Article

Arsenic Determination in Pharmaceutical Grade Barium Sulfate using Direct Solid Sampling Electrothermal Atomic Absorption Spectrometry

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Um método para determinação de arsênio em $BaSO_4$ por espectrometria de absorção atômica com aquecimento eletrotérmico e introdução de amostras sólidas (SoS-ET AAS) é descrito. Foram avaliados dois sistemas de correção de fundo (BG), deutério e efeito Zeeman (Z). Com o uso combinado de hidrogênio e Pd o BG foi diminuído. Resultados exatos e precisos foram obtidos usando Z-SoS-ET AAS. O desvio padrão relativo usando Z-SoS-ET AAS foi menor que 9,5%. O limite de detecção foi 0,005 µg g^{-1} e a massa característica foi 25,4 pg. Os resultados foram comparados com os obtidos usando o método de preparo de amostras sugerido pela Farmacopeia Europeia, com determinação usando espectrometria de emissão ótica e espectrometria de massas, ambos com plasma indutivamente acoplado, porém os resultados foram cerca de 20% menores. Vantagens como simplicidade, elevada frequência de determinações e boa exatidão foram obtidos em comparação com o método descrito na farmacopeia.

A method for arsenic determination in pharmaceutical grade $BaSO_4$ by solid sampling electrothermal atomic absorption spectrometry (SoS-ET AAS) is described. Two background (BG) correction systems, deuterium and Zeeman-effect (Z), were evaluated. Background was decreased by using hydrogen combined with Pd. Accurate and precise results were obtained using Z-SoS-ET AAS. Relative standard deviation using Z-SoS-ET AAS was lower than 9.5%. Limit of detection was 0.005 µg g^{-1} and characteristic mass was 25.4 pg. Results were also compared with those obtained using the preparation method suggested by European Pharmacopoeia for $BaSO_4$ followed by determination using inductively coupled plasma optical emission spectrometry and inductively coupled plasma mass spectrometry. Results were around 20% lower than results obtained using the proposed method. Some advantages as simplicity, higher sample throughput were found when compared with the official method currently described in pharmacopoeia.

Keywords: arsenic determination, solid sampling, barium sulfate, electrothermal atomic absorption spectrometry, pharmaceutical analysis

Introduction

Barium sulfate is a raw material widely used in pharmaceutical industry for production of suspensions for radiographic templates. In view of presence of some elements in $BaSO_4$, specially those classified as heavy metals by official pharmacopoeias, their routine control in pharmaceutical industry is mandatory in many countries.[1,2]

Arsenic is one of the most relevant elements in view of its toxicology potential.[3-5] This element is classified as a class "I" human carcinogen by World Health Organization and it has been associated with skin, lung, bladder, kidney, and liver cancers.[6] Therefore, As is included in routine analysis of limit test for heavy metals, for example, in the United States and European Pharmacopoeias.[1,2] The recommended method in pharmacopoeias for heavy metals determination is the classical reaction with thioacetamide or hydrogen sulfide in weakly acidic medium. The test should be also suitable for the determination of arsenic, but consistent results could be achieved only for relatively high As concentrations.[1,2]

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According to pharmacopoeical recommendations the limit test for heavy metals should be performed by extraction in open vessels with diluted acid solution before the reaction with sulfide.[1,2] However, this procedure is prone to several drawbacks as (*i*) risks of contamination and analyte losses; (*ii*) limit test is not specific for As, but gives only general information based on color appearance for a group of elements; (*iii*) lack of accuracy and sensitivity; (*iv*) time consuming, and (*v*) use of unstable reagents.

In addition to the general limit test, European Pharmacopoeia recommends two specific tests for arsenic in $BaSO_4$, based on the reaction with potassium iodine or arsine generation after a laborious sample preparation step.[2] In this case, the maximum As content has been set as 2 $\mu g\ g^{-1}$ for pharmaceutical grade $BaSO_4$. This test also presents some limitations as: only qualitative information is supplied, subjective interpretation is needed and high contamination risks. Furthermore, in the specific case of $BaSO_4$, this substance is practically insoluble in water and also in mineral acids making conventional wet chemistry digestion a laborious procedure.

On the other hand, electrothermal atomic absorption spectrometry (ET AAS) is a well established technique for As determination in several kinds of samples.[7,8] The conventional application of this technique involves sample digestion steps, usually ashing or acid digestion, which are time consuming and prone to contamination or analyte losses.[9] However, direct solid sampling electrothermal atomic absorption spectrometry (SoS-ET AAS) has been proposed as an alternative to the conventional methods of analysis where problems related to unsuitable limits of detection (LOD) or difficulties of sample digestion are present.[9,10] This technique has been also applied for trace element determination at low levels in a wide variety of samples.[9-15] Some advantages has been cited for SoS-ET AAS as reduced sample pretreatment and hence increased sample throughput, low contamination risk (an essential requirement when trace levels of metals must be determined), lower risks of analyte losses during the sample pretreatment, and the use of corrosive and hazardous chemicals is avoided.[9,16]

The use of SoS-ET AAS for As determination at low levels in $BaSO_4$ could present advantages over the techniques based on wet analysis, considering the matrix chemical characteristics described elsewhere. However, the sulfate matrix is often a source of interferences in ET AAS. Depending on the analyte and temperature parameters, sulfate may cause both spectral and chemical interferences.[17] Moreover, the presence of relatively low amounts of alkaline and alkaline earth metal sulfates can cause high background (BG) signals.[18-20] Thermal

decomposition of sulfates often produces compounds that cause structured or broad-band unspecific BG signals over a wide spectral range. Instruments equipped with deuterium (D_2) BG correction systems are commonly used in routine and research laboratories. However, some errors have been reported when using deuterium systems and BG correction based on Zeeman-effect (Z) has been more successfully applied for complex matrices analysis.[21] With the application of chemical modifiers and careful adjustment of temperature parameters in some specific cases deuterium BG correction could be successfully used, providing performance similar to Zeeman-effect based systems.[21-23] On the other hand, hydrogen addition shows to be effective to reduce the BG[24] or to improve the performance of Pd as chemical modifier[25] making feasible the analysis by ET AAS.

In the literature only one study was found related to As determination in a similar matrix used in the present work.[26] Authors demonstrated the feasibility of D_2-SoS-ET AAS for trace element analysis in barytes (a mineral basically constituted by $BaSO_4$). They found also that concentrated nitric acid could be used as chemical modifier for As determination. However, in spite of good results found for other elements, some figures of merit for As (accuracy, LOD and sample mass interval) were not presented. Moreover, calibration was performed using solid reference materials having different matrix composition (soil or sediments).

Based on these considerations, in this work a comparison of the performance for two instruments equipped with deuterium or Zeeman-effect BG correction systems was performed in order to develop a method for As determination in pharmaceutical grade $BaSO_4$ by SoS-ET AAS. Operational parameters were evaluated in order to achieve feasible calibration using aqueous standards. The influence of palladium combined with hydrogen addition during pyrolysis step was also investigated. Spiked samples were used to check the accuracy. However, no certified reference material with similar composition for $BaSO_4$ is available and results were compared with those obtained by inductively coupled plasma optical emission spectrometry (ICP OES) and inductively coupled plasma mass spectrometry (ICP-MS) after the extraction procedure described in European Pharmacopoeia.

Experimental

Instrumentation and operating conditions

Arsenic determination was carried out using a Model AAS 5 EA atomic absorption spectrometer equipped with a deuterium BG correction system (Analytik Jena, Jena,

Germany) and a Model AAS ZEEnit 60 atomic absorption spectrometer (Analytik Jena) equipped with Zeeman-effect BG correction system. Both equipments used transversely heated graphite heating and hollow cathode lamps for arsenic (8 mA, wavelength 193.7 nm, spectral bandpass 0.8 nm). Spectrometers were equipped with a special device for manual direct introduction of solid samples into the graphite furnace (Models SSA-5 and SSA-6Z for D_2- and Z-SoS-ET AAS, respectively, Analytik Jena). Pyrolytic coated graphite tubes (Part Nr. 407-A81.011 and 407-152.023, for D_2- and Z-SoS-ET AAS, respectively, Analytik Jena) were used throughout. Integrated absorbance was used for signal evaluation with an integration time of 10 s. Argon 99.996% of purity (White Martins-Praxair, SP, Brazil) was used for SoS-ET AAS measurements and also for ICP-MS and ICP OES determinations. Hydrogen (99.999%, White Martins-Praxair) was used during pyrolysis step for the determinations by ET AAS. A Model M2P microbalance (Sartorius, Göttingen, Germany) with a resolution of 1 μg was used for weighing the samples. The heating program for arsenic determination is in Table 1.

Table 1. Graphite furnace heating program for arsenic determination in barium sulfate by Z-SoS-ET AAS

	T / °C	Ramp / (°C s⁻¹)	time / s	Inert gas / (L min⁻¹)	Hydrogen / (L min⁻¹)
Drying 1	110	15	30	2	-
Drying 2	120	15	15	2	-
Pyrolysis	1300	400	20	2	0.5
Auto zero	1300	0	6	-	-
Atomization	2200	3000	10	-	-
Clean out	2600	3000	4	2	-

For the comparison of results sample digestion (extraction) was performed in glass vessels using a water bath according to the procedure described in 5th edition of European Pharmacopoeia (HNO_3 digestion).[2] Extracts were analyzed by the semi-quantitative recommended procedure by arsine generation and also by ICP OES and ICP-MS.

Determinations by ICP OES were performed using a Model Optima 4300 DV inductively coupled plasma optical emission spectrometer (Perkin Elmer, Shelton, USA), equipped with a cyclonic spray chamber (Glass Expansion, Inc., West Melbourne, Australia), a pneumatic nebulizer GemCone-type, and an alumina injector tube (2 mm i.d.). The operating conditions were: radiofrequency power of 1.4 kW, principal plasma gas flow rate of 15 L min⁻¹, nebulizer gas flow rate of 0.6 L min⁻¹ and auxiliary gas flow rate of 0.2 L min⁻¹. Selected spectral line was 188.979 nm and peak area was used for signal acquisition using three

points per peak and two points for BG correction. All measurements were carried out using plasma axial view.

Determinations by ICP-MS were performed using an inductively coupled plasma mass spectrometer (PerkinElmer Sciex, Model Elan DRC II, Thornhill, Canada), equipped with a concentric nebulizer (Meinhard Associates, Golden, USA), a cyclonic spray chamber (Glass Expansion, Inc., West Melbourne, Australia) and a quartz torch with a quartz injector tube (2 mm i.d.). Instrumental performance optimization, including nebulizer gas flow rate, ion lens voltage and torch alignment, was carried out following the instructions of the manufacturer. The operating conditions were: radiofrequency power of 1.3. kW, main plasma gas flow rate of 15 L min⁻¹, auxiliary gas flow rate of 1.2 L min⁻¹, and nebulizer gas flow rate of 1.12 L min⁻¹. Single ion monitoring at *m/z* 75 was used.

Samples and reagents

Powdered pharmaceutical grade $BaSO_4$ samples (purity higher than 97.5%) were purchased from pharmaceutical industries (samples "A" to "E") and they were previously dried using a conventional oven (105 °C by 2 h). The particle size distribution of $BaSO_4$ samples were checked by optical microscopy. Sample "A" was used for initial tests and adjustment of the heating program by ET AAS. Distilled and deionized water was further purified using a Milli-Q system (Millipore Corp., Bedford, USA). Reference solutions were daily prepared by serial dilution of stock As solutions (1 g L⁻¹ As in 2% HNO_3). Concentrated nitric acid used for sample digestion/extraction was doubly distilled in a sub-boiling system (Milestone, Model duoPUR 2.01 E, Bergamo, Italy). All reagents were of analytical grade (Merck, Darmstadt, Germany).

Procedures

For the proposed procedure by SoS-ET AAS test samples of barium sulfate were weighted directly on the graphite platform and transferred to the graphite tube using a manual device for solid introduction. In order to adjust the temperature parameters for As determination by SoS-ET AAS with deuterium and Zeeman-effect BG correction systems, pyrolysis and atomization curves were established with temperatures ranging from 900 to 1700 °C and from 1800 to 2500 °C, respectively. For Z-SoS-ET AAS only 2-field mode was used (field strength 0.8 T). The effectiveness of Pd (5 μg), hydrogen addition (0.5 L min⁻¹) during pyrolysis step as chemical modifiers and also the combination of both were evaluated. The chemical modifier amount was established according to literature data.[27]

Modifier solution was added directly on the solid sample after weighing on the graphite platform. In addition, the investigation of the optimum sample mass range for As determination was performed using a method similar to the described by Belarra *et al.*[28] Blanks were evaluated by simulating the same individual steps (weighing, transport, and modifier addition) using an empty platform. Arsenic reference solutions were prepared by serial dilution with water of 1000 mg mL^{-1} sodium arsenate stock solution (Merck, Catalog number 1.09939). Recovery tests were performed by adding arsenic reference solution (20 μL) to the solid BaSO$_4$ after sample weighing.

For As determination by ICP OES and ICP-MS, samples were previously treated using the procedure described in 5th edition of European Pharmacopoeia.[2] Barium sulfate (0.5 g) was transferred to glass vessels and 2 mL of concentrated HNO$_3$ and 30 mL of water were added. Vessels were heated by 2 h in a water-bath. After filtration of solution 1 mL of concentrated H$_2$SO$_4$ was added and solution was evaporated to dryness and further heated until white fumes formation. After cooling, digests were diluted with 10% (v/v) H$_2$SO$_4$ and water up to 20 mL. This solution was also analyzed by the procedure using arsine generation.[2]

In order to check the accuracy, As determination by neutron activation analysis (NAA) was performed by irradiating BaSO$_4$ sample "E" under neutron flow of 4.5×10^{12} n cm^{-2} s^{-1}, by 8 h. Before five days, gamma activity measurements were performed in a hyperpure Ge detector linked to a spectrometer. The radioisotope measured was ^{76}As at 559 keV.

Statistical analysis

Data were evaluated using analysis of variance. Tukey-Kramer multiple comparisons test (p < 0.05) was applied.

Results and Discussion

Pyrolysis and atomization profiles for arsenic in barium sulfate

Initially, the attempts to establish pyrolysis and atomization curves for As in barium sulfate without chemical modifier were not successful, mainly when using D$_2$-SoS-ET AAS. Baseline disturbance caused by relatively high BG signal did not allow the acquisition of reliable data using both BG systems. Palladium has been used in view of its effectiveness for the determination of arsenic in a wide variety of samples.[29] Therefore, palladium solution (correspondent to 5 μg) was used as chemical modifier and it was added directly on the solid sample after the

weighing on the graphite platform. However, using Pd the signals for As using D$_2$-SoS-ET AAS (Figure 1A) did not return completely to the baseline within 10 s of integration time (pyrolysis and atomization temperatures were set at 1300 and 2200 °C, respectively). Even using Z-SoS-ET AAS (Figure 1B) the BG signals were relatively high (about 0.6 in peak height) and overcorrection was observed impairing feasible determination of As. With the increase of atomization temperature up to 2500 °C the intensity of BG was also increased and a signal depression about 50% (for 2500 °C) was observed using both BG correction systems.
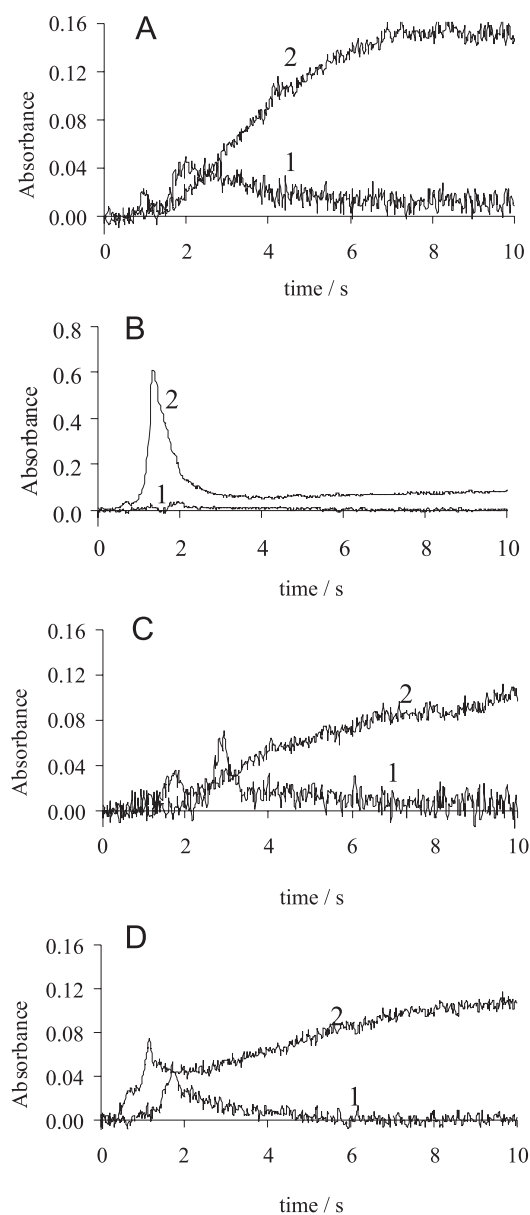

Figure 1. Analytical [1] and BG [2] signals for arsenic in barium sulfate by D$_2$-SoS-ET AAS (A and C) and Z-SoS-ET AAS (B and D). Pyrolysis was set at 1300 °C and atomization at 2200 °C (5 μg Pd was added). C and D: addition of 0.5 L min^{-1} hydrogen. Sample masses were 0.344 mg (A); 0.322 mg (B); 0.380 mg (C); 0.261 mg (D).

In a previous work it was found that 64% of the barium sulfate mass remained in the platform even with pyrolysis temperature of 1500 °C and the residual matrix vaporized concomitantly with the analyte during atomization step.[30] This is compatible with the thermal decomposition of $BaSO_4$ yielding BaO, SO_2 and O_2, at temperatures prior the melting point of barium sulfate (1580 °C).[31,32] Background signals could be originated by molecules as C_nS_m (with n>m) formed in the gas phase at high temperatures, which yields diffuse bands from 187 to 230 nm region.[19,20] Depending on the BG intensity it can not be efficiently compensated, mainly when using deuterium BG correction system. In addition, thermal treatment of metal sulfates could cause the generation of the correspondent metal sulfides and also elemental sulfur with consequent analyte losses and/or signal depression.[33] Therefore, owing the ineffectiveness of Pd alone to overcome the interferences, gaseous hydrogen was introduced during the pyrolysis step in order to minimize the matrix effects. The addition of hydrogen has been proposed for pre-reduction of Pd modifier on the surface of graphite tube yielding metallic Pd in order to increase its efficiency.[34] Contrarily to Cr determination, in this matrix[30] the use of chemical modifier and hydrogen addition were necessary due to the high matrix interference observed in the selected wavelength for As. Analytical signals for As in $BaSO_4$ with palladium and also hydrogen addition during pyrolysis step showed better profile and lower BG signals using both correction systems, specially for Z-SoS-ET AAS (Figures 1C and 1D). With the atomization temperature set at 2200 °C, the As signal was completely integrated in 10 s and no overcorrection was observed for the determinations using D_2- and Z-SoS-ET AAS.

Therefore, pyrolysis and atomization curves for solid barium sulfate were established with palladium and also with hydrogen addition during pyrolysis step. Figure 2A shows the profile of pyrolysis curve using Z-SoS-ET AAS. The maximum temperature without As losses was 1300 °C. For the atomization curve (Figure 2B) arsenic signals produced a slight increase from 2000 to 2200 °C. At 2200 °C better analytical signals considering the BG intensity, peak shape and precision (Figures 1D and 2B) were obtained. In spite of apparently higher As signal at 2400 °C (Figure 2B), intense BG signals (about 0.7 in peak height), causing overcorrection effect were observed with consequent overestimated results. Similar curve profiles were found using D_2- and Z-SoS-ET AAS. With the use of Pd and hydrogen the profile for pyrolysis and atomization curves using $BaSO_4$ were analogous to those for As aqueous standards in the same conditions. Then, the selected temperatures for subsequent studies were 1300

and 2200 °C for pyrolysis and atomization, respectively. These temperature parameters are in agreement with those previously reported for As determination using Pd as chemical modifier (without hydrogen addition).[35]
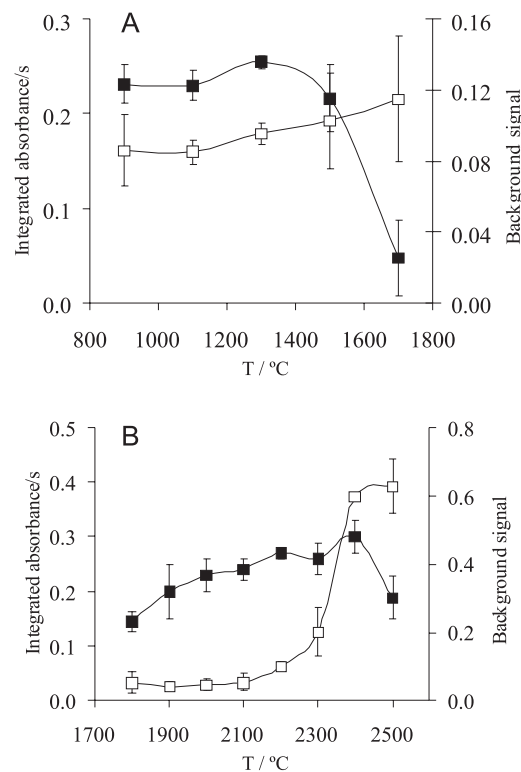

Figure 2. Pyrolysis (A) and atomization (B) curves for As in $BaSO_4$ using Z-SoS-ET AAS: ■ analytical and □ BG (peak height) signals. Pyrolysis set at 1300 °C and atomization at 2200 °C. Vertical bars are the correspondent standard deviations (n = 3). Barium sulfate mass was 0.27 ± 0.03 mg, 5 µg Pd, 0.5 L min^{-1} hydrogen.

Behavior of matrix during thermal treatment

In order to evaluate the effect of Pd and hydrogen addition on the thermal behavior of barium sulfate during pyrolysis step, the variation of sample mass was determined with increasing of pyrolysis temperatures. The dependence of mass loss with the temperature is shown in Figure 3. The curve of sample loss without Pd or H_2 was very similar to the curve using only Pd. For both conditions, up to 1300 °C, the mass of barium sulfate presented a small decrease. However, with higher temperatures the loss increased quickly achieving about 20% at 1500 °C and around 50% at 1800 °C. Using Pd the shape of mass loss curve in the range of temperatures between 1600 and 1800 °C was similar for both conditions (Figure 3). Palladium and hydrogen probably interfere in thermal decomposition of $BaSO_4$ preventing the formation of sulfur species in the gas phase which can result in diffuse bands from 187 to 230 nm region.[19,20]
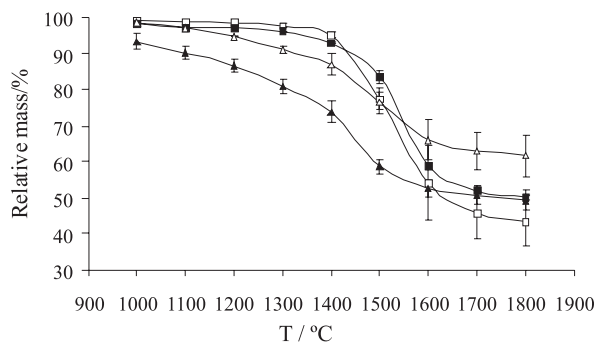
Figure 3. Relative mass loss of barium sulfate (2.5 ± 0.1 mg) after heating at temperatures between 1000 and 1800 °C. Argon flow rate was 2.0 L min^{-1}; □ without Pd or H$_2$ addition; ■ = 10 µg of Pd; △ = 0.5 L min^{-1} H$_2$; ▲ = 10 µg of Pd and 0.5 L min^{-1} H$_2$, n = 3.

When only hydrogen was used as chemical modifier the decrease of sample mass in temperatures higher than 1500 °C was less pronounced (Figure 3) although at temperatures between 1200 and 1400 °C the decrease of sample mass was bigger than at the conditions without chemical modifier or in the presence of Pd. When Pd was used with H$_2$ the shape of sample loss curve was similar with to the curve when only H$_2$ was used (Figure 3). However, for all the investigated temperatures losses were observed in a higher intensity (about 5 to 15%). Probably, the use of palladium with H$_2$ could be associated with the increase of mass losses from the platform.

In the present work the pyrolysis temperature was set at 1300 °C using Pd and H$_2$ (Figure 2A). In these conditions BG signals were relatively lower than those using only Pd as shown in Figure 1. At 1300 °C the loss of BaSO$_4$ using Pd and H$_2$ was 15% higher when compared with the same condition without H$_2$ (Figure 3). Then, after the pyrolysis step lower BaSO$_4$ remained in the platform and this fact could explain the strong reduction of BG signals using both correctors (D$_2$ and Zeeman-effect) as shown in Figure 1.

Sample mass range

The maximum sample mass that could be introduced in the graphite tube under optimized conditions was investigated and this procedure was performed similarly to that described by Belarra *et al.*[28] For both atomizers sample masses between 0.05 and 1 mg were tested. However, with sample masses higher than 0.55 and 0.8 mg for D$_2$- and Z-SoS-ETAAS, respectively, intense BG signals that could be not compensated by both correction systems were observed (error messages related to excessive BG were displayed by the software).

For tests by D$_2$-SoS-ETAASS the mass curve from 0.05 to 0.55 mg presented an unusual profile (Figure 4) and no mass interval with constant absorbance signal/sample mass ratio was identified. By evaluating the statistical data

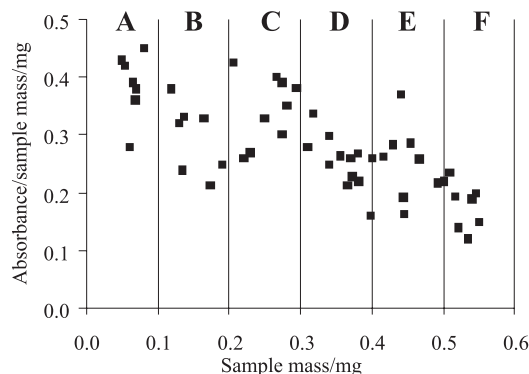(Table 2), it was observed that mass values from B- to C-block or from D- to F-block could be used.

Figure 4. Influence of sample (BaSO$_4$) mass on analytical results for As determination by the proposed D$_2$-SoS-ETAAS. Block A = 0.05 to 0.09 mg; Block B = 0.10 to 0.19 mg; Block C = 0.20 to 0.29 mg; Block D = 0.30 to 0.39 mg; Block E = 0.40 to 0.49 mg; Block F = 0.50 to 0.55 mg.

However, in both cases the precision was poor as shown in Figure 4 impairing reliable results using this technique. Therefore, the use of D$_2$-SoS-ETAASS was unreliable for the determination of As in BaSO$_4$ in the range from 0.05 to 0.55 mg.

Table 2. Analysis of variance and Tukey-Kramer test for different blocks in Figures 4 and 5. Results for D$_2$-SoS-ET AAS/Z-SoS-ET AAS

	Degrees of freedom	Sum of squares	Mean square	F test	p value
Between groups	5/7	0.2292/ 0.1680	0.04584/ 0.02400	15.634/ 24.711	0.0001/ 0.0001
Within groups	45/55	0.1319/ 0.05342	0.002932/ 0.0009712		
Total	50/62	0.3612/ 0.2214			

D$_2$-SoS-ETAAS						Z-SoS-ETAAS							
	A	B	C	D	E	F		A	B	C	D	E	F	G	H
A	+	-	+	-	-	-	A	+	-	-	-	-	-	-	-
B	-	+	+	+	+	-	B	-	+	+	+	-	-	-	-
C	+	+	+	-	-	-	C	-	+	+	+	+	+	+	-
D	-	+	-	+	+	+	D	-	+	+	+	+	+	+	-
E	-	+	-	+	+	+	E	-	-	+	+	+	+	+	-
F	-	-	-	+	+	+	F	-	-	+	+	+	+	+	-
							G	-	-	+	+	+	+	+	-
							H	-	-	-	-	-	-	-	+

(+) difference not statistically significant (95%); (-) difference statistically significant (95%).

On the other hand, using Z-SoS-ETAAS, barium sulfate masses between 0.05 and 0.8 mg could be used (Figure 5). Nevertheless, for sample masses between 0.05 to 0.2 mg

overestimated values were obtained. For sample masses higher than 0.7 mg underestimated results were found. From the statistical evaluation (Table 2), sample mass interval was higher than using D_2-SoS-ETASS (from C- to G-block). Therefore, sample masses ranging from 0.2 to 0.7 mg were used allowing more consistent results for As determination. Using Z-SoS-ET AAS, the upper limit of mass interval allowed the analysis of relatively higher sample masses when compared to previous work where $BaSO_4$ masses below 0.07 mg were applied.[26]
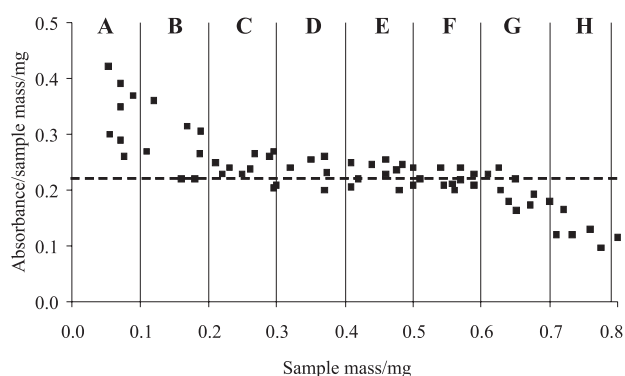

Figure 5. Influence of sample ($BaSO_4$) mass on analytical results for As determination by the proposed Z-SoS-ET AAS. Block A = 0.05 to 0.09 mg; Block B = 0.10 to 0.19 mg; Block C = 0.20 to 0.29 mg; Block D = 0.30 to 0.39 mg; Block E = 0.40 to 0.49 mg; Block F = 0.50 to 0.59 mg; Block G = 0.60 to 0.69 mg; Block H = 0.70 to 0.80 mg. The dashed line shows the mean value of absorbance/sample mass.

Sample analysis and figures of merit

Optimized conditions for As determination in barium sulfate by Z-SoS-ET AAS are shown in Table 1. Possible incomplete release of As from $BaSO_4$ matrix during the atomization was evaluated by performing a subsequent application of complete heating program without sample residue removal (the cleanout step was omitted in the first heating cycle). Analytical signals were negligible (less than 0.001 s) after application of the second heating cycle. However, in order to prevent eventual memory effects the cleaning step (2600 °C) was always applied. Calibration was feasible by

using aqueous reference standard solutions. The characteristic mass was 25.4 pg and good linearity was obtained ($R^2 = 0.995$). Limit of detection was 0.005 $\mu g\ g^{-1}$ (3σ, n = 10) and relative standard deviation was better than 9.5% using Z-SoS-ET AAS.

Arsenic concentration in pharmaceutical grade $BaSO_4$ samples ranged from 0.32 to 4.29 $\mu g\ g^{-1}$ as shown in Table 3. As no certified reference $BaSO_4$ is available, recovery tests were carried out for the proposed method. Arsenic reference solutions were added to the solid $BaSO_4$ after sample weighing and recoveries were between 96 and 102%. Since recovery tests using reference solutions could not assure the accuracy of procedure, analysis using an independent technique (NAA) was performed for $BaSO_4$ sample "E". Results were not statically different using the proposed procedure or NAA technique.

Solutions obtained after the extraction procedure described in European Pharmacopoeia were analyzed by the recommended procedure by arsine generation[2] and also by ICP OES and ICP-MS. The procedure described in European Pharmacopoeia was not feasible for the detection of As in all $BaSO_4$ samples. For ICP OES, arsenic concentration for samples B and D were below the correspondent LOD (0.8 $\mu g\ g^{-1}$). However, results for samples A and C using ICP OES and ICP-MS were around 20% below those by using the proposed Z-SoS-ET AAS method. These results were due to the low extraction efficiency and/or analyte losses during the extraction step (dried residue after extraction was analysed and As was determined by the proposed SoS-ET AAS procedure). Contrarily to results obtained using the proposed method the blank values for digests after extraction described in European Pharmacopoeia were relatively higher.[2] This aspect can be considered as an advantage for the proposed method where integrated absorbance values for blanks were always lower than 0.001 s.

It is well known that particle size and the homogenous distribution of the analyte in solid samples could influence both the accuracy and the relative standard deviation in determinations by SoS-ET AAS.[26] For samples investigated in the present work, more than 95% of particles were smaller than 30 μm. This low particle size can explain

Table 3. Results for the determination of arsenic in barium sulfate by the proposed Z-SoS-ET AAS procedure (values in $\mu g\ g^{-1}$ with mean and standard deviation), by ICP-MS and ICP OES after extraction (n =7) and by NAA

Samples	Z-SoS-ET AAS	ICP OES	ICP-MS	NAA
A	1.17 ± 0.05	0.93 ± 0.14[a]	0.98 ± 0.17[a]	-
B	0.51 ± 0.04	< 0.8	0.37 ± 0.07[b]	-
C	1.18 ± 0.09	0.89 ± 0.16[a]	0.95 ± 0.20[a]	-
D	0.32 ± 0.03	< 0.8	0.26 ± 0.06[b]	-
E	4.29 ± 0.11	3.44 ± 0.60[b]	3.58 ± 0.47[b]	4.34 ± 0.03

[a]Statistically different from Z-SoS-ET AAS (Analysis of variance, P < 0.05); [b]Statistically different from Z-SoS-ET AAS (t-test, P < 0.05).

partially the relatively low values for standard deviation obtained in this work as shown in Table 3.

Conclusions

Arsenic determination by ICP OES and ICP-MS and also the application of the limit test proposed by current pharmacopoeias require a previous sample preparation step that involves the use of corrosive and hazardous chemicals. The recommended procedure in pharmacopeias is time consuming and could introduce a source of contamination in the digestion step.

The proposed method by Z-SoS-ET AAS presented good accuracy and precision. Moreover, using optimized temperature parameters, including the use of palladium as chemical modifier and hydrogen introduction in the graphite tube during the pyrolysis step, it was possible to minimize the matrix effects for suitable As determination. In special, the use of H_2 was important to minimize the BG preventing the occurrence of overcorrection problems. In addition, calibration using aqueous reference standard solutions was feasible, avoiding the necessity of solid certified reference materials, as observed for previous works using SoS-ET AAS for a similar matrix.[26] Furthermore, in the proposed method, the absence of a sample preparation step minimizes the use of chemical reagents and allows the reduction of the analysis time to about 10 min for one sample.

Acknowledgments

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