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Single drop microextraction or solid phase microextraction–gas chromatography–mass spectrometry for the determination of iodine in pharmaceuticals, iodized salt, milk powder and vegetables involving conversion into 4-iodo-*N*,*N*-dimethylaniline

Paramita Das, Manju Gupta, Archana Jain, Krishna K. Verma*

Department of Chemistry, Rani Durgavati University, Jabalpur 482001, Madhya Pradesh, India

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Abstract

A rapid sequence of oxidation and iodination using 2-iodosobenzoate as an oxidizing agent and *N*,*N*-dimethylaniline as an iodine scavenger at pH 6.4, when 4-iodo-*N*,*N*-dimethylaniline is formed, has been used for the determination of iodide by GC–MS. Solid phase microextraction (SPME) and single drop microextraction (SDME) have been used for the extraction of the iodo-derivative and their relative efficiencies compared. Pharmaceutical samples were subjected to solid phase extraction (SPE) for cleanup and the eluate analyzed for iodide. Iodate in salt samples was reduced to iodide with ascorbic acid. Milk powder and dried vegetables were wet combusted with peroxydisulfate to liberate covalently bound iodine as iodate which was reduced before derivatization. A rectilinear calibration graph was obtained for 0.1 μg–10 mg l^{-1} iodide by both extraction methods, the correlation coefficient and limit of detection (LOD) were 0.9995 and 25 ng l^{-1} iodide by SPME method, and 0.9998 and 10 ng l^{-1} iodide by SDME method, respectively. SDME appeared to be more efficient technique than SPME for the present system. From the pooled data, the average recovery of spiked iodide to real samples was 100.7% (range 96.5–107.0%) with an average R.S.D. of 3.1% (range 2.6–4.5%).

Keywords: Solid-phase microextraction; Single-drop microextraction; Derivatization, GC; Iodine; 4-Iodo-*N*,*N*-dimethylaniline

1. Introduction

Iodide is an essential trace element and is necessary for the synthesis of thyroxine and triiodothyronine. Lack of these hormones causes poor mental and physical development in children and enlargement of the thyroid (goitre) in adults [1,2]. On the contrary, excessive intake can cause toxic goitre (thyrotoxicosis) and thyroid cancers [3,4]. Out of 239 districts surveyed in India, 197 were found to be endemic for goitre. About 150 million of the Indian population is at risk of iodide deficiency, 55 million for goitre, 2.2 million for cretinism and 6.6 million for milder neurological defects [5]. Stillbirths and spontaneous abortions are associated with iodine deficiency during pregnancy [6]. Daily adult requirement is 100–300 μg iodide. An intake consistently below 50 μg per day results in endemic goitre. Lower limit of safe daily dietary intake of iodine has been suggested in many countries, viz. 160 μg in Canada [7], 150 μg in the USA [8], and values between 150 and 200 μg in the European Union [9] and other countries. Determination of iodine in pharmaceuticals, table salt, milk powder and vegetables is of considerable interest and it can be utilized as intake monitor.

Ion chromatography has been used for the direct determination of iodide [10,11]. High levels of chloride in the medium affect the efficiency of chromatography but this has been avoided by adding chloride to the eluent. Inadequate sensitivity of detection, such as by conductivity, amperometry or potentiometry limits the routine use of this technique [12]. Post-column reaction and spectrophotometry [13] or conversion of iodide to a more detectable organic derivative are two ways to overcome detection problems [14–18]. As long as 20–30 min reaction time is required to form the derivative. Moreover, the limits of detection of these methods are not sufficient to enable their use at

* Corresponding author. Tel.: +91-761-2323103; fax: +91-761-2313252.
E-mail address: arichna@sancharnet.in (K.K. Verma).

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trace level determination of iodine in samples, such as milk and vegetables. The former inconvenience was avoided by derivatization of iodine to 4-iodo-*N*,*N*-dimethylaniline, when the reaction was complete within 1 min, and the latter by a concentration step in the procedure [19].

Sample preparation is a necessary step in trace analysis that results in an extract which is fully compatible with the final method of determination, usually chromatography. There has been growing interest in trace enrichment techniques using solid phase extraction (SPE) that was originally developed as an alternative to liquid–liquid extraction (LLE) since the latter is labor intensive, time consuming and making use of large volumes of ozone depleting solvents but now SPE is a powerful standard method for sample cleanup, analyte enrichment and phase transfer [20–22]. To overcome the sensitivity problems of off-line SPE, in which a part of final extract is subjected to the chromatography, SPE is performed in mini-columns packed with a suitable sorbent and also coupled on-line to enable transfer of the whole extract into the analytical column. Such couplings are often cumbersome and require elaborated instrumentation [23,24]. Two sample preparation techniques, solid phase microextraction (SPME), which is a solventless extraction method, and single drop microextraction (SDME), that uses a single drop of organic solvent of up to a few microliters volume, combine sampling and concentration in the same step and whole of the extracted analyte(s) is used in determination in a simple manner [22,25,26]. As always a fresh drop of solvent is used for extraction there is of course no chance of analyte carryover in SDME.

The aim of the present work was to utilize SPME and SDME in the determination of iodine present as (i) iodide, as in pharmaceuticals, (ii) iodate, as in iodized table salt, and (iii) covalently bound to organic compounds, as in milk and vegetables. Iodination of aromatic amines is a faster reaction than of phenols and usually results with the formation of only one isomer [27]; with *N*,*N*-dimethylaniline the reaction completes within 1 min and 4-iodo-*N*,*N*-dimethylaniline thus formed is suitable for SPME/SDME and for its sensitive detection by GC–MS. Mineralization of covalently bound iodine by oxidation with peroxydisulfate has been employed in this work.

2. Experimental

2.1. Equipment

The GC–MS instrumentation used consisted of a Hewlett Packard G1800B GCD system (HP 5890 series II with a quadrupole mass detector). HP-5 (5% phenyl substituted methylpolysiloxane) 30 m × 0.25 mm × 0.25 μm capillary column and helium (99.999%) carrier gas at a flow rate of 1 ml min^{-1} were used. The injector temperature was maintained at 250 °C and all injections were made in splitless mode. The GC oven temperature was held at 90 °C for 3 min and then programmed to 220 °C at 20° min^{-1} and hold for further 2 min. The GC–MS transfer line was maintained at 300 °C, electron ionization at 70 eV and the mass spectrum scanned from *m/z* 45–450. Chromatographic data were acquired using a HP ChemStation software G1074B version A.01.00. C_{18} SPE cartridges (2.8 ml) containing 200 mg of the sorbent were obtained from Merck, Darmstadt, Germany. Before analysis, all aqueous samples were filtered through a 0.45 μm membrane filter (Millipore-India, Mumbai, India). The Supelco (Bellefonte, PA, USA) SPME fibre holder for manual use (57330-U) was employed with Supelco fibres 100 μm polydimethylsiloxane (PDMS), 7 μm polydimethylsiloxane (PDMS) and 85 μm polyacrylate (PA). Before their first use, the fibres were conditioned at 300 °C in the GC injector for 1 h under the flow of helium. Extraction vials, 4 ml, with PTFE silicone septum and screw cap with a hole (Supelco), 8 mm × 1.5 mm magnetic stir bars, a magnetic stirrer and an in-house made syringe/fibre holder stand were used.

2.2. Reagents, standards and samples

Sodium 2-iodosobenzoate reagent was made by stirring 400 mg of the free acid (Sigma, St. Louis, MO, USA) with a slight molar excess of sodium hydroxide (7.6 ml of 0.2 M sodium hydroxide) and diluting to 100 ml with water in a calibrated flask. It was filtered through a 0.45 μm membrane filter. This solution was stable for at least 4 months at ambient temperature.

A solution of 20 μl of *N*,*N*-dimethylaniline (Aldrich, Milwaukee, WI, USA) in 100 ml of methanol was used as halogen scavenger. The phosphate buffer contained 10 g each of KH_2PO_4 and K_2HPO_4 (both from Qualigens, Mumbai, India) in 250 ml water and was adjusted to pH 6.4. The ascorbic acid (Qualigens) solution was made by dissolving 50 mg of reagent in 100 ml of water. Potassium peroxydisulfate was analytical reagent grade (Qualigens). GC grade *n*-hexane, iso-octane and methylene chloride were obtained from Merck, India. 4-Bromo-*N*,*N*-dimethylaniline (Aldrich), 100 mg in 100 ml of methanol, was used as internal standard. Analytical reagent grade potassium iodide (Qualigens) was oven-dried and 130.7 mg of the substance was dissolved in 100 ml of water to give 1000 mg l^{-1} iodide. Less concentrated solutions were made by sequential dilution and stored in a cool place. All drugs, table salts, vegetables and milk powder samples were purchased from the local market.

2.3. Derivatization procedure and microextraction

A 0.5–2 ml aliquot of sample solution was mixed with 200 μl of phosphate buffer, 250 μl of *N*,*N*-dimethylaniline, 400 μl of 2-iodosobenzoate and 2 μl of the internal standard, and diluted to 4 ml with de-ionized water in the extraction vial. The solution was mixed well and kept for 1 min at ambient temperature (26 °C). For SDME, the needle of a 10 μl Hamilton syringe containing 1 μl of iso-octane was

penetrated through the septum of the vial until the tip protruded 1 cm below the meniscus of solution. The plunger was depressed to cause the solvent to form a drop suspended from the tip. After 15 min of equilibration (stir rate 300 rpm), the drop was drawn back into the syringe and immediately transferred into the GC injection port for analysis. For SPME, the fibre was kept dipped for 15 min for equilibration (stir rate 300 rpm). The fibre was retracted and the analytes were desorbed by placing the fibre in GC injector for 5 min.

2.4. Determination of iodide in pharmaceuticals

A known number of tablets were weighed and ground into a fine powder. A known amount of powder or a known aliquot of liquid formulation was mixed with 25 ml of de-ionized water and stirred for about 5 min. It was filtered (Whatman No. 42 filter paper) into a 50 ml calibrated flask, the residue was washed with 2–5 ml of water, and the filtrate and washings were diluted to volume with water. If the formulation contained iodine as iodate, the combined filtrate and washings were treated with 1 ml of 1% acetic acid and 2 ml of 0.2% ascorbic acid, shaken for about 5 min and diluted to volume. A 1 ml aliquot of this solution was loaded on to C_{18} cartridge that was previously activated by passing 2 ml of methanol and equilibrated with 2 ml of de-ionized water, allowed to flow under a gentle positive pressure and the eluate was collected. The sorbent was washed with 1 ml of de-ionized water and washings were combined with the eluate. A 1 ml portion of this solution was subjected to derivatization and analysis as described in Section 2.3.

2.5. Determination of total iodine in table salt

A 1 g portion of homogenized table salt was dissolved in about 50 ml of de-ionized water, mixed with 1 ml of 0.5% EDTA (disodium salt), 1 ml of 1% acetic acid, 1 ml of 0.5% ascorbic acid, shaken well for 1 min and finally diluted to 100 ml in a calibrated flask. A 1 ml portion of this solution was subjected to derivatization and analysis as described in Section 2.3.

2.6. Determination of organic-iodine in milk powder and vegetables

Raw vegetables were weighed, cut into small pieces and dried in an air oven at 60 °C. The dried mass was ground into a fine powder. About 500 mg of powdered sample was taken together with 30 ml of de-ionized water in a 100 ml Kjeldahl flask and swirled to form slurry. It was mixed with 3 g of potassium hydroxide, pre-dissolved in 10 ml of water, and 3 g of powdered potassium peroxydisulfate, and heated gently to boiling. After 15 min, 1.5 g of peroxydisulfate and 10 ml of water were added and the solution was again boiled gently for 20 min; this oxidation process was repeated once more. The solution was cooled to the room temperature, mixed with 3 ml of 9 M sulfuric acid and 5 ml of 0.5% ascorbic acid, shaken well, filtered (Whatman No. 42 filter paper) into a 250 ml calibrated flask and diluted to the mark with de-ionized water. A 10 ml portion of this solution was adjusted to about pH 6 by addition of sodium hydroxide and finally diluted to 20 ml. A 1 ml aliquot of this solution was subjected to clean-up by SPE on C_{18} cartridge as before (Section 2.4) and derivatization and analysis as described in Section 2.3.

3. Results and discussion

The chemistry of derivatization has been described previously [19]. *N*,*N*-Dimethylaniline was considered as an appropriate organic substrate for iodination because tertiary amines gave better GC and extraction property of the derivative by SDME and SPME compared to their primary amine analogues.

3.1. Mineralization of organic-iodine

Two methods have been evaluated for mineralization of organic-iodine, reaction with potassium hydroxide and with potassium peroxydisulfate. The former reaction involved nucleophilic displacement of iodine by hydroxide ion giving free iodide while the latter is based on oxidation of organic compound leading to the formation of iodate. Milk powder samples (about 200 mg) were refluxed with 3 g of potassium hydroxide in aqueous medium, and the final analysis was done as described in peroxydisulfate method. Though iodine is a good leaving group, the recovery of iodide was about 50% as compared to that found by the peroxydisulfate method. It appeared that the tertiary structure of milk protein did not allow hydroxide ion at many places on the macromolecular structure to occupy a stereochemically favourable position necessary for a bimolecular nucleophilic displacement of iodine [28]. Peroxydisulfate ion being one of very powerful oxidizing agents, redox potential 2.01 V [29], resulted in the wet combustion of organic compound. Iodine attached to aliphatic molecules was only oxidized to iodate as aromatic iodo-compounds, such as 2-iodobenzoic acid gave $<$50% recovery for its iodine. Since the oxidation was carried out in alkaline medium and iodine was oxidized to iodate, losses due to the formation of volatile iodine were not evident. On prolonged boiling peroxydisulfate was decomposed to sulfate. Thus peroxydisulfate oxidation was best suited to mineralize organic-iodine as present in vegetables and milk powder.

3.2. Single drop/solid phase microextraction

There are several parameters common to SDME and SPME which control the optimum performance of extraction including nature of liquid or fibre material, size of extractant, sorption time, stirring and ionic strength of

solution, etc. These parameters were separately evaluated to develop optimized extraction condition.

Both 4-iodo-*N*,*N*-dimethylaniline and the internal standard 4-bromo-*N*,*N*-dimethylaniline, being weak tertiary bases, exist mostly in molecular form in phosphate buffer of pH 6.4. This view was corroborated by agreement within 4.5% of extraction recoveries for the two compounds at pH 6.4 and 8.0 by SDME using 1 μl of iso-octane. Good partitioning of analytes took place in methylene chloride, *n*-hexane and iso-octane when 1 mg l^{-1} of iodide was analyzed, the optimum value being obtained at 2, 1.5 and 1 μl drop size, respectively, of solvents in a 15 min equilibration time which indicated that iso-octane is the best solvent. A 1 μl drop of iso-octane was used in subsequent experiments. The optimum extraction was reached in 15 min of equilibration time with stirring rate of 300 rpm. In the pooled data peak area ratios within ±2.5% were obtained when the internal standard was spiked to the aqueous sample solution or added to iso-octane. Since spiking the internal standard to the aqueous solution is the only way in SPME, this technique was also used in SDME.

Three SPME fibres 85 μm PA, 7 and 100 μm PDMS were evaluated for the extraction of 1 mg l^{-1} iodide, after derivatization, and the solution spiked with equal concentration of the internal standard in a 4 ml vial. All fibres were exposed to the same length of time, 15 min, for extraction and analytes were thermally desorbed in GC injector at 250 °C for 5 min. The results are shown in Fig. 1. Optimum peak areas were obtained with 100 μm PDMS fibre and it was used in later experiments. Both 4-iodo- and 4-bromo-*N*,*N*-dimethylaniline act as non-polar molecules in aqueous solution of pH 6.4 and this ostensibly explains their best extraction in non-polar phases iso-octance and PDMS fibre, and least extraction in more polar PA fibre.

A time profile of the extraction of both 4-iodo- and 4-bromo-*N*,*N*-dimethylaniline by 100 μm PDMS fibre was determined in order to assess the optimum SPME sampling period. Direct insertion of fibre into the derivatized analyte solution (4 ml) was carried out at room temperature (26 °C) and after sampling periods between 5 and 60 min the fibre was withdrawn for GC. Desorption time was set to 5 min at 250 °C in these experiments. The equilibrium was found to be reached in 15 min and thereafter it was practically constant. Optimum temperature of GC injector for the desorption of analytes was 250 °C for a period of 5 min, further increase in temperature to 280 °C and time to 15 min did not affect the peak areas. No carryover in a subsequent blank desorption was seen.

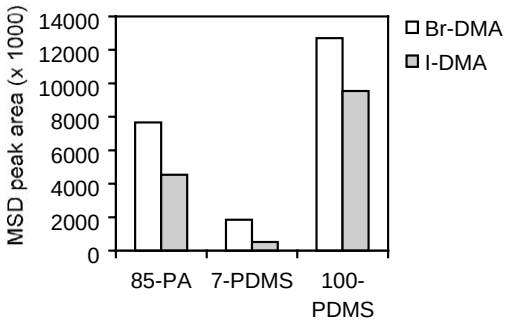

Fig. 1. Effect of fibre material on the SPME of 1 mg l^{-1} iodide after derivatization; 85-PA = 85 μm polyacrylate, 7-PDMS = 7 μm polydimethylsiloxane, and 100-PDMS = 100 μm polydimethylsiloxane. Equilibration time, 15 min and GC desorption time 5 min. Br-DMA = 4-bromo-*N*,*N*-dimethylaniline (1 mg l^{-1}) and I-DMA = 4-iodo-*N*,*N*-dimethylaniline.

Addition of salt is an important parameter to affect the extraction efficiency. Sodium sulfate was taken as a typical salt since it was found not to contain any detectable iodine species. About 16 mg of potassium phosphate was already present in 4 ml of extraction solution, addition of 25 and 50 mg of sodium sulfate to the solution decreased peak areas by 1.1 and 5.7%, respectively, by either extraction method. Extraction of both 4-iodo- and 4-bromo-*N*,*N*-dimethylaniline by SDME and SPME progressively decreased upon adding increasing masses of salt, the decrease being 50 and 99% on adding 0.7 and 1.0 g of salt to the derivatized iodide solution as compared to when no salt was added, respectively. This behavior has earlier been recorded [30,31]. Salt in water perhaps changed the nature of Nerst diffusion film around the drop or solid fibre, making it successively more polar with increasing ionic concentration that reduced the rate of diffusion of target molecules. The high sensitivity of the present method was an advantage that allowed dilution of iodized salt samples to bring down ionic concentration before extraction.

3.3. Validation

The chromatogram obtained for 10 μg l^{-1} iodide, after derivatization and SPME, is shown in Fig. 2 (the excess of *N*,*N*-dimethylaniline was eluted within 5 min); the inset are the mass spectra corresponding to iodo-derivative and the internal standard peaks. The electron impact (70 eV) mass spectrum contained the molecular ion as base peak along with diagnostic fragment ions. Laboratory table salt samples were prepared by adding known amounts of iodate to sodium chloride that was found to be free from any iodide or iodate by blank determinations, and mixing thoroughly. Agreement between the standard additions to table salts, pharmaceuticals and milk powder samples, and the mass of iodine found by the present method served to validate the new method; the average recovery found was 100.7% (range 96.5–107.0%) with an average R.S.D. of 3.1% (range 2.6–4.5%). The results obtained are given in Tables 1 and 2. The peroxydisulfate mineralization method was validated by analyzing a certified milk powder sample (Lactogen, Table 2) when iodine found by this method agreed well with the reference value; the average recovery being 101.2% with an R.S.D. of 3.6%.

Table 1
Determination of total iodine in table salts

Sample	Iodine[a]/(mg kg^{-1})	Iodine spiked[a]/(mg kg^{-1})	Iodine found[b]/(mg kg^{-1})	Sample preparation	Recovery (%)	R.S.D. (%)
Laboratory prepared samples						
1	0	15.0	15.2	SPME	101.4	3.3
2[c]	0	15.0	14.7	SPME	98.0	2.9
3	0	20.0	19.5	SDME	97.5	2.8
4[d]	0	20.0	19.7	SDME	98.5	2.5
5	0	25.0	24.6	SDME	98.4	2.6
6[e]	0	25.0	24.8	SDME	99.2	2.3
Commercially available samples[f]						
7	30	0.0	28.5	SDME		2.9
		15.0	43.2	SDME	98.0	3.2
8	50	0.0	47.7	SPME		2.7
		10.0	58.3	SPME	106.0	3.4
		25.0	73.5	SPME	103.2	3.1

[a] Iodine present/spiked as iodate; results expressed as equivalent mass of iodine.
[b] Each result is the average of five determinations.
[c] Salt sample mixed with bromide (10 mg), iron(II) (5 mg) and nitrate (15 mg).
[d] Salt sample mixed with iron(III) (5 mg), thiosulfate (5 mg) and nitrite (2 mg).
[e] Salt sample mixed with sulfide (3 mg) and thiocyanate (5 mg).
[f] Masses of iodine as claimed on the label are given.

Table 2
Determination of free iodide in pharmaceuticals and total iodine in milk powder and vegetables

Sample	Label claim	Iodide spiked (μg)	Found[a]	Recovery (%)	R.S.D. (%)
Pharmaceuticals					
Cyltabs (Duphar)[b]	65 μg/tablet		64.7 μg/tablet[c]		2.2
		10	74.6 μg/tablet[c]	99.0	2.9
		20	85.4 μg/tablet[c]	103.5	3.1
Revital (Ranbaxy)[d]	100 μg/tablet		110.0 μg/tablet[e]		2.7
		25	134.3 μg/tablet[e]	97.2	3.8
		40	148.6 μg/tablet[e]	96.5	4.5
Workadine (Wockhardt)	5 mg/g		5.34 mg/g[c]		1.2
Betadine (Win Medicare)	5 mg/g		5.95 mg/g[c]		4.1
Cipladine (Cipla)	5 mg/g		5.02 mg/g[e]		1.4
Collosal iodine (Duphar)	8 mg/5 ml		7.89 mg/5 ml[e]		2.5
Milk powder/flour					
Everyday (Nestle)	–		378 μg/g[c]		3.2
Lactogen (Nestle)	92 μg/g		93.8 μg/g[e]		3.8
		10	104.0 μg/g[e]	102.0	2.9
		20	113.5 μg/g[e]	98.5	3.6
Lactogen (Nestle)	92 μg/g		92.5 μg/g[c]		3.4
		10	103.2 μg/g[c]	107.0	3.5
		20	112.4 μg/g[c]	99.5	3.9
Water nut flour	–		159 μg/g[e]		4.0
Vegetables[f]					
Aubergine (purple fruit)	–		1.05 mg/g[e]		5.2
Lotus seeds	–		367 μg/g[c]		4.8
Lotus stem	–		242 μg/g[e]		5.6
Potato	–		2.13 mg/g[e]		5.3

[a] Each result is the average of five determinations.
[b] Each tablet contains Vitamin A (2500 units), Vitamin B1 (1 mg), Vitamin B2 (2 mg), Vitamin B6 (0.5 mg), Vitamin B12 (1 μg), folic acid (0.2 mg), niacinamide (15 mg), Vitamin C (30 mg), manganese(II) sulfate (1.35 mg), magnesium sulfate (1.25 mg), ferrous sulfate (16.75 mg), copper(II) sulfate (2.5 μg), ammonium molybdate (5 μg) and calcium fluoride (325 μg).
[c] Sample preparation by SPME.
[d] Each tablet contains Vitamin A (2500 units), Vitamin B1 (1 mg), Vitamin B2 (1.5 mg), Vitamin B6 (1 mg), Vitamin B12 (1 μg), Vitamin C (50 mg), nicotinamide (10 mg), iron(II) fumarate (30 mg), copper(II) (as sulfate) (0.5 mg) and zinc (as oxide) (10 mg).
[e] Sample preparation by SDME.
[f] Mass of iodine in dried mass of vegetable is given.

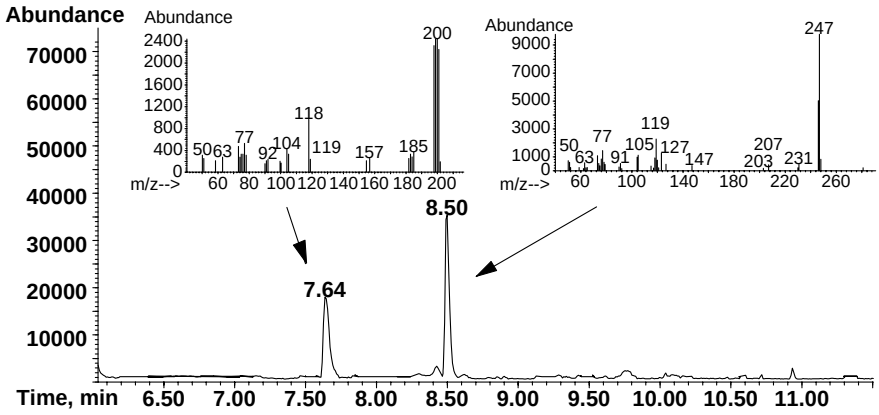

Fig. 2. Standard total ion chromatogram of 10 μg l^{-1} iodide after derivatization to 4-iodo-*N*,*N*-dimethylaniline (retention time 8.50 min) and 2.5 μg l^{-1} 4-bromo-*N*,*N*-dimethylaniline (retention time 7.64 min), used as the internal standard, after SPME on 100 μm PDMS fibre. The inset are corresponding electron impact mass spectra of peaks.

3.4. Calibration graph and detection limits

Ratio of peak areas of iodo-derivative to that of 4-bromo-*N*,*N*-dimethylaniline internal standard was plotted against the concentration of iodide. A rectilinear calibration graph (twenty concentration levels; sample size 2 ml) was obtained for 0.1 μg–10 mg l^{-1} iodide by both extraction methods, the correlation coefficient and limit of detection (LOD) [32] were 0.9995 and 25 ng l^{-1} iodide by SPME method, and 0.9998 and 10 ng l^{-1} iodide by SDME method, respectively. The LOD was no better than found earlier [19], 8 ng l^{-1} iodide, however, the sample volume required was 10 ml. In precision studies, six aliquots of the same sample were separately derivatized and one injection each was made. The R.S.D. for 0.1 and 5 μg l^{-1}, 0.1, 1 and 10 mg l^{-1} iodide standards found by SPME (SDME) methods were respectively 5.2% (2.8%), 4.3% (2.7%), 3.7% (1.8%), 3.3% (2.0%) and 2.5% (1.7%). Data on LOD and precision of two methods served to indicate that SDME was more efficient technique than SPME for the present system. Moreover, the SDME was simpler to perform and cost effective.

3.5. Analysis of real samples

The present method has been applied to determine total iodine in table salt, pharmaceuticals, milk powder and vegetables (Table 2). Standard addition method was used for the validation of results. Typical chromatograms obtained for these analyses involving sample preparation by SDME are given in Fig. 3. Many of the active substances and

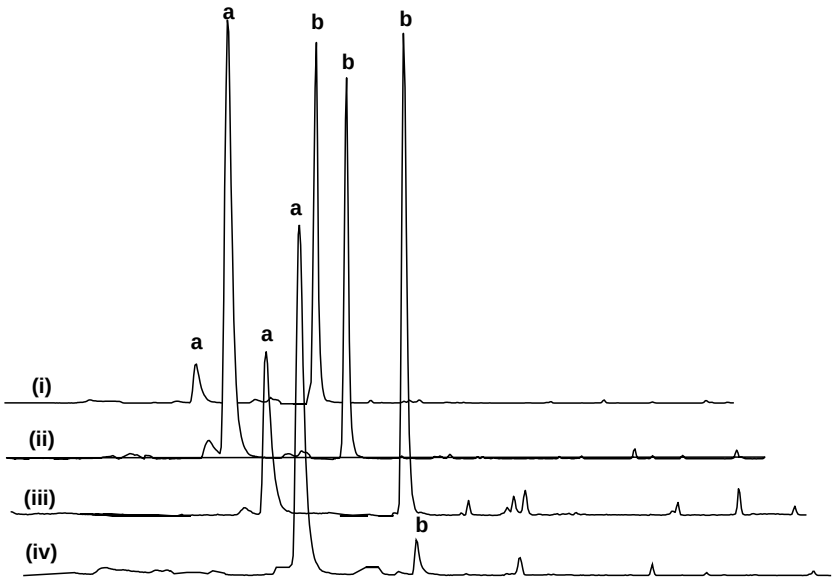

Fig. 3. Total ion chromatograms obtained for the determination of iodide in (i) revital and (ii) cipladine drug formulations, (iii) lactogen milk power and (iv) aubergine (purple fruit) (last two samples involving mineralization by peroxydisulfate oxidation) by derivatization and SDME; peaks designation (a) the internal standard 4-bromo-*N*,*N*-dimethylaniline, and (b) 4-iodo-*N*,*N*-dimethylaniline.

excipients of drug samples did not affect the results nor impaired with the quality of the chromatogram.

4. Conclusions

The proposed reaction scheme is a straightforward conversion of iodide into 4-iodo-*N*,*N*-dimethylaniline that is rapid and unaffected by the presence of many ionic substances as present in salts and pharmaceuticals, or get into the sample during mineralization of milk powder and vegetables. 4-Iodo-*N*,*N*-dimethylaniline is a good candidate for extraction by SPME and SDME, and for GC–MS for its sensitive detection and identification. The aqueous sample can be subjected to cleanup by SPE with a C_{18} cartridge when organic matter as found in pharmaceuticals are removed. Derivatization and extraction results in simple chromatogram. Elevated ionic concentrations decrease the extraction efficiency by both methods, however, the high sensitivity of the present method allows dilution of such samples before extraction to minimize this effect. SDME is more efficient than SPME for the present system as it has better limit of detection and precision. Moreover, the SDME is simpler to perform, naturally free from memory effects and cost effective.

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