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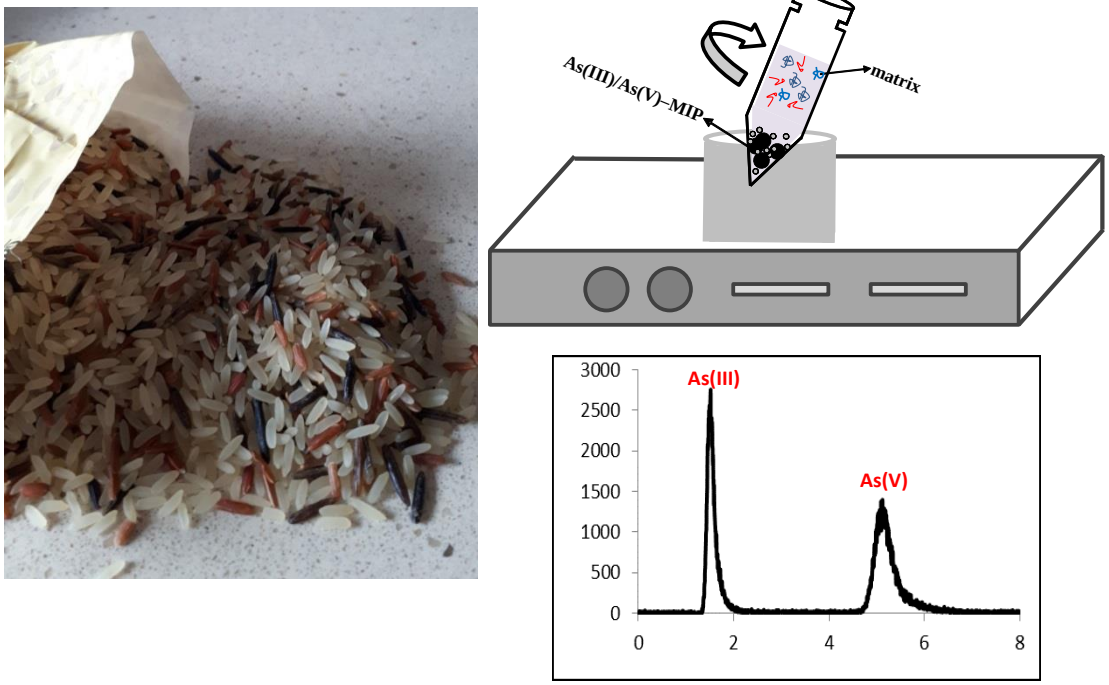
Highlights:

- A vortex-assisted dispersive micro-SPE was used to separate and pre-concentrate iAs
- The ion-imprinted polymeric sorbent was selective for iAs
- iAs (As(III) plus As(V)) can be assessed by ICP-MS
- As(III) and As(V) species can be assessed by HPLC-ICP-MS
- The LOQ of the method is lower than the iAs levels in rice set by safety authorities

Graphical Abstract (for review)



Ionic imprinted polymer – vortex-assisted dispersive micro-solid phase extraction for inorganic arsenic speciation in rice by HPLC-ICP-MS

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Abstract

This study combines ultrasound-assisted extraction and vortex-assisted dispersive micro-solid phase extraction using an ionic imprinted polymer as a selective sorbent for rapid isolation and pre-concentration of inorganic arsenic species (As(III) and As(V)) in extracts from rice samples prior to their determination by high performance liquid chromatography coupled to inductively coupled plasma mass spectrometry. All factors affecting the ultrasound assisted extraction of the species from rice (ultrasound amplitude, sonication time and sonication mode) and their selective pre-concentration by ionic imprinted polymer-based vortex-assisted dispersive micro-solid phase extraction (sorbent amount, extract pH, vortex extraction time and speed, eluting solution and vortex elution time and speed) were optimized. The analytical performance of the procedure was studied at optimum conditions: ultrasound continuous sonication at 40% amplitude for 1.0 min using 1:1 methanol/ultrapure as an extractant, 50 mg of sorbent, extract pH at 8.0, vortex loading at 1000 rpm for 1.0 min, and elution with ultrapure water by vortexing at 1000 rpm for 1.0 min, pre-concentration procedure which leads to a pre-concentration factor of 10. The limits of detection obtained for As (III) and As (V) were 0.20 and 0.41 μg kg^{-1}, respectively, and were well below the maximum levels

established by the European Union in rice and rice containing products. The method was found to be precise (intraday and interday relative standard deviations ≤ 11%) and selective. The accuracy was confirmed by analysing the ERM-BC211 (rice, As species) certified reference material, and the method was successfully applied to commercial rice samples.

Keywords

Dispersive micro-solid phase extraction, inorganic arsenic, ionic imprinted polymer, rice

1. Introduction

Consumption of contaminated water and food is one of the major sources of exposure to toxic contaminants such as arsenic (As) for humans [1]. Arsenic toxicity depends on its chemical form, solubility and many other intrinsic and extrinsic factors, and the most toxic forms of arsenic are the inorganic arsenic species (iAs) [trivalent arsenite As(III), which is 2-10 times more toxic than pentavalent arsenate As(V)] [2].

Rice is one of the major staple foods for about 50% of the world population, mainly from the Asian and African countries [3]. Approximately 50% of total arsenic in rice is inorganic arsenic, ranging from 0.4 to 100%. Therefore, the development of simple, sensitive, rapid and reliable methods for the determination and speciation of iAs in rice is of great relevance.

The determination of iAs species in rice requires close attention to sample preparation strategies [4], and there are several sample preparation methods that have been used for As extraction from rice with different heating devices [5-8], or by speeding up the extraction with ultrasound [9,10] or microwave energy [11-13] assistance.

Conventional solid-phase extraction (SPE) is one of the most common and popular sample pre-treatment techniques, and drawbacks of conventional cartridges-based SPE can be overcome by dispersing the sorbent into the liquid sample/extract. The technique, referred to

as dispersive solid phase extraction (DSPE) [14], and as dispersive micro solid-SPE (D-μ-SPE) when using a small amount (μg or mg range) of micro- or nanosorbents in the sample [15]. D-μ-SPE is an environmentally-friendly and miniaturized extraction technique that speeds up mass transference, reduces the extraction and desorption times, and can be used for extract clean-up and targets pre-concentration [16, 17]. A wide range of materials can be used as sorbents for D-μ-SPE, such as silica nanoparticles, carbon nanotubes, graphene, graphene oxide, metal organic and zeolite imidazolate frameworks, immunosorbents, and molecularly or ionic-imprinted polymer (MIP/IIP), the latter proposed for selectivity improvement [16].

Dispersion can be enhanced by applying ultrasound (ultrasound-assisted dispersive micro-solid phase extraction, UA-D-μ-SPE), air (air-assisted dispersive micro-solid phase extraction, AA-D-μ-SPE), and vortex stirring (vortex-assisted dispersive micro-solid phase extraction, VA-D-μ-SPE) [15,18]. Most applications have been described for organic target pre-concentration [15-17]. Regarding metals, pure nanosilica and nanosilica-ionic liquid hybrid material, and carbon nanotubes have been used for D-μ-SPE of Se(IV) [19,20] and As(V) [21] before electrothermal atomic absorption spectrometry (ETAAS).

The high selectivity offered by MIP as sorbents for D-μ-SPE and the simplicity and speed of the technique can be an appealing combination for efficient and fast clean-up and pre-concentration purposes. Some examples can be found in the literature such as those that use magnetic MIPs and VA-D-μ-SPE for screening of dicofol in tea samples [22] and ciprofloxacin in human serum, plasma, urine and pharmaceutical samples [23]. The benefits of imprinted polymer combined with D-μ-SPE for metallic species have been yet not explored, and the aim of the current study has been the development and application of an IIP selective to iAs (As(III) and As(V)) as a sorbent for VA-D-μ-SPE. Arsenic species (As(III) and As(V) included) have been isolated from rice by ultrasound-assisted extraction (UAE) before the selective pre-concentration of iAs by the proposed IIP-VA-D-μ-SPE. Pre-

concentrated iAs species were then separated and determined by high-performance liquid chromatography-inductively coupled plasma mass spectrometry (HPLC-ICP-MS).

2. Materials and methods

2.1. Instrumentation

The ICP-MS was a NexIon 300X (Perkin Elmer, Waltham, MA, USA) with a SeaFast SC2 DX autosampler (Elemental Scientific, Omaha, NB, USA). The chromatographic system consisted of a Flexar LC HPLC instrument (LC pump, column oven, and LC autosampler) from Perkin Elmer, equipped with a PRP×100 column (10 µm, 100 Å SS, 4.1× 100 mm) and a PRP×100 guard column (10 µm, 25 × 2.3 mm) from Hamilton (Reno, NV, USA). A low-profile roller (Stovall, Greensboro, NC, USA), placed inside a Boxcult temperature-controlled chamber (Stuart Scientific, Surrey, UK), was used for IIP synthesis. Fourier transform infrared spectrometry (FT-IR) with ATR correction (instrument Spectrum-Two, Perkin Elmer), and scanning electron microscopy (SEM) with a ZEISS EVO LS 15 instrument (Carl Zeiss, Oberkochen, Germany) were used for IIP characterization. Other devices were: a VibraCell VCx 130 ultrasonic processor (Sonics, Newtown, CT, USA), an USC60TH ultrasonic cleaner bath (45 kHz, 120 W) from VWR (Leuven, Belgium), a Reax top vortex mixer (Heidolph, Schwabach, Germany), a 2K15 ultracentrifuge (Sigma, Osterode, Germany), a Basic 20 pH meter (Crison, Barcelona, Spain), an oven model 207 from Selecta (Barcelona, Spain), a Taurus 850 domestic blender (Taurus, Barcelona, Spain), a Miniplus 3 peristaltic pump (8 channels) from Gilson (Middleton, WI, USA), and a Classic ML analytical balance (Mettler Toledo, Columbus, OH, USA).

2.2. Reagents

Ultrapure water (resistivity of 18.2 MΩ cm) was from a Milli Q-A10 system (Millipore Co., Billerica, MA, USA). Sodium (meta)arsenite and divinylbenzene (DVB) were from Sigma-

Aldrich (St. Louis, MO, USA); 1-vinyl imidazole and 2,2'-azobisisobutyronitrile (AIBN) from Fluka (Buchs, Switzerland); ammonium chloride, ammonium hydroxide and methanol from Merck (Darmstadt, Germany); ammonium hydrogen carbonate, acetic acid from Panreac (Barcelona, Spain); and ammonium dihydrogen phosphate from BDH (Poole, United Kingdom). As(III) standard solution in hydrochloric acid (1000 mg L^{-1}) and As(V) standard solution in water (1000 mg L^{-1}) were from Merck, while monomethyl arsenic (MMA) and dimethyl arsenic (DMA) standard solutions (1000 mg L^{-1} as arsenic**)** were prepared by dissolving appropriate amounts of >98% $CH_3AsO(ONa)_2 \cdot 6H_2O$ (Carlo Erba, Milan, Italy) and >98% $C_2H_6AsNaO_2 \cdot 3H_2O$ (Merck), respectively. Single stock standard solutions (1000 mg L^{-1}) of Ca, Co and Mg (Merck), Cr, Hg, K, P, Pb and Zn (Scharlab, Barcelona, Spain), Cd, Cu, Fe, Ge, Sc, and Rh from Perkin Elmer (Shelton, CT, USA). The certified reference material ERM-BC211 (rice, As species) was from the Institute for Reference Materials and Measurements (Geel, Belgium). Other consumables were Durapore 0.22 µm membrane filters (Millipore), 2.0 mL polypropylene microtubes tubes (Labbox, Barcelona, Spain), 1.52 mm i.d. PVC 2-stop tubing (SCP Sciences, Baie-D'Urfe, Quebec, Canada), replacement Teflon frits (Supelco, Bellefonte, PA, USA), and 5.0 mL disposable syringes (Dispomed, Gelnhausen, Germany).

2.3. Synthesis of the ionic imprinted polymer

Details regarding As (III)-based IIP synthesis can be found elsewhere [24] and consisted of a template/bifunctional monomer/cross-linker molar ratio fixed at 1:4:20 [1.6 mmol of $NaAsO_2$ (template), 6.5 mmol of 1-vinylimidazole (bi-functional monomer), and 32 mmol of DVB (cross-linker)] and 20 mL 1:3 acetic acid/methanol porogen. The presence of N moieties in the bifunctional monomer 1-vinylimidazole allows the interaction with the hydroxyl groups in oxyanions such as As(III) and As(V) [25]. After adding the initiator (AIBN, 40 mg) and purging (N_2 for 10 min), polymerization was performed in a low-profile roller (rotation of the

tubes at 33 rpm around the long axis) placed inside a temperature-controllable chamber at 60°C for 12 h. The resulting polymer was washed with 5.0 mL methanol three times, and oven-dried at 40ºC overnight. Template removal was performed by packaging approximately 200 mg of IIP into 5.0 mL syringes between two Teflon frits, and by passing 200 mL of 2.0 M HNO_3 at a flow rate of 1.0 mL min^{-1} until the last leachate solution was free of As (ICP-MS analysis). The polymer particles were washed with ultrapure water and dried in a desiccator. Non-imprinted polymers (NIPs) were synthesized using the same procedure but in the absence of the As(III). Details regarding IIP characterization is given in Electronic Supplementary Information (ESI).

2.4. Rice samples

Rice samples were purchased in local supermarkets at Santiago de Compostela. Portions of 100 g were first ground to fine powders using a domestic blender, and powdered samples were then stored in pre-cleaned polyethylene bottles with hermetic seals at 4°C before use.

2.5. Microwave assisted acid digestion

Portions of 0.500 g of rice samples and CRM (three replicates each one and at least two reagent blanks in each microwave acid digestion set) were directly weighted in the Teflon reactors and were mixed with 3.0 mL of 69 %(m/v) nitric acid, 1.0 mL of 33 %(m/v) hydrogen peroxide, and 4.0 mL of ultrapure water. After closing the reactors they were subjected to microwave energy (800 W power) in a four-stage heating program involving a first heating ramp from room temperature to 90°C in 4.0 min, followed by a second heating ramp from 90°C to 150°C in 7.0 min, and a third heating ramp from 150°C to 200°C in 8.0 min. Finally, the reactors were heated at 200°C for 20 min, and were then allowed to cool down for 1.0 h. The acid digests were finally made up to 25 mL with ultrapure water and stored in polyethylene flasks.

2.6. Ultrasound assisted extraction (UAE)

Rice sub-samples of 1.000 g were weighed into a 15 mL centrifuge tube, and 10 mL of the extracting solution (1:1 methanol/water [26]) were added. The ultrasound probe operating in continuous mode (frequency of 20 kHz with a power of 68 W, and amplitude at 40% of the maximum range) was immersed into the solution that was irradiated by ultrasonic waves for 1.0 min (the test tubes were immersed in an ice-bath to avoid temperature increases). Then, the extract was isolated from the solid residues by ultracentrifugation (4°C, 3000 rpm, 10 min) before further VA-D-µ-SPE pre-concentration.

2.7. Vortex-assisted dispersive micro-solid phase extraction (VA-D-µ-SPE)

For VA-D-µ-SPE, portions of 50 mg of IIP (or NIP in some experiments) in 2 mL microtubes were conditioned by adding 1.5 mL of ultrapure water (pH 8.0, adjusted using 0.1M/0.1 M NH_3/NH_4Cl buffer solution), and subjecting the mixture to vortex stirring (1000 rpm, 1 min) and ultracentrifugation (4 °C, 12000 rpm, 10 min) to discard the liquid supernatant. A volume of 1.5 mL of rice extract (pH fixed at 8.0) was added, and the mixture was vortexed (1000 rpm, 1 min) and ultracentrifuged (4 °C, 12000 rpm, 10 min). After discarding the liquid phase, elution was performed using 150 µL of ultrapure water and vortexing (1000 rpm, 1 min) and centrifugation (4 °C, 12000 rpm, 10 min). The supernatants were isolated and direct measured by HPLC-ICP-MS. The experiments were performed in triplicate and at least two reagent blanks were prepared for each experiment set.

2.8. ICP-MS and HPLC-ICP-MS measurements

The determination of total As in acid digests from rice, and the multi-element determinations when studying the imprinting effect and cross-reactivity were performed by ICP-MS (operating conditions listed in Table S1 (ESI) by using 1.0 %(v/v) nitric acid matched calibrations covering the 0-100 µg L^{-1} concentrations range.

As(III) and As(V) in the extracts from rice were determined by HPLC-ICP-MS under operating conditions listed in Table 1. Quantification was performed using the standard

addition technique by spiking rice extracts with As(III) and As(V) concentrations within the 0.1 – 2.0 μg L^{-1}, and subjecting the spiked extracts to the VA-D-μ-SPE process (standard addition calibration covering As(III) and As(V) concentrations from 1.0 to 20 μg L^{-1}, taking into account a pre-concentration factor of 10). External calibration curves (used during the optimization of VA-D-μ-SPE and UAE conditions) consisted of mobile phase ($(NH_4)H_2PO_4$, 15 mmol, pH 6.0) matched standards covering As(III) and As(V) concentrations within the 1.0 – 20 μg L^{-1} range. Chromatograms for an aqueous standard (1.0 μg L^{-1}), an extract from the CRM and two rice samples (basmati and wild rice) are given in Figure 1(a-d).

3. Results and discussion

3.1. Optimization of VA-D-μ-SPE

The VA-D-μ-SPE procedure was optimized using rice extracts aliquots (1.5 mL each one) spiked with iAs (2.0 μg L^{-1} for As(III) and As(V)). For As(III) and As(V) analytical recovery assessment, un-spiked rice extracts were also analysed in each set of conditions. Extracts from rice (Jasmin) were obtained by applying non-optimised UAE conditions (continuous sonication at 60% amplitude for 5.0 min). Several parameters affecting the VA-D-μ-SPE process (rice extract pH, loading vortex stirring time and speed, eluting vortex time and speed, and IIP amount)were fully evaluated (experiments performed in triplicate and at least two blanks prepared for each set of tested conditions). As(III) and As(V) concentrations (analytical recoveries) were assessed using aqueous calibrations and after subtracting the As(III) and As(V) contents in the un-spiked rice extracts.

3.1.1. Rice extract pH and loading vortex stirring time and speed

Variables affecting the loading stage were studied using un-optimized eluting conditions (water as extractant, and elution vortex stirring speed at 2000 rpm for 2.0 min). The pH of the rice extract plays an important role for favouring the interactions between dissolved analytes (As(III) and As(V)) and IIP particles during dispersion. The influence of the extract pH was

tested by varying the pH from 6.0 (extract pH after UAE) to 10.0 (pHs higher than 6.0 were obtained by adding a few drops of ammonia to the 10 mL extract obtained after UAE). The spiked 1.5 mL aliquots of rice extracts after pH adjustment were mixed with 50 mg of IIP, and the loading step was carried out by vortexing at 2000 rpm for 3.0 min (non-optimized elution conditions as explained above). Figure 2(a) shows that As (V) analytical recovery is high (approximately 40%) when fixing the pH within the 6.0-8.0 range, and decreases at the highest tested pHs (9.0 and 10.0). However, As (III) analytical recovery is highest (approximately 40%) when loading rice extracts at pH 8.0. These findings agree with As(III)/As(V)-pH dependence [27], which implies As(V) and As(III) species prevalent at neutral pH and/or at slightly alkaline pHs. The highest iAs analytical recoveries were observed at pH 8.0, and this pH was selected.

The role of the vortex agitator is to disperse the IIP into the sample solution to improve the extraction efficiency. By fixing the extract pH at 8.0 and the loading vortex time at 2.0 min, several loading vortex speeds (from 500 to 2500 rpm, 500 rpm intervals) were tested. Analytical recoveries for As(III) and As(V) were found to be dependent of the vortex speed (Figure 2(b)). Low vortex speed (500 rpm) and vortex speeds higher than 1000 rpm led to poor extraction yields. The low analytical recoveries when vortexing at the lowest speed is attributed to an inefficient contact between As ions and the dispersed IIP particles. In addition, analyte-sorbent desorption (back diffusion), reported for several microextraction techniques [28-30], are responsible for the low extraction yields when using high vortex speeds. Taking into account these findings, the loading vortex speed was fixed at 1000 rpm.

Finally, the vortex rotational speed was fixed at 1000 rpm, and loading experiments (rice extract at pH 8.0) were performed by varying the vortex stirring time from 1.0 to 5.0 min. Calculated iAs analytical recoveries (Figure 2(c)) show that the effect of the vortexing time during the loading stage is not significant, and the loading vortex time was set at 1.0 min.

3.1.2. Eluting vortex stirring time and speed

In the current experiments, 150 µL of ultrapure water were used for iAs species elution. Several elution times (within the 1.0-5.0 min range) and elution speeds (from 500 to 2500 rpm) were tested under optimized loading vortex conditions. As shown in Figure 3(a,b), iAs analytical recoveries were not significantly different within the time/speed range studied, and elution vortex conditions were finally fixed at 1000 rpm for 1.0 min.

3.1.3. Effect of the IIP sorbent amount

It is well known that the use of appropriate amounts of the IIP sorbent affects the extraction efficiency of the VA-D-µ-SPE procedure [16]. Therefore, several amounts of IIP (10, 20, 50 and 100 mg) were used to evaluate the recovery of As(III) and As(V) using the above optimized conditions. Experiments in triplicate (Figure 3(c)) showed that iAs species recoveries were gradually increased up till 50 mg of IIP sorbent, and there were no statistically significant differences between the recoveries of As(V) when using 50 or 100 mg of IIP. Hence, 50 mg of IIP was found to be adequate to quantitatively retain iAs. This mass of polymer was thus selected for further studies.

3.2. Optimization of ultrasound-assisted extraction (UAE)

Despite water is a common extractant for iAs from biological matrices, methanol/water mixtures (typically 1:1 ratio) have been found to be effective for extracting both iAs and organic As species from solid matrices, rice included [31]. A 1:1 methanol/water mixture was selected as an extract for isolating all As species from rice (MMA and DMA included) and demonstrating the high selectivity capacity of the prepared IIP for iAs. The extractive procedure has been assisted by ultrasound (ultrasonic probe) which highly enhances the extractive capabilities of solvents, which also guarantees an efficient extraction of iAs using methanol/water mixtures instead of water. In addition, the use of an ultrasound probe for assisting As species isolation from rice could lead to a more efficient As species extraction,

and the efficiency of the As species releasing could not be affected by the rice's matrix (white, brown rice types).

Three factors affecting the extractive process (use of ultrasound probe for assisting the extraction), ultrasounds amplitude (20, 30, 40, 50, 60, 70 and 80%), sonication time (2, 5, 7, 10, 15 min), and sonication mode (continuous and non-continuous), have been fully evaluated using 10 mL of 1:1 methanol/ultrapure water as an extractant. Experiments were performed in triplicate with 1.0000 g subsamples spiked with As (III) and As (V) at 5.0 µg L^{-1}, and the obtained extracts were further subjected to the optimized VA-D-µ-SPE. Un-spiked rice subsamples were also subjected to the tested conditions in order to properly assess the analytical recovery of the spiked As(III) and As(V) concentrations after HPLC-ICP-MS (use of an aqueous calibration). The test tubes containing the extractant and the sample were immersed in an ice-bath during the ultrasonication process to avoid temperature increases and solvents evaporation.

Results (As(III) and As(V) analytical recoveries for each set of conditions) show that ultrasounds amplitude (Figure S3(a), ESI) and continuous and non-continuous sonication (Figure S3(c), ESI) do not affect iAs extraction from rice. A continuous sonication at 40% ultrasound amplitude was chosen. Regarding the sonication time, Figure S3(b)(ESI) shows similar As(III) and As(V) analytical recoveries within the 2.0 – 10 min range; whereas the extraction efficiency of both species is impaired at high sonication times (15 min). The optimum sonication (extraction) time was therefore fixed at 2.0 min.

3.3. Imprinting effect and cross-reactivity (IIP selectivity) studies

The imprinting effect (iAs adsorption onto IIP particles through the imprinted recognition cavities) and the selectivity (avoidance of adsorption of other elements and/or arsenic species through the imprinted recognition cavities) were evaluated by subjecting aqueous standards of As(III) and As(V) at 5 µg L^{-1}, aqueous standards containing microelements (Cd, Co, Cr,

Cu, Mn, Ni, Pb, Hg, and the As species DMA and MMA) at concentrations of 2.0 µg L^{-1}, and aqueous standards containing macro-elements (Al, Ca, Fe, K, Mg, and Zn) at concentrations of 5.0 µg L^{-1}, to the optimized VA-D-µ-SPE procedure using IIP and NIP as sorbents (experiments in triplicate for MMA and DMA experiments, and experiments replicated six times for other elements). Extracts regarding MMA and DMA experiments were directly analysed by HPLC-ICP-MS (conditions in Table 1); whereas, extracts when testing other elements were analysed by ICP-MS (conditions listed in Table S1, electronic supplementary information, ESI). In the latter case, two eluates (150 µL each one) were combined and diluted up to 2.0 mL with 1.0 %(v/v) nitric acid before ICP-MS analysis.

Imprinting effect and selectivity were assessed by calculating the extraction efficiency (EF) or analytical recovery, the distribution ratio ($D_{(M)}$), and the selectivity coefficient ($S_{(M)}$) according to

$$EF\ (\%)=\frac{A_2}{A_T}\times 100 \quad \text{Equation 1}$$

$$D_{(M)}=\frac{A_2}{A_1} \quad \text{Equation 2}$$

$$S_{(M)}=\frac{D_{(As(III))}}{D_{(M)}} \quad \text{Equation 3}$$

where, A_1 is the amount of metal ion in aqueous solution at equilibrium, A_2 is the amount of metal ion extracted by the IIP/NIP at equilibrium, A_T is the total amount of metallic ion used in the extraction, $D_{As(III)}$ is the distribution ratio for As(III) (template), and D_M is the distribution ratio for other elements/DMA and MMA species.

As expected (Table 2), As(III) and As(V) showed the highest EFs (100% when using IIP as a sorbent); whereas, EFs fall to 31 and 41% for As(III) and As(V), respectively, when using NIP as a sorbent. These finding imply that the interactions between the IIP particles and As(III) (template) and also As(V) are mainly through the imprinted recognition cavities

generated in IIP, and the non-specific interactions (adsorption) are a minority. In addition, the IIP sorbent offers high selectivity against other arsenic species present in rice, such as MMA and DMA, which are not retained in the IIP (EFs lower than 10%) and against other elements, with EFs range from 0 to 20% (Table 2). The low $D_{(M)}$ ratios and high $S_{(M)}$ factors assessed for As(III) and As(V), and the high $D_{(M)}$ ratios and low $S_{(M)}$ factors for MMA and DMA, and other elements (Table 2) confirm that the prepared IIP sorbent is highly selective to iAs.

3.4. Analytical performances of the UAE-VA-D-µ-SPE method

3.4.1. Calibration and matrix effect

As(III) and As(V) aqueous calibrations (pH 8.0, concentrations ranging from 1.0 to 20 µg L^{-1}) and standard addition calibrations (10 mL of rice extracts spiked with As(III) and As(V) within the 0.1 – 2.0 µg L^{-1} range and subjected to the VA-D-µ-SPE procedure) were prepared in triplicate. Taking into account the pre-concentration factor of 10. the concentration levels of the standard addition calibrations varied from 1.0 to 20 µg L^{-1}. The mean slopes for aqueous standards were 865±35 and 812±36 for As(III) and As(V), respectively; whereas, slopes for the standard addition calibration were 627±71 for As(III) and 718±63 for As(V). These differences are attributed to the matrix effect and suggest that a calibration based on standard additions throughout the VA-D-µ-SPE procedure is needed for achieving accurate results. Good linearity (correlation coefficient from 0.995 to 1.00) was observed for aqueous and standard addition curves for both arsenic species.

3.4.2. Limit of detection (LOD) and limit of quantification (LOQ)

The limit of detection (LOD) and limit of quantification (LOQ) were based on the 3σ/10σ criteria (σ is the standard deviation of the measurement of eleven blank samples after applying VA-D-µ-SPE). Instrumental LOD and LOQ for As(III) and As(V) were then obtained by dividing the 3σ/10σ values by the mean slope of the standard addition for each As species, and values of 0.20 µg L^{-1} and 0.67 µg L^{-1} for As(III), and 0.41 µg L^{-1} and 1.38 µg

L^{-1} for As(V) were obtained. LOD/LOQ values after considering the pre-concentration factor of 10 (VA-D-µ-SPE) and the whole UAE process were 0.20 µg kg^{-1} and 0.67 µg kg^{-1} for As(III), and 0.41 µg kg^{-1} and 1.38 µg kg^{-1} for As(V).

As shown in Table S2 (ESI), the assessed LOD for As(III), and in some cases for As(V), is lower than those reported by other authors using HPLC-ICP-MS [6,8,12], electrothermal atomic absorption spectrometry (ETAAS) [32] or hydride generation atomic absorption spectrometry (HG-AAS) [33]. In addition, the LODs are lower than the maximum levels set by the EU [34], the government of Canada [35], and by the U.S. Food and Drug Administration (FDA) [36].

3.4.3. Precision and accuracy

Inter-day precision of the VA-D-µ-SPE and HPLC-ICP-MS procedure was evaluated after the analysis of rice extracts spiked with both iAs species at three concentration levels (0.1, 0.5 and 2.0 µg L^{-1}), and was expressed as the relative standard deviation (RSD) of seven spiking VA-D-µ-SPE experiments for each concentration tested. Similarly, intraday precision was performed by preparing seven standard addition calibrations through the VA-D-µ-SPE procedure in consecutive days, and by replicating three times each concentration level (0.1, 0.2, 0.5, 1.0 and 2.0 µg L^{-1}). RSDs listed in Table 3 show satisfactory inter-day and intraday precision (RSDs lower than 11% for As(III) and lower than 7% for As(V)).

Inter-day and intraday analytical recovery were also obtained from the same experiments performed for inter-day and intraday precision assessment. After subtracting the As(III) and As(V) found in the un-spiked rice extracts, the analytical recovery was assessed by applying the equation 4

$$AR = \frac{[As\ species]_{found}}{[As\ species]_{added}} x100 \quad Equation\ 4$$

where [As species]$_{found}$ is the As(III) or As(V) measured after spiking experiments, and [As species]$_{added}$ is the spiked As(III) or As(V) concentrations.

As shown in Table 3, analytical recoveries within the 89-103% range were obtained for all cases. Because RSDs values lower than 20% for inter-day/intraday precision assays, and analytical recoveries within the 80-120% range for inter-day/intraday analytical recovery assays were obtained, precision and analytical recovery of the proposed method is acceptable. Accuracy was also evaluated by analysing a certified reference material ERM-BC211 with a certified value of iAs of 124±11 μg kg^{-1}. Three subsamples of ERM-BC211 were subjected to the optimised UAE, VA-D-μ-SPE and HPLC-ICP-MS procedure, and the found iAs concentration was 120±5 μg kg^{-1} (concentration calculated by summing the As(III) and As(V) concentrations, 107±5 and 13±1 μg kg^{-1}, respectively, and taking into account the propagation of error for assessing the standard deviation). Results show that there are no statistically significant differences between the certified and the experimental value ($P > 0.05$, t-test, 95% confidence level). As an example, Figure 1(c) shows a chromatogram for an extract obtained from the ERM-BC211. In addition, as listed in Table 4, total As concentration (252±2 μg kg^{-1}) is not statistically different ($P > 0.05$, t-test, 95% confidence level) to the certified total As content in the CRM (260±13 μg kg^{-1}).

Despite the fact that ERM-BC211 is not certified for single As(III) and As(V) concentrations, the As(III) and As(V) concentrations found in the current research are in good agreement with those reported by Maher et al. (106 ±18 μg kg^{-1} of As(III) and 16±6 μg kg^{-1} of As(V)) after a microwave-assisted extraction with 2%(v/v) nitric acid and HPLC-ICP-MS analysis [13]. These authors confirmed the validity of their results using X-ray absorption near edge spectroscopy (XANES) [13]. However, our results are quite different from those reported by Vu et al. (< LOD for As(III) and 134.79 ±10.93 μg kg^{-1} for As(V)) [8]. The high

concentration of As(V) found by these authors could possibly be due to the fast oxidation of As(III) to As(V) during the sample preparation and analysis steps [4,37].

3.4.4. IIP reusability

Reusability of the IIP sorbent was tested by using three single IIP portions (50 mg each) which were used in successive days at the same time that inter-day and intraday assays were performed. In this experiment, rice extracts spiked with 1.0 μg L^{-1} As(III) were subjected to the proposed VA-D-μ-SPE procedure for over 10 days, implying 23 sorption-desorption cycles each. As shown in Figure S3 (ESI), analytical recoveries for As(III) were found to be within the 80-100% range during at least 20 sorption-desorption cycles. Therefore, the same IIP portion can be reused 20 times with quantitative results.

3.5. Application

The UAE-VA-D-μ-SPE procedure was used for the determination of As (III) and As (V) ions in three rice samples: two white rice (Basmati and Jasmin), and a wild rice (a mixture of white and brown rice). As(III), As(V), and iAs, and also total As concentrations (microwave assisted acid digestion and ICP-MS) are listed in Table 4. In general, As(III) concentrations were higher than As(V) levels in the three rice samples. The iAs concentrations ranged from 30±5 to 213±16 μg kg^{-1}, and are in agreement with the iAs concentrations found in the literature [4]. These results show that the iAs levels in some of the studied commercial rice samples is quite close to the EU/EC regulated values (200 μg kg^{-1} for white rice, 250 μg kg^{-1} for husked rice [34]). Basmati rice surpasses the EU limit for rice destined for the production of food for infants and young children, and the recommended action level guidance by FDA (100 μg kg^{-1} of iAs) [36]. In addition, iAs level in wild rice is also close to the limit proposed by FDA.

Conclusions

The proposed VA-D-µ-SPE procedure based on IIPs as sorbents has demonstrated to offer excellent selectivity for both As(III) and As(V) ions. It can be implemented for the selective assessment (pre-concentration) of iAs without the need for pre-oxidation and/or pre-reduction steps to ensure a quantitative iAs pre-concentration/isolation. Although HPLC-ICP-MS was used as a hyphenated analytical technique for assessing As(III) and As(V) in the current research, the proposed selective pre-concentration method can be used as a previous step for selective and direct iAs quantification by atomic spectrometry techniques such as ICP-MS, inductively coupled plasma – optical emission spectrometry (ICP-OES), electrothermal atomization atomic spectrometry (ETAAS), and hydride generation based atomic spectrometry techniques. VA-D-µ-SPE is a low cost procedure because it does not require sophisticated laboratory devices. In addition, IIP synthesis is not expensive and each 50 mg subsample can be reused at least 20 times. Regarding the proposed UAE procedure for isolating As species from rice, the selected conditions and extractants have proved to avoid As(III) oxidation during the sample pre-treatment (UAE) and pre-concentration step (VA-D-µ-SPE). Finally, the developed sample pre-treatment procedure and HPLC-ICP-MS provided quantitative iAs recoveries and showed good accuracy when analysing the ERM-BC211 certified reference material, and LOD/LOQ values lower than the maximum iAs levels established by several international regulations in rice and rice-based products.

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Conflict of interest

The authors have declared no conflict of interest.

Figure captions

Figure 1. HPLC-ICP-MS chromatograms for a 20 µg L^{-1} As(III) and As(V) aqueous standard (a), and a pre-concentrated extract from ERM-BC211 CRM (b), wild rice (c), and basmati rice (d)

Figure 2. Effect of the extract pH (a), loading vortex speed (b), and loading vortex time (c) on the analytical recovery of As(III) and As(V)

Figure 3. Effect of the elution vortex time (a), elution vortex speed (b), and IIP amount (c) on the analytical recovery of As(III) and As(V)

Table 1. Operating HPLC-ICP-MS parameters

ICP-MS	
Radio frequency power (W)	1600
Ar flow rate (plasma/auxiliary/nebulizer) (L/min)	16/1.2/0.92
KED mode, He flow rate (mL/min)	4
Integration time (ms)	250
Mass monitored	^{75}As
HPLC	
Column	Hamilton PRP×100, 10 µm, 4.1×100 mm
Mobile phase	$(NH_4)H_2PO_4$, 15 mmol, pH 6.0
Flow rate	1 mL min^{-1}, 8.5 min
Injection volume	20 µL

Table 2. Values of extraction efficiencies (%), distribution ratios and selectivity coefficients of IIP and NIP after the VA-D-μ-SPE procedure

	Extraction Efficiency (%)		Distribution ratio (D_M)		Selectivity Coefficient ($D_{As(III)}/D_M$)	
	IIP	NIP	IIP	NIP	IIP	NIP
As (III)	100	31	∞	0.46	-	-
As(V)	100	41	∞	0.70	1	98
MMA	11	2	0.12	0.03	564	2675
DMA	0	2	0	0.03	∞	2684
Al	0	0	0	0	∞	∞
Ca	0	0	0	0	∞	∞
Fe	0	1	0	0.01	∞	6278
K	0	0	0	0	∞	∞
Mg	13	0	0.16	0	441	∞
Zn	18	0	0.22	0	306	∞
Cd	0	0	0	0	∞	∞
Co	0	0	0	0	∞	∞
Cr	0	0	0	0	∞	∞
Cu	0	0	0	0	∞	∞
Mn	5	0	0.05	0	1403	∞
Ni	0	0	0	0	∞	∞
Pb	0	0	0	0	∞	∞
Hg	0	20	0	0.25	∞	280

Table 3. Inter-day and intraday precision and analytical recovery

		As(III)		As(V)	
	Concentration (μg L^{-1})	Analytical recovery (%)	RSD (%)	Analytical recovery (%)	RSD (%)
Interday	0.1	89	11	103	7
	0.5	94	11	97	7
	2.0	93	10	96	7
Intraday	0.1	91	8	99	7
	0.2	99	9	98	5
	0.5	95	8	95	7
	1.0	99	4	97	6
	2.0	89	9	97	7

Table 4. Concentration of total As, iAs, As(III) and As(V) in ERM-BC211 certified reference material and commercial rice samples

Rice type	Total As (µg kg^{-1})	iAs percentage (%)	As(III) (µg kg^{-1})	As(V) (µg kg^{-1})	iAs (µg kg^{-1})[a]
ERM-BC211[b]	252±2	48±2	107±5	13±1	120±5
Wild rice	92±11	101±15	76±17	17+3	93±17
Basmati rice	139±6	92±9	120±13	7±1[c]	127±13
Jasmin rice	51±2	59±10	30±11	< LOD[d]	30±11

(a) Concentration obtained as a sum of As(III) and As(V) concentrations; (b) Certified total As concentration of 260±13 µg kg^{-1}; (c) Concentration between the LOD and the LOQ of the method; (d) Lower than 2.2 µg kg^{-1}

Figure 1

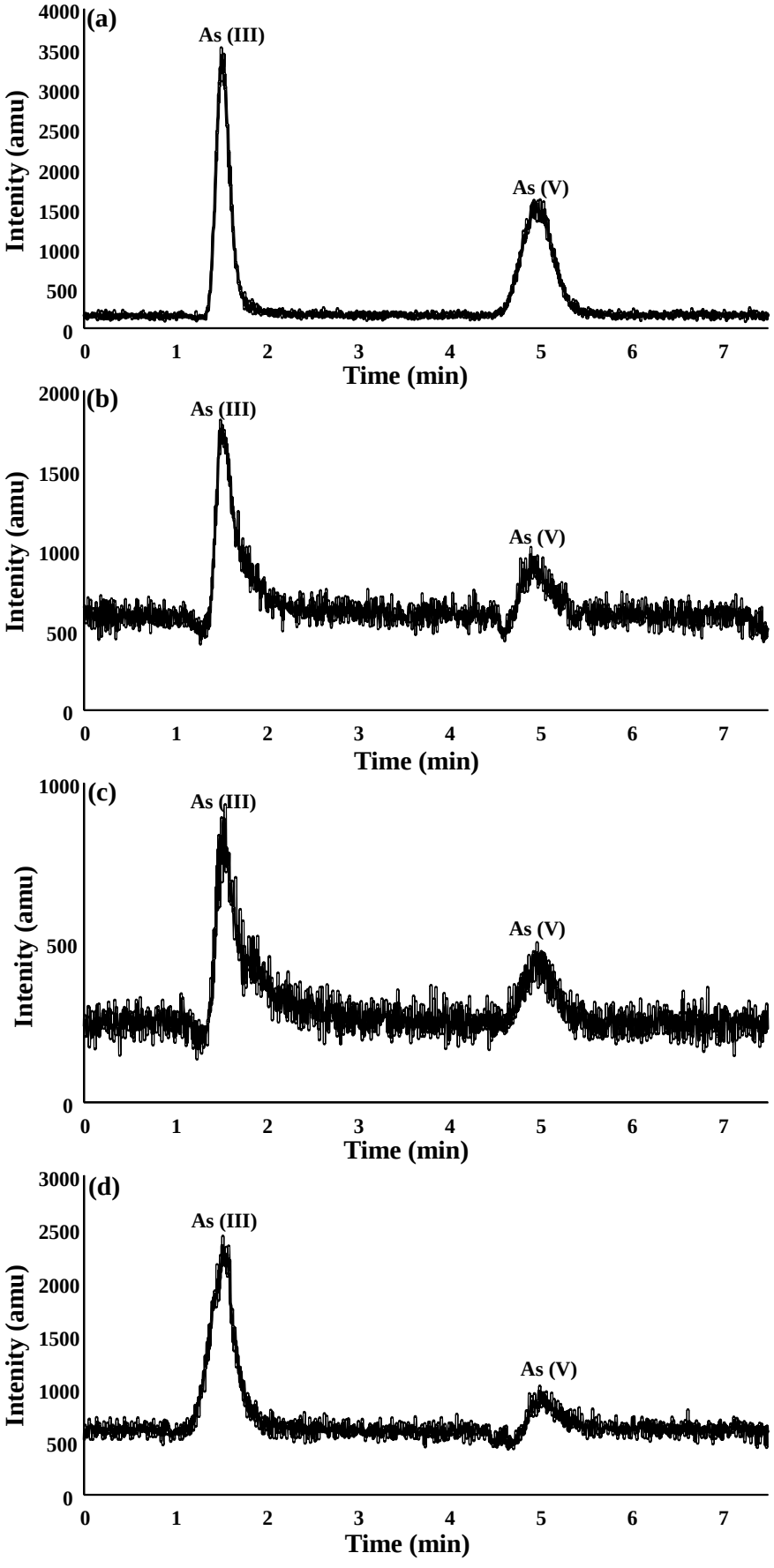
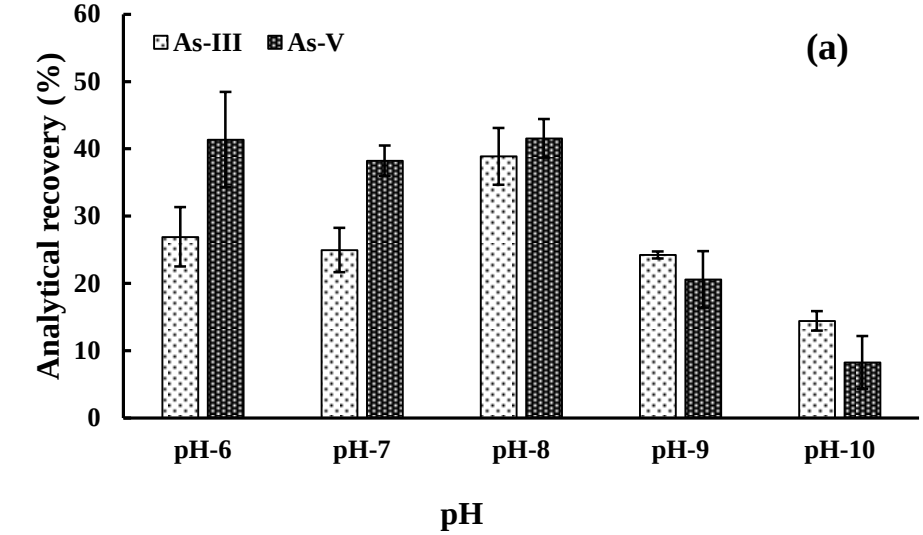
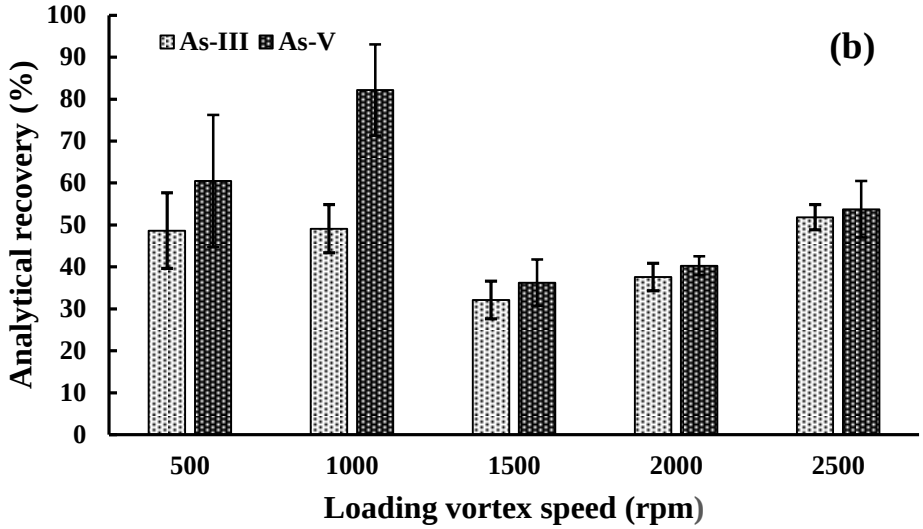

(a)
As (III)
As (V)
Intenity (amu)
Time (min)
(b)
As (III)
As (V)
Intenity (amu)
Time (min)
(c)
As (III)
As (V)
Intenity (amu)
Time (min)
(d)
As (III)
As (V)
Intenity (amu)
Time (min)

Figure 2


As-III
As-V
(a)
Analytical recovery (%)
60
50
40
30
20
10
0
pH-6
pH-7
pH-8
pH-9
pH-10
pH


As-III
As-V
(b)
Analytical recovery (%)
100
90
80
70
60
50
40
30
20
10
0
500
1000
1500
2000
2500
Loading vortex speed (rpm)

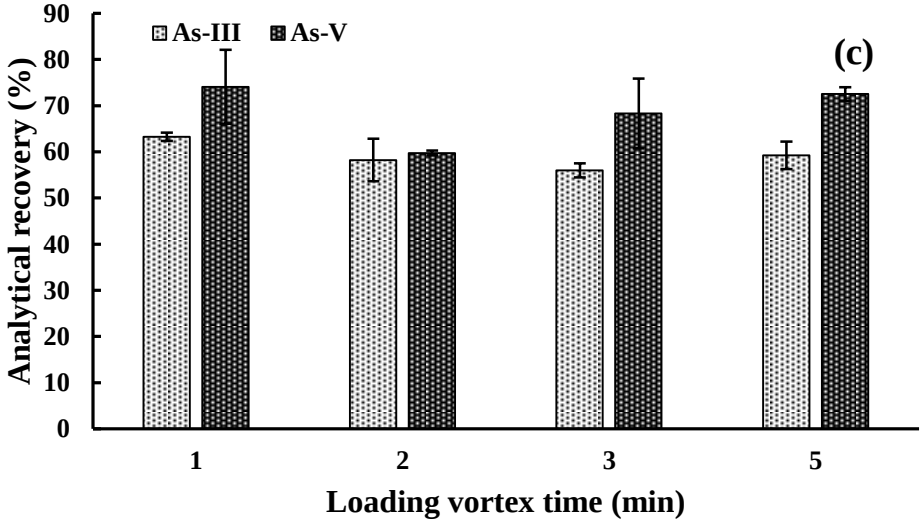
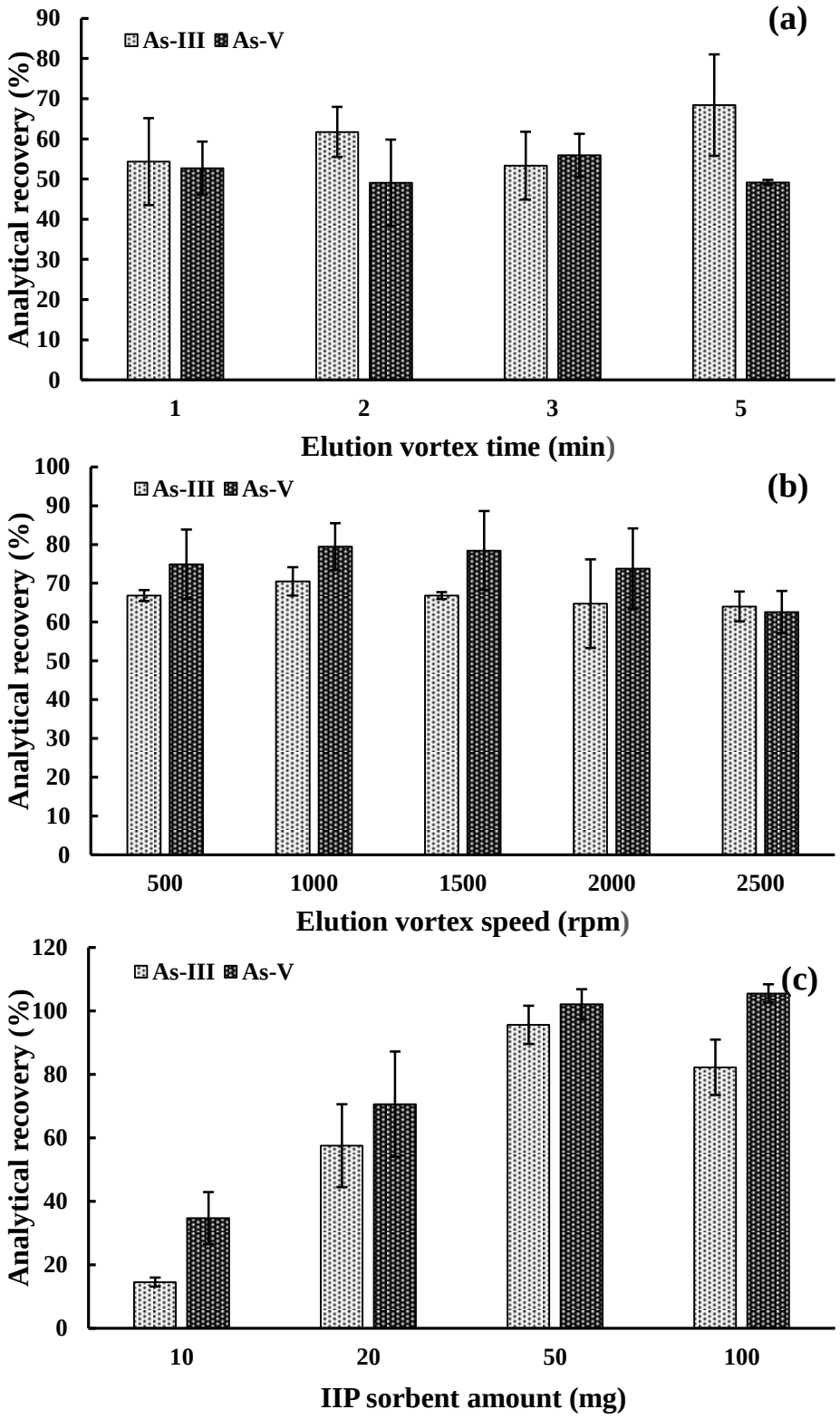

As-III
As-V
(c)
Analytical recovery (%)
90
80
70
60
50
40
30
20
10
0
1
2
3
5
Loading vortex time (min)

Figure 3


(a)
As-III
As-V
Analytical recovery (%)
0
10
20
30
40
50
60
70
80
90
1
2
3
5
Elution vortex time (min)
(b)
As-III
As-V
Analytical recovery (%)
0
10
20
30
40
50
60
70
80
90
100
500
1000
1500
2000
2500
Elution vortex speed (rpm)
(c)
As-III
As-V
Analytical recovery (%)
0
20
40
60
80
100
120
10
20
50
100
IIP sorbent amount (mg)

References

[1] S. Hensawang, P. Chanpiwat, Health impact assessment of arsenic and cadmium intake via rice consumption in Bangkok, Thailand. Environ. Monit. Assess. 189 (2017) 599. https://doi.org/10.1007/s10661-017-6321-8.

[2] P.B. Tchounwou, C.G. Yedjou, A.K. Patlolla, D.J. Sutton, Heavy metal toxicity and the environment, in: A. Luch (Ed.), Molecular, clinical and environmental toxicology, Experientia Supplementum, vol 101, Springer, Basel, 2012, pp. 133-164. https://doi.org/10.1007/978-3-7643-8340-4_6.

[3] T.N. Maraseni, R.C. Deo, J. Qu, P. Gentle, P.R. Neupane, An international comparison of rice consumption behaviours and greenhouse gas emissions from rice production. J. Clean. Prod. 172 (2018) 2288-2300. https://doi.org/10.1016/j.jclepro.2017.11.182.

[4] M. Welna, A. Szymczycha-Madeja, P. Pohl, Comparison of strategies for sample preparation prior to spectrometric measurements for determination and speciation of arsenic in rice, Trends Anal. Chem. 65 (2015) 122-136. https://doi.org/10.1016/j.trac.2014.11.007.

[5] T. Narukawa, A. Hioki, K. Chiba. Speciation and monitoring test for inorganic arsenic in white rice flour, J. Agric. Food Chem. 60 (2012):1122-1127. https://doi.org/10.1021/jf204240p

[6] S.C. Sofuoglu, H. Güzelkaya, Ö. Akgül, P. Kavcar, F. Kurucaovalı, A. Sofuoglu, Speciated arsenic concentrations, exposure, and associated health risks for rice and bulgur, Food Chem.Toxicol. 64 (2014) 184-191. https://doi.org/10.1016/j.fct.2013.11.029.

[7] K. Baba, T. Arao, Y. Maejima, E. Watanabe, H. Eun, M. Ishizaka, Arsenic speciation in rice and soil containing related compounds of chemical warfare agents, Anal. Chem. 80 (2008) 5768-5775. https://doi.org/10.1021/ac8002984.

[8] H.A. Vu, M.H. Nguyen, H.A. Vu-Thi, Q. Do-Hong, X.H. Dang, T.N.B. Nguyen, H.Q. Trinh, T. L. Bich, T.T. Nguyen, D. Le-Van, M.B. Tu, D.B. Chu, Speciation analysis of

arsenic compounds by high-performance liquid chromatography in combination with inductively coupled plasma dynamic reaction cell quadrupole mass spectrometry: application for vietnamese rice samples, J. Anal. Meth. Chem., 2019 (2019) 5924942. https://doi.org/10.1155/2019/5924942.

[9] E. Yilmaz, Use of hydrolytic enzymes as green and effective extraction agents for ultrasound assisted-enzyme based hydrolytic water phase microextraction of arsenic in food samples, Talanta. 189 (2018) 302-307. https://doi.org/10.1016/j.talanta.2018.07.006.

[10] E. Sanz, R. Muñoz-Olivas, C. Cámara, A rapid and novel alternative to conventional sample treatment for arsenic speciation in rice using enzymatic ultrasonic probe, Anal. Chim. Acta. 535 (2005) 227-235. https://doi.org/10.1016/j.aca.2004.12.021.

[11] T. Narukawa, K. Inagaki, T. Kuroiwa, K. Chiba, The extraction and speciation of arsenic in rice flour by HPLC–ICP-MS, Talanta 77 (2008) 427–432. https://doi.org/10.1016/j.talanta.2008.07.005.

[12] G. Raber, N. Stock, P. Hanel, M. Murko, J. Navratilova, K.A. Francesconi, An improved HPLC–ICPMS method for determining inorganic arsenic in food: Application to rice, wheat and tuna fish, Food Chem. 134 (2012) 524-532. https://doi.org/10.1016/j.foodchem.2012.02.113.

[13] W. Maher, S. Foster, F. Krikowa, Measurement of inorganic arsenic species in rice after nitric acid extraction by HPLC-ICPMS: verification using XANES, Environ. Sci. Technol. 47 (2013) 5821−5827. https://doi.org/10.1021/es304299v.

[14] M. Anastassiades, S.J. Lehotay, D. Štajnbaher, F.J. Schenck, Fast and easy multiresidue method employing acetonitrile extraction/partitioning and “dispersive solid-phase extraction” for the determination of pesticide residues in produce, J. AOAC Int. 86 (2003) 412-431.

[15] A. Chisvert, S. Cárdenas, R. Lucena, Dispersive micro-solid phase extraction, Trends Anal. Chem. 112 (2019) 226-233. https://doi.org/10.1016/j.trac.2018.12.005.

[16] T. Khezeli, A.Daneshfar, Development of dispersive micro-solid phase extraction based on micro and nano sorbents, Trends Anal.Chem.89 (2017) 99-118. http://dx.doi.org/10.1016/j.trac.2017.01.004.

[17] M. Ghorbani, M. Aghamohammadhassan, M. Chamsaz, H. Akhlaghi, T. Pedramrad, (2019). Dispersive solid phase microextraction, Trends Anal. Chem. 118 (2019) 793-809. http://dx.doi.org/10.1016/j.trac.2019.07.012.

[18] M. Rutkowska, K. Owczarek, M. Guardia, J. Płotka-Wasylka, J. Namieśnik, Application of additional factors supporting the microextraction process, Trends Anal. Chem. 97 (2017) 104-119. http://dx.doi.org/10.1016/j.trac.2017.09.005.

[19] M. Llaver, R.G. Wuilloud, Separation and preconcentration of inorganic Se species in tap and natural waters using unfunctionalized nanosilica as sorption material in dispersive micro-solid phase extraction, Microchem. J.146 (2019) 763–770. https://doi.org/10.1016/j.microc.2019.01.066.

[20] M. Llaver, E.A. Coronado, R.G. Wuilloud, High performance preconcentration of inorganic Se species by dispersive micro-solid phase extraction with a nanosilica-ionic liquid hybrid material, Spectrochim. Acta Part B 138 (2017) 23–30. https://doi.org/10.1016/j.sab.2017.10.003.

[21] A.C. Grijalba, L.B. Escudero, R.G. Wuilloud, Ionic liquid-assisted multiwalled carbon nanotube-dispersive micro-solid phase extraction for sensitive determination of inorganic As species in garlic samples by electrothermal atomic absorption spectrometry, Spectrochim. Acta Part B 110 (2015) 118–123. http://dx.doi.org/10.1016/j.sab.2015.06.005.

[22] X. Cheng, H.Yan, X. Wang, N. Sun, X. Qiao, Vortex-assisted magnetic dispersive solid-phase microextraction for rapid screening and recognition of dicofol residues in tea products, Food Chem. 162 (2014) 104–109. http://dx.doi.org/10.1016/j.foodchem.2014.04.023.

[23] R. Mirzajani, A. Keshavarz, The core–shell nanosized magnetic molecularly imprinted polymers for selective preconcentration and determination of ciprofloxacin in human fluid samples using a vortex-assisted dispersive micro-solid-phase extraction and high-performance liquid chromatography. J. Iran. Chem. Soc. 16 (2019), 2291-2306. http://dx.doi.org/10.1007/s13738-019-01701-7.

[24] K.K. Jinadasa, E. Peña-Vázquez, P. Bermejo-Barrera, A. Moreda-Piñeiro, Ionic imprinted polymer solid-phase extraction for inorganic arsenic selective pre-concentration in fishery products before high-performance liquid chromatography –inductively coupled plasma-mass spectrometry speciation, J. Chromatogr. A (2020). doi.org/10.1016/j.chroma.2020.460973 (in the press)

[25] Y.K. Tsoi, Y.M. Ho, K.S.Y. Leung, Selective recognition of arsenic by tailoring ion-imprinted polymer for ICP-MS quantification, Talanta, 89 (2012) 162-168. https://doi.org/10.1016/j.talanta.2011.12.007.

[26] A. Moreda-Piñeiro , E. Peña-Vázquez , P. Hermelo-Herbello , P. Bermejo-Barrera , J. Moreda-Piñeiro , E. Alonso-Rodríguez , S. Muniategui-Lorenzo , P. López-Mahía, D. Prada-Rodríguez , Matrix solid-phase dispersion as a sample pretreatment for the speciation of arsenic in seafood products, Anal. Chem. 80 (2008) 9272–9278. https://doi.org/10.1021/ac801622u.

[27] P.L. Smedley, D.G. Kinniburgh, A review of the source, behaviour and distribution of arsenic in natural waters. Appl. Geochem. 17 (2002) 517–568.

[28] C. Basheer, J. Lee, S. Pedersen-Bjergaard, K.E. Rasmussen, H.K. Lee, Simultaneous extraction of acidic and basic drugs at neutral sample pH: A novel electro-mediated microextraction approach, J. Chromatogr. A 1217 (2010) 6661–6667. https://doi.org/10.1016/j.chroma.2010.04.066.

[29] J. Sánchez-González, S. García-Carballal, P. Cabarcos, M.J. Tabernero, P. Bermejo-Barrera, A. Moreda-Piñeiro, Determination of cocaine and its metabolites in plasma by porous membrane-protected molecularly imprinted polymer micro-solid-phase extraction and liquid chromatography—tandem mass spectrometry, J. Chromatogr. A 1451 (2016) 15–22. https://doi.org/10.1016/j.chroma.2016.05.003.

[30] J. Sánchez-González, S. Odoardi, A.M. Bermejo, P. Bermejo-Barrera, F.S. Romolo, A. Moreda-Piñeiro, S. Strano-Rossi, Development of a micro-solid-phase extraction molecularly imprinted polymer technique for synthetic cannabinoids assessment in urine followed by liquid chromatography–tandem mass spectrometry, J. Chromatogr. A 1550 (2018) 8–20. https://doi.org/10.1016/j.chroma.2018.03.049.

[31] I. Pizarro, M. Gómez, C. Cámara, M.A. Palacios, Arsenic speciation in environmental and biological samples: Extraction and stability studies, Anal. Chim. Acta, 495 (2003) 85-98. https://doi.org/10.1016/j.aca.2003.08.009.

[32] I.N. Pasias, N.S. Thomaidis, E.A. Piperaki, Determination of total arsenic, total inorganic arsenic and inorganic arsenic species in rice and rice flour by electrothermal atomic absorption spectrometry, Microchem. J. 108 (2013) 1-6. https://doi.org/10.1016/j.microc.2012.11.008.

[33] R.R. Rasmussen, Y. Qian, J.J. Sloth, SPE HG-AAS method for the determination of inorganic arsenic in rice—results from method validation studies and a survey on rice products, Anal. Bioanal. Chem. 405 (2013) 7851-7857. https://doi.org/10.1007/s00216-013-6936-8.

[34] EU/EC, Commission Regulation (EU) 2015/1006 of 25 June 2015 amending Regulation (EC) No 1881/2006 as regards maximum levels of inorganic arsenic in foodstuffs, Off. J. European Union, L161 (2015) 14-16.

[35] Government of Canada, Health Canada's proposal to add maximum levels for inorganic arsenic in polished (white) and husked (brown) rice to the List of contaminants and other adulterating substances in foods, https://www.canada.ca/en/health-canada/services/food-nutrition/public-involvement-partnerships/proposal-add-maximum-levels-inorganic-arsenic-white-and-brown-rice-list-of-contaminants-other-adulterating-substances/document.html, Last visited: 17/01/2020.

[36] Food and Drug Administration (FDA), Draft guidance for industry: Action level for inorganic arsenic in rice cereals for infants, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-guidance-industry-action-level-inorganic-arsenic-rice-cereals-infants, Last visited: 17/01/2020.

[37] U. Araujo-Barbosa, E. Peña-Vazquez, M.C. Barciela-Alonso, S.L. Costa Ferreira, A.M. Pinto Dos Santos, P. Bermejo-Barrera, Simultaneous determination and speciation analysis of arsenic and chromium in iron supplements used for iron-deficiency anemia treatment by HPLC-ICP-MS, Talanta 170 (2017) 523-529. http://dx.doi.org/10.1016/j.talanta.2017.04.034.

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Antonio Moreda-Piñeiro: Conceptualization, Methodology, Software, Validation, Writing-Reviewing and Editing, Supervision

Pilar Bermejo-Barrera: Resources, Project administration, Funding acquisition, Writing-Reviewing and Editing