Journal of Pharmaceutical and Biomedical Analysis 52 (2010) 747–751

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

journal homepage: www.elsevier.com/locate/jpba

Short communication

Speciation analysis of Sb(III) and Sb(V) in antileishmaniotic drug using Dowex 1 × 4 resin from hydrochloric acid solution

L. Łukaszczyk, W. Żyrnicki*

Chemistry Department, Analytical Chemistry Division, Wroclaw University of Technology, Wybrzeze Wyspianskiego 27, 50-370 Wroclaw, Poland

ARTICLE INFO

Article history:
Received 9 September 2009
Received in revised form 5 February 2010
Accepted 6 February 2010
Available online 13 February 2010

Keywords:
Speciation analysis of antimony
Meglumine antimoniate
Solid phase extraction
Dowex 1 × 4
Inductively coupled plasma optical emission spectrometry

ABSTRACT

A new and simple method for the direct and simultaneous determination of Sb(III) and Sb(V) in meglumine antimoniate, the first-choice drug for leishmaniasis treatment, was developed. Speciation analysis was carried out using the quantitative separation of inorganic trivalent and pentavalent antimony on Dowex 1 × 4 resin from 1.5 mol l^{-1} hydrochloric acid solution. The inductively coupled plasma optical emission spectrometry (ICP-OES) was used for determination of antimony. The interfering effects of As, Bi, Cd, Cu, Mn, Pb and Zn were examined and only Bi was found to be a significant interferent. The liberation of Sb(V) and Sb(III) from organoantimonial compounds without changing of oxidation state was carried out by means of 1.5 mol l^{-1} hydrochloric acid solution. The spike recovery values obtained for Sb(III) in pharmaceutical sample varied from 92 to 100%. The method was successfully applied for the direct determination of antimony(III) and of antimony(V) in meglumine antimoniate.

1. Introduction

Leishmaniasis is a serious parasitic disease occurring in the Mediterranean region, Africa, Asia, and Central and South America. For leishmaniasis treatment, antimonial drugs have been applied for a long time. As the first, trivalent antimonial drugs like: antimony potassium tartrate (Tartar emetic), pentasodium bis[4,5-dihydroxybenz-1,3-disulfonate]antimonate (Stibophen) and lithium antimony thiomalate (Antiomaline) for this purpose have been used [1]. For the last 50 years, two pentavalent antimonial drugs, meglumine antimoniate (Glucantime) and sodium stibogluconate (Pentostam) as the first-choice medicines for leishmaniasis therapy were used. Binding with organic molecule as well as pentavalent oxidation state of antimony make these drugs much less toxic, because inorganic forms of antimony are more toxic than the organic ones and antimony(III) is generally more harmful than antimony(V) [2]. In spite of existence of antimony in less toxic form in actually using drugs, instability of these drugs causes a risk of occurrence of some toxic contaminants. In meglumine antimoniate, antimony exists as a mixture of pentavalent organoantimonial compounds [3], but also inorganic Sb(V) [4] and, worse, trivalent antimony as contaminants have been found [5–11]. Therefore, determination of trivalent and pentavalent antimony in such pharmaceutical formulation is important.

Several analytical methods have been proposed for monitoring of antimony(III) and/or antimony(V) in antileishmaniotic drug of meglumine antimoniate. The method of UV–Vis spectrophotometry coupled with liquid–liquid extraction flow analysis (LLE-FA) based on ion pair formed between hexachloroantimoniate anion and rhodamine B cation was used for determination of Sb(V) only [12].

Some of the methods applied for Sb species determination in meglumine antimoniate were based on the direct determination of only one species, obtaining the second one indirectly [5–8]. For example, the concentrations of Sb(III) and total Sb (after reduction of Sb(V) to Sb(III)) were determined by hydride generation – atomic absorption spectrometry (HG-AAS) [5,6], as well as hydride generation – inductively coupled plasma optical emission spectrometry (HG-ICP-OES) [7]. The measurement of Sb(III) content was based on the assumption that the Sb(V) signal in citric acid was totally suppressed and only Sb(III) was able to produce antimony hydride. The concentration of Sb(V) was calculated from difference between total Sb and Sb(III). Santos et al. [8] measured the concentrations of Sb(III) and total Sb in meglumine antimoniate by using the method of potentiometric stripping analysis (PSA) with the use of carbon nanotube electrode. The Sb(V) concentration was obtained by calculation.

For the direct Sb(III) and Sb(V) determination in meglumine antimoniate, the methods such as: ion chromatography – inductively coupled plasma mass spectrometry (IC-ICP-MS) [4], UV–Vis spectroscopy based on the reaction of Sb(III) with bromopyrogallol red [9], UV–Vis spectroscopy [10] and adsorptive stripping

* Corresponding author. Tel.: +48 71 320 24 94; fax: +48 71 320 24 94.
E-mail address: wieslaw.zyrnicki@pwr.wroc.pl (W. Żyrnicki).

0731-7085/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.jpba.2010.02.009

voltammetry (DPAdSV) [11] (both with partial least squares (PLS) regression and pyrogallol as complexing agent) were proposed until now. Although the UV–Vis spectroscopy and DPAdSV were successfully applied for the direct determination of antimony species in meglumine antimoniate, the low selectivity can be a serious disadvantage of these methods. The IC-ICP-MS is a method of high selectivity, sensitivity and appropriate applicability for the direct determination of antimony species. However, this method cannot be used for samples with the complex matrices and only diluted solutions can be analysed. Therefore, the Sb(III) in meglumine antimoniate samples was not detected by this method, although the Sb(III) content around 1% of the total Sb was found by hydride generation – inductively coupled plasma mass spectrometry (HG-ICP-MS) [4]. Anyway the IC-ICP-MS is expensive in laboratory use because of high cost of equipment and its maintenance.

Solid phase extraction (SPE) is considered as an alternative technique to liquid–liquid extraction (LLE), but in contrast to LLE, SPE avoids exposure to and use of large volumes of organic solvents. Furthermore, owing to its versatility, SPE is used for matrix removal as well as for separation and/or preconcentartion of species. In some particular application, SPE is a valuable tool for differentiation of species of many metals and metalloids [13–15]. The coupling of SPE with sensitivity detected system as atomic absorption spectrometry (AAS), optical emission spectrometry (OES) or atomic fluorescence spectrometry (AFS), makes the direct speciation analysis of Sb possible. It should be also emphasized that the use of SPE allows for storage of the samples for several days before detection with stability of the retained species [16], which is crucial in speciation analysis and impossible by methods for antimonial drug analysis until now reported.

Due to higher reliability and more universal application in speciation analysis, the methods enabling the direct measurements of analyte contents are superior in comparison to those based on indirect determination. Furthermore, the indirect determination of Sb species can not assure a high quality of results and lead to significant errors, especially if the Sb(III) and Sb(V) contents differ substantially. Considering the global trends and requirements addressed to analytical methods, there is a strong need for development of direct and reliable methods being highly sensitive, economic, simple and in agreement with green chemistry.

In comparison to previous studies, a simple, low cost, safety, sensitive, and selective method was developed for the direct and simultaneous determination of Sb(III) and Sb(V) in meglumine antimoniate using the SPE separation and ICP-OES detection. In addition, to the best of our knowledge, this work presents the first application of SPE in analysis of meglumine antimoniate. This study was carried out based on selective retention of chloro-complexes of trivalent antimony on a strongly basic anion exchange resin, enabling for Sb(III) separation from a high concentration of Sb(V).

2. Experimental

2.1. Reagents and samples

De-ionized water (18.3 MΩ cm) obtained from EASYpure™ system (Barnstead, USA) was used throughout this study. All reagents were of analytical grade. The stock 1000 mg l^{-1} solutions of Sb(III) and Sb(V) were prepared by dissolving antimony potassium tartrate hemihydrate (POCH, Poland) and potassium hexahydroxyantimonate (Riedel-de Haën, Germany), respectively, in water. The working standards of antimony were prepared daily from their stock solutions. The single-element solutions of interfering ions were prepared by dissolving appropriate amounts of nitrate salts of As(V), Bi(III), Cd(II), Cu(II), Mn(II), Pb(II), Zn(II) (Chempur, Poland). The concentrated hydrochloric acid (Merck, Germany) was used to prepare loading solutions as well as conditioning and rinsing solutions. After SPE percolation and before ICP-OES measurements, the solutions collected in the flasks were acidified to 0.7 mol l^{-1} with Suprapure nitric acid (Merck, Germany). The resin employed was Dowex 1 × 4-200 (Sigma–Aldrich, Germany), a strong base anion exchange resin with 4% cross linking; chloride ion form and 100–200 mesh size of particles. The glassware and plasticware filled with 10% (v/v) of HNO_3 were washed in ultrasonic bath during 30 min and rinsed several time by distilled and de-ionized water consecutively. The sample of meglumine antimoniate (Glucantime), an injectable antimonial drug was analysed. This pharmaceutical formulation, manufactured by Sanofi-Aventis (France), was commercialized in 5 ml ampoules. Each ampoule of the drug contained about 81 mg ml^{-1} of Sb(V) as meglumine antimoniate in aqueous solution.

Table 1
Analytical parameters of the ICP-OES spectrometer.

Instrumental parameters	
Spray chamber	Cyclone
Nebulizer	Burgener
RF power (W)	1000
Generator frequency (MHz)	40.68
Plasma gas flow rate (l min^{-1})	13
Auxiliary gas flow rate (l min^{-1})	0.20
Nebulizer gas flow rate (l min^{-1})	0.25
Nebulizer pressure (bar)	3.0
Sample uptake (ml min^{-1})	1.3
Sample downtake (ml min^{-1})	1.0

2.2. Instrumentation

The Jobin Yvon sequential spectrometer ICP-OES (JY 38S) with 1 m monochromator was used in measurements. The instrumental parameters were summarized in Table 1. Determination of antimony and other elements was performed using the following analytical lines: Sb(206.833 nm), Sb(217.581 nm), As(197.262 nm), Bi(223.061 nm), Cd(228.802 nm), Cu(324.754 nm), Mn(259.373 nm), Pb(220.353 nm), Zn(213.856 nm). Two analytical lines of antimony were employed to ensure better quality of measurements. The antimony concentrations presented in this study were expressed as averages of the values from the both analytical lines measured three times.

The ultrasonic bath, model Ultrasons-H from J.P. Selecta (Spain), operating at 50 Hz, was applied here to test influence of the ultrasound energy on antimony liberation from organic complexes and for cleaning of glassware and plasticware.

The column system was used for separation of antimony species. A short glass column with the inner diameter of 10 mm and length of 100 mm, ended with frit, was filled with suspension of 2.0 g of Dowex 1 × 4-200 resin in water. Before using, the column was washed with 20 ml of water, next with 10 ml of 2.0 mol l^{-1} hydrochloric acid, and finally rinsed with 30 ml of water. The solutions were passed through the resin at a flow rate of 1 ml min^{-1} by using four-channel peristaltic pump (Perimax, Germany).

2.3. Sorption studies: influence of HCl concentration on Sb retention

For the sorption studies, 10 ml of 8.0 mg l^{-1} Sb(III) or Sb(V) standard solutions, prepared in 0.1, 0.5, 1.0, 1.5, 2.0, 4.0, 6.0, 8.0, 10.0 mol l^{-1} HCl, were passed through the columns. After sorption, the resin was washed two times with 5 ml of the rinsing solutions containing the same concentration of hydrochloric acid as the standard solutions passed.

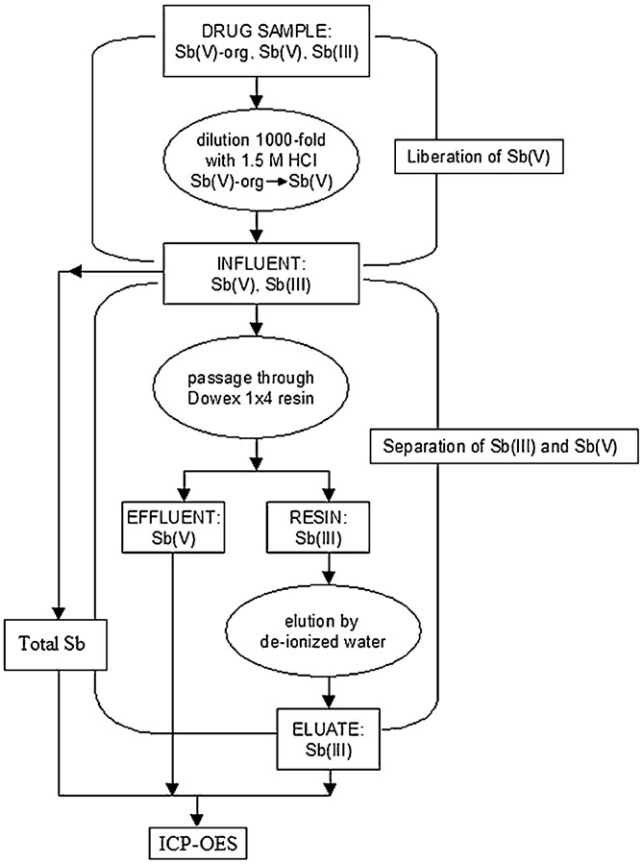

Fig. 1. Scheme of analytical procedure of antimony speciation in drug formulation.

2.4. Separation procedure

For separation of inorganic antimony forms off-line procedure was used. The volume of 10 ml of loading solution containing 1.5 mol l^{-1} HCl was passed through the column. After solution percolation, the column was washed two times with 5 ml of 1.5 mol l^{-1} HCl solution. The retained chloro-complexes of antimony(III) were eluted with 10 ml of de-ionized water.

2.5. Interferents

For this study, the working solutions of 8.0 mg l^{-1} Sb(III) or Sb(V) containing 80.0 mg l^{-1} of As(V), Bi(III), Cd(II), Cu(II), Mn(II), Pb(II) or Zn(II) were prepared in 1.5 mol l^{-1} hydrochloric acid solution and the separation procedure (see Section 2.4.) was applied.

2.6. Drug sample preparation

The analytical procedure of the drug analysis (Fig. 1) consisted of two steps. The first was dilution of meglumine antimoniate to 1:1000 (v/v) with 1.5 HCl, when Sb(III) and Sb(V) could be liberated from organoantimonial compounds. The second step was a percolation of 10 ml of such solution through the column enabling separation of inorganic Sb(III) and Sb(V).

3. Results and discussion

3.1. Sorption efficiency of Sb(III) and Sb(V) as a function of HCl concentration

Conditions for quantitative separation of Sb(III) and Sb(V) on Dowex 1 from HCl solution have been studied here. The results

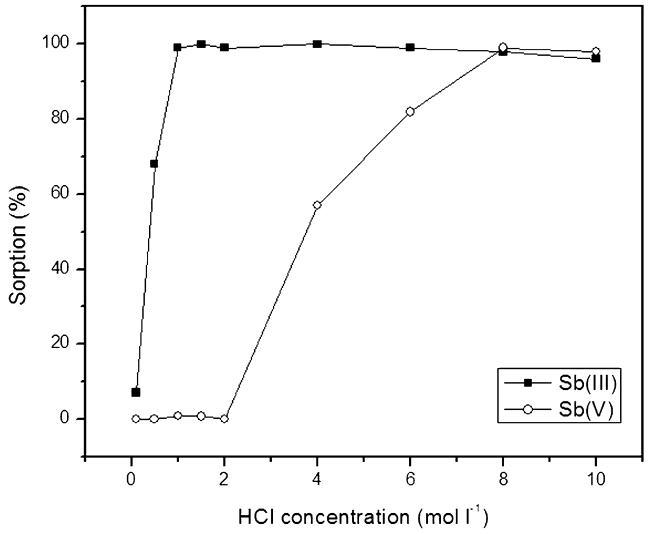

Fig. 2. Effect of hydrochloric acid concentration on retention of Sb(III) and Sb(V) on Dowex 1 × 4-200.

were shown in Fig. 2. In the concentration range of hydrochloric acid from 1.0 to 2.0 mol l^{-1}, the sorption of antimony(III) was practice quantitative (approximately 100%), while antimony(V) was not taken up at all. Therefore, for the next study 1.5 mol l^{-1} hydrochloric acid was selected. It was found that with the use of 10 ml of water, total elution of the retained antimony(III) could be achieved.

Taking into consideration the previous reports [17,18], it seems most likely that at 1.5 mol l^{-1} HCl, Sb(III) may be retained on anion exchanger as $SbCl_6^{3-}$ and $SbCl_4^-$, whereas Sb(V) could pass through the resin without retention as $Sb(OH)_xCl_{(5-x)}0\,(aq)$.

3.2. Influence of interferents

In previous studies of some commercial meglumine antimoniate samples, Al, As, Bi, Cd, Cu, Cr, Mn, Ni, Pb, Zn as contaminants have been found [4,8]. Therefore, interferent effects were investigated here in order to evaluate an influence of foreign ions on Sb(III) and Sb(V) recovery during anion exchange separation. Kraus and Nelson [19] reported that using Dowex 1 no sorption of aluminum and nickel, and negligible sorption of chromium from HCl solutions have been observed. Therefore, influences of As, Bi, Cd, Cu, Mn, Pb, Zn were only examined.

The results presented in Table 2 indicated that the influence on recovery of pentavalent antimony was not observed in the presence of examined ions at the interferent to Sb(V) mass ratio of 10. Similarly, no effects were observed if the mixture of Sb(III) with the interferents was investigated, with Bi exception. Bismuth(III) caused a significant decrease of recovery of antimony(III), probably

Table 2
Effect of foreign ions on the recoveries of Sb(III) and Sb(V) in the presence of potential interferents to Sb mass ratio of 10.

Element	Recovery (%)	
	Sb(III)[a]	Sb(V)[a]
As	95	106
Bi	56	102
Cd	94	100
Cu	92	102
Mn	90	101
Pb	93	100
Zn	95	101

[a] Concentration of Sb = 8.0 mg l^{-1}.

because of antimony oxysalt coprecipitation with bismuth oxysalt precipitated during the water elution.

In addition to interference effects caused by the As, Bi, Cd, Cu, Mn, Pb, Zn ions, their sorption on Dowex 1 × 4 was also investigated. It was found that As, Cu, Mn totally passed through the column and were found in the effluent, while the total contents of Bi, Cd, Pb and Zn were retained by the anion exchanger and, with exception of bismuth, eluted with Sb(III).

3.3. Working concentration range of Sb(III)

In order to check a level of antimony(III) concentration that could be retained on Dowex 1 × 4 and effectively separated from an excess of Sb(V) by proposed method, the working concentration range for trivalent antimony was investigated. In the literature it was reported that meglumine antimoniate (Glucantime) may contain from 0.24 to 10.5 mg ml^{-1} of Sb(III) [5–11]. In our research, the extended range of Sb(III) concentration (0.15, 1.0, 10.0, 50.0 mg ml^{-1}) in the presence of 100 mg ml^{-1} of Sb(V) was studied. The recoveries of Sb(III) in the examined working concentration range varied from 90 to 97%.

3.4. Antimony liberation from organoantimonial compounds and oxidation state stability

The meglumine antimoniate is a complex mixture of carbohydrate–antimony(V) oligomers (Sb(V)-org) existing in equilibrium in aqueous solution, with general formulas of $(NMG–Sb(V))_n–NMG$, $(NMG–Sb(V))_n$, $(Sb(V)–NMG)_n–Sb(V)$ [3,4,20], where Sb(V) and NMG represent pentavalent antimony and N-methyl-D-glucamine, respectively. The mentioned complexes characterize by considerable lability [3,5]. In order to apply the proposed separation procedure, Sb(V) as well as Sb(III) should be liberated from the organoantimonial compounds by hydrochloric acid dilution [6,9].

Trivelin et al. [12] reported that recovery of Sb(V) higher than 92% was obtained if the meglumine antimoniate sample was diluted 1:100 (v/v) with 6.0 mol l^{-1} HCl and exposed for 15 min on ultrasound energy (55 kHz) before analysis. Therefore, the influence of sonication time on recovery of antimony from meglumine antimoniate with 1.5 and 6.0 mol l^{-1} HCl was investigated previously diluting the drug 1:100 (v/v). The samples after sonication were diluted 1:10 (v/v) to 1.5 mol l^{-1} HCl and treated according to the separation procedure described in Section 2.4.

The recoveries of pentavalent antimony were expressed as a per cent of the total antimony content, due to the fact that the pentavalent organoantimonial compounds are the major constituents of examined pharmaceutical formulation. The obtained recovery rates for antimony(V) varied from 96 to 101% for the samples diluted with 1.5 mol l^{-1} HCl without sonication, from 93 to 99% for the samples diluted with 1.5 mol l^{-1} HCl with sonication and from 97 to 101% for the samples diluted with 6.0 mol l^{-1} with and without sonication.

In order to stability control of antimony(III) during the sample preparation, a recovery test for diluted (1:1000, v/v) drug samples spiked with 2.0 mg l^{-1} of Sb(III) was applied. For the reason of increasing of trivalent antimony concentration in drug samples exposed on ultrasound energy, the recoveries of antimony(III) were determined after subtraction of the base value of Sb(III) received for no spiked samples without sonication.

As shown in Fig. 3, the recoveries of Sb(III) were close to 100% for the samples containing 1.5 mol l^{-1} HCl, without sonication activity. For the samples exposed on ultrasound energy before analysis, the increase in recovery rate of Sb(III) with the time was observed. The recoveries of Sb(III) varied from 105 to 130% and from 114 to 184% for samples diluted in 1.5 and 6.0 mol l^{-1} HCl, respectively. Therefore, for further analysis of pharmaceutical formulation, dilution

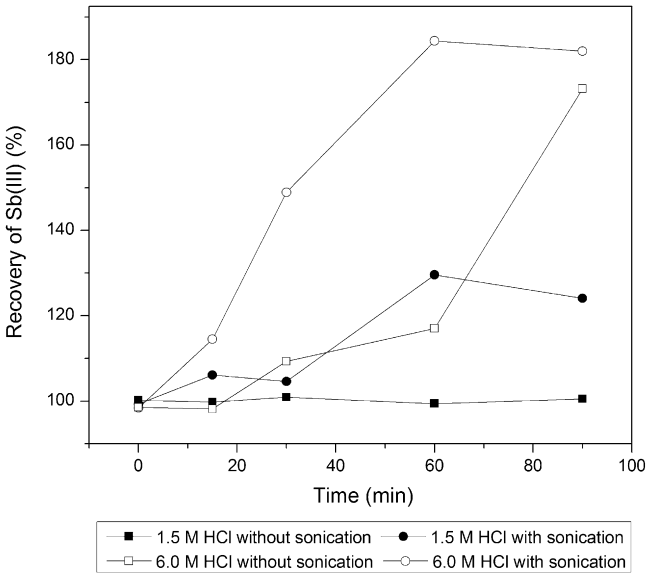

Fig. 3. Effect of the sonication time and hydrochloric acid concentration on Sb(III) recovery from diluted 1:1000 (v/v) meglumine antimoniate samples spiked with 2.0 mg l^{-1} of Sb(III) standard.

1:1000 (v/v) with 1.5 mol l^{-1} HCl without sonication was used to assure that Sb(V) will not be converted to Sb(III).

3.5. Analytical figures of merits

For the both measured analytical lines of Sb, some validation criteria like: precision, linearity of external calibration graph, detection limit, specificity, accuracy and working concentration range were evaluated. The analytical performance parameters were presented in Table 3.

The precision (repeatability) of measurements was expressed as the relative standard deviation. The limit of detection was defined as the concentration of analyte giving signals equivalent to three times the standard deviation of the blank plus the net blank intensity, for six independent replicates. The method was selective for Sb(III) and Sb(V) determination in meglumine antimoniate samples as conformed by the interferent study (Section 3.2).

Since the standard reference materials with certificated contents of antimony species are not available a recovery test is a valid alternative to check accuracy [21]. Therefore, for this study the spike recoveries of Sb(III) were examined. Pentavalent antimony is a major constituent of the drug, therefore the samples were not spiked by Sb(V). Pretty good recoveries of Sb(III) in all instances were obtained, as shown in Table 4.

3.6. Sample analyses

The proposed method was applied for analysis of the commercial antileishmanial drug samples. With five replicates, the mean

Table 3
Analytical performance parameters.

Analytical parameters	Sb(206.833)	Sb(217.581)
Working concentration range of Sb(III) (mg l^{-1})	0.15–50.0	
Correlation coefficient[a]	0.9998	
Limit of detection of Sb(III) (μg l^{-1})	32	44
Limit of detection of Sb(V) (μg l^{-1})	42	52
Precision (% RSD, n = 5, concentration of Sb = 8.0 mg l^{-1})	2.7	

[a] Correlation coefficient of external calibration graph (0.10–100 mg l^{-1}).

Table 4
Determination of Sb(III), Sb(V) and total Sb in diluted (1:1000, v/v) drug samples. Spike recovery data for Sb(III).

Sb(III)		Sb(V) found ($mg\,l^{-1}$)[a]	Total Sb found ($mg\,l^{-1}$)[a]
Added ($mg\,l^{-1}$)	Found ($mg\,l^{-1}$)[a]		
0	0.20 ± 0.01	80.0 ± 2.1	81.2 ± 3.3
0.15	0.34 ± 0.01	80.4 ± 2.4	81.5 ± 3.0
0.50	0.66 ± 0.03	80.0 ± 2.3	82.9 ± 0.3
2.0	2.20 ± 0.04	79.9 ± 3.0	82.3 ± 0.6
4.0	4.31 ± 0.11	79.7 ± 1.1	85.1 ± 1.2

[a] Mean ± standard deviation; $n = 3$.

values of concentrations and their standard deviations for Sb(III) and Sb(V) were found to be 0.20 ± 0.01 and $80.0 \pm 2.1\,mg\,ml^{-1}$, respectively. The mean concentration of the total antimony was equal to $81.2 \pm 3.3\,mg\,ml^{-1}$ ($n = 5$) being in good agreement with content given by manufacturer ($81\,mg\,ml^{-1}$ of Sb). As one may easily deduce and see clearly from the results obtained here, the Sb(III) contents can not be determined reliably from the difference between the total Sb and Sb(V) values, taking into account standard deviation uncertainties. This fact substantiates the development of methods to the direct determination of Sb(III).

4. Conclusions

The described work, in our knowledge, presents the first application of the solid phase extraction on anion exchange resin for speciation analysis of antimony in the commercial drug of meglumine antimoniate. The proposed separation procedure of inorganic antimony species, as well as Sb(V) and Sb(III) liberation from organic compounds, were found to occur without changing of antimony oxidation states. It confirms that a kinetic of exchange between Sb(III) and Sb(V) in HCl solution is rather slow [22].

The proposed protocol is distinguishable by such advantages as: simplicity, reliability, low cost of analysis and selectivity. The using SPE permits a quantitative separation of Sb(III) from Sb(V). The method can be applied to the direct determination of antimony(III) in its wide concentration range, and determination of antimony(V) existing in large excess in pharmaceutical formulation of meglumine antimoniate.

References

[1] C. Demicheli, T.L. de Figueiredo, S. Calvalho, R.D. Sinesterra, J.C.D. Lopes, F. Frézard, Physico-chemical characterization of meglumine antimoniate, BioMetals 12 (1999) 63–66.
[2] P. Smichowski, Antimony in the environment as a global pollutant: a review on analytical methodologies for its determination in atmospheric aerosol, Talanta 75 (2008) 2–14.
[3] W.L. Roberts, W.J. McMurray, P.M. Rainey, Characterization of the antimonial antileishmanial agent meglumine antimonate (glucantime), Antimicrob. Agents Chemother. 42 (1998) 1076–1082.
[4] N. Mikeley, S.R. Mortari, A.O. Schubach, Monitoring of total antimony and its species by ICP-MS and on-line ion chromatography in biological samples from patients treated for leishmaniasis, Anal. Bioanal. Chem. 372 (2002) 495–502.
[5] E.M.M. Flores, E.P. Santos, J.S. Barin, R. Zanella, V.L. Dressler, C.F. Bittencourt, Determination of antimony(III) and total antimony by hydride generation atomic absorption spectrometry in samples of injectable drugs used for leishmaniasis treatment, J. Anal. At. Spectrom. 17 (2002) 819–823.
[6] E.M.M. Flores, F.R. Paula, E.F.B. Silva, D.P. Moraes, J.N.G. Paniz, E.P. Santos, V.L. Dressler, C.F. Bittencourt, Selective determination of Sb(III) in drugs by flow injection hydride generation AAS, At. Spectrosc. 24 (2003) 15–21.
[7] L.M. Cabral, V.N.M. Juliano, L.R.S. Dias, C.B. Dornelas, C.R. Rodigues, M. Villardi, H.C. Castro, T.C. Santos, Speciation of antimony(III) and antimony(V) using hydride generation for meglumine antimoniate pharmaceutical formulations quality control, Mem. Inst. Oswaldo Cruz 103 (2008) 130–137.
[8] V.S. Santos, W.J.R. Santos, L.T. Kubota, C.R.T. Tarley, Speciation of Sb(III) and Sb(V) in meglumine antimoniate pharmaceutical formulations by PSA using carbon nanotube electrode, J. Pharmaceut. Biomed. Anal. 50 (2009) 151–157.
[9] S. Rath, W.F. Jardim, J.G. Dórea, A simple spectrophotometric procedure for the determination of antimony(III) and (V) in antileishmanial drugs, Fresenius J. Anal. Chem. 358 (1997) 548–550.
[10] M.J.G. Gonzáles, O.D. Renedo, M.J.A. Martinez, Simultaneous determination of antimony(III) and antimony(V) by UV–Vis spectroscopy and partial least squares method (PLS), Talanta 68 (2005) 67–71.
[11] M.J.G. Gonzáles, O.D. Renedo, M.J.A. Martinez, Speciation of antimony by adsorptive stripping voltammetry using pyrogallol, Talanta 71 (2007) 691–698.
[12] L.A. Trivelin, J.J.R. Rohwedder, S. Rath, Determination of pentavalent antimony in antileishmaniotic drugs using an automated system for liquid–liquid extraction with on-line detection, Talanta 68 (2006) 1536–1543.
[13] B.C. Mondal, D. Das, A.K. Das, Synthesis and characterization of a new resin functionalized with 2-napthol-3,6-disulfonic acid and its application for the speciation of chromium in natural water, Talanta 56 (2002) 145–152.
[14] J.L. Gómez-Ariza, J.A. Pozas, I. Giraldez, E. Morales, Use of solid phase extraction for speciation of selenium compounds in aqueous environmental samples, Analyst 124 (1999) 75–78.
[15] K. Zih-Perényi, P. Jankovics, É. Sugár, A. Lásztity, Solid phase chelating extraction and separation of inorganic antimony species in pharmaceutical and water samples for graphite furnace atomic absorption spectrometry, Spectrochim. Acta B 63 (2008) 445–449.
[16] V. Camel, Solid phase extraction of trace elements, Spectrochim. Acta B 58 (2003) 1177–1233.
[17] M. Filella, P.M. May, Computer simulation of the low-molecular-weight inorganic species distribution of antimony(III) and antimony(V) in natural waters, Geochim. Cosmochim. Acta 67 (2003) 4013–4031.
[18] E.H. Oelkers, D.M. Sherman, K.V. Ragnarsdottir, C. Collins, An EXAFS spectroscopic study of aqueous antimony(III)-chloride complexation at temperatures from 25 to 250 °C, Chem. Geol. 151 (1998) 21–27.
[19] K.A. Kraus, F. Nelson, Proceedings of the First United Conference on the Peaceful Uses of Atomic Energy, vol. 7, 1956, pp. 113–131.
[20] F. Frézard, P.S. Martins, M.C.M. Barbosa, A.M.C. Pimenta, W.A. Ferreira, J.E. de Melo, J.B. Mangrum, C. Demicheli, New insights into the chemical structure and composition of the pentavalent antimonial drugs, meglumine antimonate and sodium stibogluconate, J. Inorg. Biochem. 102 (2008) 656–665.
[21] M. Thompson, S.L.R. Ellison, R. Wood, Harmonized guidelines for single laboratory validation of methods of analysis, Pure Appl. Chem. 74 (2002) 835–855.
[22] M. Filella, N. Belzile, Y.-W. Chen, Antimony in the environment: a review focused on natural waters. I. Occurrence, Earth-Sci. Rev. 57 (2002) 125–176.