fe can be measured with a precision of 0.2 (parts per 10000)	[268]
Aridus^{TM}/DIN	Drug substances containing chlorine, bromine and iodine / Revered phase HPLC ICP-MS	DIN was less sensitive to analyte structure than the Aridus^{TM}	[11]
Aridus^{TM}	Uranium isotopic ratios in geological samples / Multicollector ICP-MS	A precise $^{234}U/^{238}U$ analysis was carried out with 200 ng of sample. The precision (2 σ) of the isotopic measurements was 0.8 ‰	[269]
Aridus^{TM}	Uranium and plutonium in soils / ICP-SFMS	By working at a 100 µl/min liquid flow rate, limits of detection were 0.2 pg/l and 0.04 pg/g for uranium and plutonium, respectively	[177]
Aridus^{TM}	Si isotope ratios in silica, diatomite and sponges / Multicollector ICP-MS	Variations in the $^{28}Si/^{29}Si$ are determined with precisions better than 0.1 ‰. This procedure requires	[169]

		only 3 μg Si.	
Aridus™	$^{236}U/^{238}U$ ratios in uranium minerals / ICP-SFMS	With a 100 μl/min sample consumption rate, the uranium isotope ratio was measured down to the level of 10^{-7}.	[170]
Aridus™ with a PFAN	^{239}Pu in urine / ICP-SFMS	For a sample with a Pu concentration as low as 7.6 pg/l, the error with respect to the expected value was lower than 2%.	[176]
Aridus™/ MMN/ DIHEN	$^{236}U/^{238}U$ isotope ratio in soil simples / ICP – QMS with an hexapole reaction cell, ICP – SFMS and Multicollector ICP-MS	These experiments can be carried out with uranium levels as low as fg/g	[230]
Aridus™	Thorium isotopic measurements in volcanic rocks / Multicollector ICP-MS	A liquid flow rate moderately low (*i.e.*, 0.5 ml/min) was used.	[184]
Demountable DIN	Nickel and bismuth in sediments / preconcentration lab-on-valve ICP-MS	With a 2.0 ml sample volume consumed, the LODs obtained were 15 and 4 ng/l for Ni and Bi, respectively.	[247]
DIHEN / MMN	Uranium, thorium and plutonium isotope ratios in radioactive wastes and uranium isotope ratios in soils / ICP-QMS	The $^{240}Pu/^{239}Pu$ ratio was measured for concentrations as low as 12 ng/L.	[220]
DIHEN / MM	Concentration and isotope ratios for long-lived radionuclides in radioactive wastes	Polyatomic interferences were removed by extracting the analytes (*e.g.*, U, Th and ^{99}Tc) through a liquid extractant or by means of a solid exchanger	[229]
DIHEN / MMN	Concentration and isotope ratios for long-lived radionuclides in radioactive wastes	Polyatomic interferences were removed by extracting the analytes (*e.g.*, U, Th and ^{99}Tc) through a liquid extractant or by means of a solid exchanger	[229]
DIHEN	Sn and Cr isotopes in human lung fibroblast cells/ ICP-TOF MS	Precise isotope ratios can be obtained by measuring simultaneously fast (12.75 ms) transient signals for several isotopes	[218]
Demountable DIN	Selenium speciation in human urine samples / ion pairing ICP- Quadrupole MS	Four identified selenium compounds and an unidentified one were separated and detected working at 50 μl/min and injecting 3 μl of sample.	[212]

Demountable DIN/ MMN + cyclonic spray chamber	Selenium speciation in human urine samples / reversed phase, ion pairing LC- and CE-ICP- Quadrupole MS	Two selenium metabolites were identified at 50 μl/min and injecting 3 μl of sample.	[214]
DIN	Boron in undigested blood plasma and urine samples /isotope dilution ICP-Quadrupole MS	The total sample volume required was 1 ml and the injected volume was 50 μl. 94% of the carbon was removed by protein precipitation.	[204]
MCN 6000 /DIN / MCN + cyclonic spray chamber	Enriched ^{77}Se yeast samples / Reversed Phase LC – ICP-Quadrupole MS	More than 30 selenium containing compounds were separated by consuming just 3 μl of sample and working at a 50 μl/min liquid flow rate.	[178]
dDIHEN / DIHEN	Trace metals in urine samples / ICP-QMS	No nebulizer clogging was observed for 1:5 diluted urine samples and good recoveries are achieved	[218]
LB-DIHEN	Trace metals in herbal extracts / ICP-QMS	The sample volume required was 20 μl. A standard additions methodology was applied.	[224]
DIHEN	Cd^{2+} in seawater samples / Anodic stripping voltammetry – ICP-QMS	The obtained concentration (26 ± 4 ppt) was in accord with the actual one (25 ± 3 ppt).	[243]
DIHEN / MMN	Long lived radionuclides in radioactive wastes / ICP-DFMS	With a 20 μl of waste sample it was possible to determine ^{237}Np concentrations as low as 10 ng/l with good precision (*i.e.*, RSD 2.0%, n=5).	[229]
Demountable DIHEN	Ni and Bi in river sediments (CRM 320) and urine samples	Matrix elimination and analyte preconcentration were carried out by means of a 'lab-on-valve' methodology. The aspirated sample volume of 2.0 ml was reduced to 60 μl through the preconcentration step. Limits of detection were on the order of ng/l.	[247]
Demountable DIHEN	Cd and Pb in urine samples / Sequential injection ICP-QMS	Matrix was removed and the analytes preconcentrated by means of a suspension of PTE beads. 3 ml of sample were aspirated and the retained analyte was eluted with 40 μl of a nitric acid solution. The LODs were 2.9 and 6.0 ng/l for Cd and Pb, respectively.	[248]
DIHEN	^{31}P in a phosphopeptide mixture and ^{127}I in a synthetic tryoxine / micro- and nano-LC-ICP-	Eleven phosphorous compounds were separated and detected by injecting 5 μl of sample the liquid flow	[241]

	SFMS	rate being just 4 μl/min. Absolute LOD for ^{127}I was 40 fmol.	
DIHEN	Hg in freeze-dried urine (NIST SRM 2670), I and B in bovine muscle (NIST SRM 8414), Hg and I in seahorse genital tonic pills and B in rodent liver samples / Flow injection ICP-QMS	Good recoveries were found for the determination of these memory prone elements	[236]
DIHEN	Na, Mg, K, Ca, Fe , Mg in homeopathic nerve tonic tablets / ICP-QMS under cool conditions	Unlike under normal conditions, when operated under cool conditions, the background levels were low enough to allow the precise analysis of these kinds of samples.	[221]
DIHEN	^{56}Fe, ^{52}Cr, ^{59}Co, ^{64}Cu, ^{208}Pb, ^{27}Al, ^{55}Mn, ^{65}Zn, ^{108}Ag, ^{88}Sr in silicon wafer surfaces / ICP-QMS with hexapole collision cell	A 100 μl drop scanned the sample surface and dissolved the contaminants. It was then diluted to 2 ml and analyzed by the method of standard additions. The analytes surface concentration range was 0.49 to 6.5 * 10^9 atoms / cm^{-2}.	[219]
DIHEN	Sn and Cr in human fibroblast cells / ICP-TOFMS	Only 10 μl of sample allowed for a precise determination of isotopic ratios.	[218]
DIHEN	Cr bound to human lung DNA / microscale flow inyection analysis (μFIA) ICP-QMS	Using a 20 μl injection loop, the achieved LOD was 980 fg/injection	[**¡Error! Marcador no definido.**]
DIN	Ba, Cu, Pb and Zn in undigested honey samples / ID ICP-QMS	A 50 μl diluted sample aliquot was injected into the system and results were in good agreement with those obtained with a conventional digestion based method	[205]
DIN	Lead speciation in rainwater / ICP-QMS	At a 40 μl/min delivery liquid flow rate, limits of detection for inorganic lead and triethyllead were 90 and 200 ng/l, respectively.	[209]
DIN / MCN	Palladium in road dust and car exhaust fumes / ICP-QMS	The injected sample volume ranged from 1.5 to 5 μl, the Pd concentration being on the order of 20 μg/l.	[207]
DIN	Chromium speciation in freeze dried urine	The injected volume was 2.5 μl and the liquid flow	[211]

(NIST SRM 2670) / HPLC – ICP-QMS rate was 100 μl/min.

Figures and Captions

Figure 1

Schematic of different pneumatic aerosol generation principles. (a) Concentric nebulizer; (b) cross-flow nebulizer.

Figure 2

Variation of the aerosol surface mean diameter ($D_{3,2}$) with the liquid flow rate (Q_l) for three different pneumatic nebulizers: conventional concentric nebulizer type A (A), conventional concentric nebulizer type K (B) and micromist (C). Nebulizer gas flow rate, Q_g: 0.8 l/min.

Figure 3

Simulation of the evolution of the drop size distribution with time caused by solvent evaporation. (a) Distilled water Q_l = 30 μl/min; (b) distilled water Q_l = 1000 μl/min; (c) 2 mol/l nitric acid Q_l = 30 μl/min. Q_g = 0.7 l/min. Dotted line: primary aerosol distribution; continuous line: simulated aerosol distribution 1 second after the aerosol generation; grey line: aerosol distribution 6 seconds after the aerosol production for (a) and (c) and 2 seconds after the aerosol generation for (b). Nebulizer: PFA. All calculations have been performed at 25ºC.

Figure 4

Drop size distributions for different pneumatic micronebulizers. (1) High Efficiency Nebulizer, HEN; (2) PFA micronebulizer; (3) MicroMist. Q_g = 0.75 l/min; Q_l = 300 μl/min.

Figure 5

Change in the drop diameter with time caused by droplet coagulation for several initial droplet diameters at 30 μl/min (a) and 1 ml/min (b). Nebulizer: PFA. Gas flow rate: 0.7 l/min. Initial drop diameters, in μm: (A) 1.41; (B) 1.64; (C) 1.9; (D) 2.95.

Figure 6

Relative change of the drop diameter caused by coalescence versus time for the data presented in Figure 5.

Con formato: Fuente: Sin Negrita

Eliminado: Figure 5

Figure 7

Different pneumatic micronebulizers. (a) Microconcentric Nebulizer, MCN; (b) High Efficiency Nebulizer, HEN; (c) detailed top view of the HEN nozzle; (d) Micromist, MM; (e) PFA nebulizer.

Figure 8

Schematic of the concentric capillary nebulizer (CCN). Taken from ref. 74 with permission.

Figure 9

Schematic of the high efficiency cross-flow micronebulizer, HECFMN, reprinted with permission from ref. 77, © 2001 American Chemical Society (a); Burgener parallel path micronebulizer, PPMN, Mira Mist (b); Sonic Spray Nebulizer, SSN (c); Multi Micro Spray Nebulizer, MMSN (d).

Figure 10

Spray chambers used for the analysis of microsamples coupled with ICP techniques. (A) double pass; (B) cyclonic; (C) single pass.

Figure 11

Pictures of two low inner volume spray chambers. (a) cyclonic spray chamber (Cinnabar); (b) single pass spray chamber;

Figure 12

Schematic of the Torch Integrated Sample Introduction System (TISIS). Design and dimensions of the TISIS. (a) different components of the TISIS; (b) complete mounted system. (1) nebulizer; (2) evaporation cavity and aerosol; (3) PTFE adapter for the nebulizer; (4) drain exit; (5) PTFE adapter for the injector; (6) plasma injector; (7) torch main body; (8) plasma. Taken from reference 155.

Figure 13

(a) Two step desolvation system. (1) nebulizer; (2) spray chamber; (3) thermocouple; (4) source; (5) drain; (6) Liebig condenser. (b) schematic of the Aridus^{TM} desolvation assembly.

Figure 14

ICP-AES emission signal (a) and limits of detection (b) measured for three different sample introduction systems. Liquid flow rate: 55 μl/min. Black bars: direct injection nebulizer, nebulizer gas flow rate: 0.25 l/min; White bars: MCN6000, aerosol heating temperature: 70ºC, membrane temperature: 160ºC, nebulizer gas flow rate: 0.87 l/min; Grey bars: MCN coupled to a double pass spray chamber, nebulizer gas flow rate: 0.7 l/min.

Figure 15

Layout of the direct injection high efficiency nebulizer, DIHEN (a) scheme of a demountable DIHEN taken from ref. 249 with permission (b) and reduced length torch (c).

Figure 16

Flow chart illustrating how to select a micronebulizer and an aerosol transport device to carry out a given application.

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