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Total and Inorganic Arsenic in Marketed Food and Associated Health Risks for the Catalan (Spain) Population

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ABSTRACT: Inorganic arsenic (iAs) is considered to be a human carcinogen. In this paper, total (As) and iAs contents of 215 food products and drinks (i.e., seafood, fruits and vegetables, meat products, oils and fats, rice and rice products, seasonings, and alcoholic drinks) marketed in Catalonia (Spain) were quantified by inductively coupled plasma−mass spectrometry. The analytical method described was used for different food products, obtaining feasible results without the need to couple LC-ICP-MS for iAs. Daily As and iAs intakes for the average adult Catalan consumer were estimated at 354 and 6.1 μg/day/person, respectively, using consumption data from the Catalan Nutrition Survey (ENCAT). The highest As content was found in seafood, contributing 96% of dietary As intake, whereas rice presented the highest iAs values, corresponding to 67% of dietary iAs intake. As cooking process may affect iAs content, boiled rice was evaluated, showing an iAs reduction (up to 86%) when using higher water volumes (30:1 water/rice ratio) than those used in previous studies. This iAs exposure was slightly below the exposure risk range stated by the European Food Safety Authority (0.3−8 μg/kg of body weight/day), although the possibility of a risk to the population with high rice consumption cannot be excluded.

KEYWORDS: arsenic, inorganic arsenic, dietary exposure, food safety, risk assessment, cooked rice

INTRODUCTION

Arsenic (As) is a ubiquitous metalloid, naturally present in water, soil, and air in a variety of diverse organic and inorganic forms; its natural occurrence may be increased by anthropogenic activity (i.e., agricultural chemicals, atmospheric release from incineration facilities, and industrial activity).[1] Inorganic As species (arsenite or As(III) and arsenate or As(V)) are considered to be the most dangerous forms due to its biological availability and physiological and toxicological effects (iAs is classified as a nonthreshold, class 1 human carcinogen).[1] Food and drinking water remain the greatest source of exposure to inorganic As (iAs) in the general population.[1] In 1989, the Joint Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO) Expert Committee on Food Additives (JECFA) established a provisional tolerable weekly intake (PTWI) of 15 μg/kg body weight (bw) for iAs. However, the European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM Panel) no longer considers this PTWI appropriate for iAs risk assessment as data[2] have linked lung and bladder cancer and skin effects (dermal lesions, hyperpigmentation, keratosis) to levels of iAs exposure previously considered to be safe. As an alternative method for iAs assessment, THE EFSA has suggested the use of margins of exposure (MOEs), taking MOEs as a comparison between population exposure and the iAs dose at which the cancer risk is raised.

Although As toxicology depends mostly on the chemical form, most countries' food regulations do not define a maximum allowed concentration in terms of specific As species, but only in terms of total As. This distinction is important because iAs is the main contributor to As toxicity. As a result, data from official food control sources are reported as total As. In addition, most of these data correspond to aquatic organisms with concentrations 2−3 orders of magnitude higher than those in foods of terrestrial origin.[3] However, within aquatic organisms, most As occurs as organic compounds; only a small proportion of As (from 0.02 to 6.8%) is in the inorganic form.[4,5] Speciation of As in food groups other than aquatic organisms has been less studied, although THE EFSA estimated that iAs content in these other food products may range from 50 to 100% of total As.[2] In the past decade, iAs accumulation in rice has attracted much attention. Baseline levels of total As in rice, with reported levels ranging from 0.13 to 0.32 μg/g dw, are estimated to be 10-fold higher than those in other grain crops,[6] partly due to the flooded anaerobic conditions in rice cultivation, which facilitate As mobilization.[7]

In regions without high As levels in their drinking water supplies, rice is considered to be the primary source of iAs in the human diet.[8,9] Consequently, some authors have highlighted the risk to frequent rice consumers[10] and to populations with subsistence diets based on As-contaminated paddy rice.[11] Recently, iAs content has also been reported in derivative rice products such as rice crackers,[12] puffed rice,[12] or baby rice[13] (levels ranging from 0.06 to 0.21 μg/g dw) as well as in rice milk (7.0−20.7 μg/L).[14]

Moreover, it must be considered that iAs content may vary with cooking processes, even increasing its content for some foods.[15,16] For rice, previous studies described a reduction of iAs content with prewashing processes (rinsing or soaking) and

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subsequent cooking with several volumes of distilled water up to a 6:1 ratio of water/rice.[17−20] However, the prewashing process before cooking is not a common technique in Catalonia, and these studies were not performed with tap (decontaminated) water. In the present study, both tap water and distilled water were used to assess the boiling process of Spanish white rice samples (short and long grain), without prewashing steps, and larger ratios of water/rice were considered.

This study quantified the total As and iAs content of a broad range of raw food products and drinks. Our goal was to contribute to the knowledge of As and iAs content in food, especially in less studied groups, and to provide information that may be useful in setting future standards. Furthermore, because dietary food choices vary substantially among different countries, the health risk associated with dietary As and iAs exposure in the population of Catalonia (Spain) was estimated using food consumption information for this population[21] because no iAs dietary estimations have been performed in Catalonia using iAs analysis results instead of theoretical extrapolation factors from As data. A commonly used rice boiling process in Spain was assessed to evaluate whether volumes of water higher than those used in previous studies[17−20] produce a greater iAs reduction. Moreover, we aimed to show that our analytical method could be used for different food products, obtaining feasible results without needing to couple liquid chromatography to inductively coupled plasma mass spectrometry (LC-ICP-MS) for iAs.

MATERIALS AND METHODS

Sampling. Food samples were collected and analyzed by the authors as part of the Food Health Quality Surveillance Program (IQSA program) of the Public Health Agency of Barcelona (ASPB). Samples were collected in the city of Barcelona from various marketing channels (municipal markets, supermarkets, and other retail stores) covering distinct origins (local, national, and European Union and imports from other countries) from March 2007 to July 2010. For total As and iAs intake estimation, 215 samples were analyzed from the following food groups: fresh fish (n = 27), canned fish (n = 10), bivalves (n = 28), cephalopods (n = 20), crustaceans (n = 19), spices (n = 29), vegetables and fruits (n = 28), meat products (n = 9), oils and fats (n = 6), rice and derivative rice products (n = 27), and alcoholic drinks (n = 12). In addition, more limited numbers of some other samples were collected, such as wheat flour (n = 4) and baby food containing rice (n = 5), to obtain preliminary values of their As concentration. These foods were chosen either because they are commonly consumed in Catalonia[21] or because they have a high level of As and few data published (e.g., seasonings). Other products such as edible seaweeds, which may have high levels of total and inorganic As, were not collected because their consumption in Western countries is not common nowadays[22] and because their As content has been published.[22,23] In addition, five extra white rice samples from different Spanish brands were collected to estimate the final iAs content after cooking.

Samples were brought to the laboratory the same day of collection and kept for not more that a day in the refrigerator until sample preparation.

Chemicals and Reagents. Deionized water (18.2 MΩ cm) was used to prepare reagents and standards. All glassware was treated with 10% v/v nitric acid (HNO_3) for 24 h and was then rinsed three times with deionized water before use. Concentrated superpure HNO_3 (Carlo Erba, Rodano, Italy) and 30% w/w hydrogen peroxide (H_2O_2) (Merck, Darmstadt, Germany) were used for microwave digestions, and isopropanol (Merck) was used within the ICP-MS method. For iAs extractions, hydrazine sulfate and 48% hydrobromic acid (HBr) (both Sigma-Aldrich, Madrid, Spain), concentrated suprapure hydrochloric acid (HCl) (Carl Roth GmbH & Co. KG, Karlsruhe, Germany), and chloroform (Merck) were used. External calibration standards were prepared weekly by dilution of a multielement plasma stock solution traceable to the National Institute of Standards and Technology, with 100 mg/L of As (J. T. Baker, Phillipsburg, NJ) in 5% (v/v) HNO_3 (Carlo Erba). A diluted solution (0.2 mg/L in 40% v/v of isopropanol) of a 100 mg/L multielement internal standard stock solution (Agilent Technologies, Barcelona, Spain) containing Ge was used as an online internal standard to correct possible instrumental drifts and matrix effects.

Sample Preparation. *Raw Samples.* All samples were analyzed in a raw state (wet weight) without lyophilization or other pretreatments. Only edible parts of each food were used for the analysis. Vegetables were washed with water and the outer leaves discarded. Canned fish was drained. Only the meat of fresh fish and shellfish was considered, and viscera and mantle were discarded in cephalopods. Subsequently, vegetables and seafood samples were minced using a commercial mincer (Moulinex, vidrafoc, Barcelona, Spain) until complete homogenization, and cereals and spices were crushed to a fine powder in a coffee mill. Samples were stored in the refrigerator at 4−10 °C until analysis (a maximum of 2 days for perishable samples and 15 days for stable samples).

In general, the results for As and iAs presented in this study are shown in wet weight (ww) because dietary intake data are also expressed on a wet basis. However, the results for rice are also expressed in dry weight (dw) to compare them with previous data published on a dry basis. The moisture percentage in these samples was determined using a WTC oven with natural convection (Binder Inc., Bohemia, NY) at 102 °C until constant weight was reached (24 h).

Cooked Rice Samples. To assess changes in iAs content in cooked rice, five white Spanish rice samples were boiled for 15 min. After a 2 min draining, iAs was determined in the boiled rice. The cooking process was carried out in a hot electric plate with a stainless steel pot of 2 L, using 25 g of rice and different volumes (100, 400, and 750 mL) of both distilled and tap water, and the following ratios of water volume/sample weight were obtained: 4:1 w/s_w, 16:1 w/s_w, and 30:1 w/s_w.

To compare the iAs content in cooked rice with that in the original raw sample, the analytical weight used for iAs content calculation (w) was normalized, considering the analytical portion of boiled rice (r_1), the initial sample weight before boiling (r_2), and the final weight after boiling and draining (r_3): $w = r_1 \times r_2/r_3$.

Total As Digestion. A total of 0.5 g from every homogenized sample (as described under Sample Preparation) was weighed, and 9 mL of 16% HNO_3 and 1 mL of 30% H_2O_2 were added to perform a microwave digestion using an Ethos 1 microwave system (Milestone, Gomensoro, Barcelona, Spain). The digestion method was as follows: 15 min up to 200 °C and held for 15 min, working with a maximum potency of 800 W. Finally, the digested sample was made up to 30 g with deionized water.

Inorganic As Extraction. The extraction method was based on selective extraction of inorganic species.[24] Samples (4.0 g for seafoods, vegetables, and cooked rice or 1.0 g for the remaining foods) were stirred with 35 mL of 10 mol/L HCl for 30 min using a multipoint magnetic stirrer (SBS, Barcelona, Spain) and were left to stand overnight. Hydrazide sulfate 1.5% w/v (1.5 mL) and concentrated HBr (3 mL) were added and stirred for at least 2 min. Chloroform (10 mL) was added and vigorously stirred for at least 5 min. The chloroformed phase was collected after 5 min at 2500 rpm in a Rotina 46 R centrifuge (Hettich, Tuttlingen, Germany). The extraction was repeated twice. When separation was difficult, 20 mL of chloroform was used instead for each step. The residual acid phase was completely removed from the chloroform with a pipet (a very important step in sea products). The organic phase was filtered through a 0.45 μm (low protein birding durepore (pvdf) membrane Millex- HV). HCl 1 mol/L (10 mL) was added and vigorously stirred for at least 5 min. The acid phase was separated after centrifugation for 5 min at 2500 rpm. The extraction was

Table 1. Mean Concentrations of Inorganic Arsenic (iAs) and Total Arsenic (As), iAs Contribution, Mean Consumption, and Estimated Daily Intake (Daily Consumption × Mean As or iAs Concentration) by Seafood Individually and Food Groups

		mean concn (μg/g ww) (range given in parentheses)				As daily intake (μg/day)	
	N	iAs	total As	iAs (%)	daily consumption (g/day)	iAs	total As
fresh fish	**27**	**0.004 (0−0.07)**	**4.94 (0.90−20.6)**	**0.1**	**39.7**[a]	**0.16**	**196**
monkfish	3	<LQ[b]	11.1		3.40	0	37.7
hake	5	<LQ[b]	2.37		3.68	0	8.73
red mullet	1	<LQ[b]	9.90		0.25	0	2.48
salmon	5	<LQ[b]	1.26		2.00	0	2.53
sardines	5	0.02	6.41	0.4	2.80	0.06	17.9
sole	3	<LQ[b]	5.54		5.14	0	28.5
tuna	4	<LQ[b]	1.39		1.50	0	2.09
tope shark	1	<LQ[b]	17.7		0.10	0	1.77
canned fish	**10**	**0**	**1.29 (0.46−2.79)**	**0**	**8.39**[a]	**0**	**10.8**
mackerel	1	<LQ[b]	0.46		0.03	0	0.01
sardines	4	<LQ[b]	1.99		0.51	0	1.02
tuna	5	<LQ[b]	0.89		7.24	0	6.45
bivalves	**28**	**0.04 (0−0.15)**	**3.37 (1.37−26.4)**	**1.1**	**2.49**[a]	**0.09**	**8.40**
clams	3	0.05	10.6	0.5	0.46	0.02	4.90
cockle	2	0.09	2.04	4.4	0.18	0.02	0.36
razor clam	2	0.11	2.16	5.2			
mussels	19	0.02	2.56	0.8	1.40	0.03	3.59
oyster	2	0.05	2.75	1.9	0.01	0	0.03
cephalopods	**20**	**0**	**9.6 (0.35−66.8)**	**0**	**7.38**[a]	**0**	**70.9**
cuttlefish	4	<LQ[b]	6.52		3.46	0	22.6
European squid	3	<LQ[b]	1.57		3.24	0	5.09
octopus	13	<LQ[b]	12.4		0.67	0	8.37
crustaceans	**19**	**0.02 (0−0.9)**	**11.1 (0.2−54.0)**	**0.2**	**4.67**[a]	**0.10**	**53.5**
crab	3	0.01	22.9	0	0.20	0	4.63
Norway lobster	4	0.02	7.83	0.2	0.80	0.01	6.30
red shrimp	7	0.05	16.1	0.3	1.62	0.08	26.1
triple-grooved shrimp	5	<LQ[b]	0.96		0.52	0	0.50
total seafood (Lb/Ub)[c]	**104**					**0.35/1.51**	**339/339**

[a] These mean consumptions correspond to the total consumption for the Catalan population according to the Catalan Nutrition Survey (ENCAT) and not only to the individual consumption of species shown in the table. [b] <LQ, below the limit of quantification. [c] Lb, lower bound estimate (considering samples <LQ = 0); Ub, upper bound estimate (considering samples <LQ = $^1/_2$LQ).

repeated twice, all acidic portions were collected, and this final acidic extract was made up to 50 g with deionized water. The sample was diluted 1/5 with water prior to analysis to reduce the chloride content in the ICP-MS analysis.

Determination of As and iAs by ICP-MS. Arsenic was determined on an Agilent quadrupole inductively coupled plasma mass spectrometer (ICP-MS) 7500 cx (Agilent Technologies, Barcelona, Spain) at 1500 kW, measuring mass 75 *m*/*z* and using helium as a collision gas to remove ArCl. Moreover, specific conditions such as high helium flow (4.5−4.8 mL/min) and high energy difference (3 V) between the octapole exit and quadrupole entrance were needed to eliminate chloride interferences properly. The sample introduction system consisted of a micromist concentric nebulizer and a Scott-type spray chamber using a total flow (make up plus auxiliary gas) of 1.10 mL/min. Data were collected and processed using Agilent Chemstation ICPMS software rev. B.04.00.

The results were quantified using external calibration standards of 0.25, 0.5, 1, 5, 10, 25, 50, 100, 150, and 200 μg/L prepared in HNO_3 5%

for total As or prepared in HCl 0.1 mol/L for iAs to simulate the chloride content in samples due to the extraction process with HCl. A solution of 5 μg/L of germanium is used as an internal standard and measured at 72 m/z.

The instrumental detection limit was 0.03 μg/L (calculated as 3 times the standard deviation of a blank sample). The lower concentration levels validated (above which our results were quantified) were 0.02 mg/kg for total As and 0.04 mg/kg for iAs.

The final solutions (standards and samples) were prepared with 2% isopropanol (or 40% if introduced within the online internal standard) to minimize the effects of the dissolved carbon on As response.[25,26]

Quality Control Procedures. The method developed in our laboratory is fully validated and accredited by ISO 17025. For this reason, all types of analyzed foods were spiked with standards at several concentration levels, and no important differences were detected among different samples. Average recoveries of 101% for total As and 95% for iAs were obtained. Average relative standard deviations under reproducibility conditions of 11% for total As and 12% for iAs were obtained. Furthermore, some certified reference materials have been analyzed during validation: NIST SRM 1568a Rice with a certified value of 290 ± 30 μg/kg for total As, obtaining 275 ± 15 μg/kg (n = 3); TORT-2 Lobster hepatopancreas with a certified value of 21.6 ± 1.8 mg/kg for total As, obtaining 22.9 ± 2.3 mg/kg (n = 3); NMIJ CRM 7503-a Rice with a certified value of 84.1 ± 3.0 μg/kg for iAs (as sum of certified values for As(III) and As(V) ± the square sum of their uncertainties), obtaining 80.1 ± 8.0 μg/kg (n = 3).

Moreover, the total As method is tested several times a year with participation in different proficiency tests (FAPAS, JRC-irmm) analyzing a wide range of foods with satisfactory results (z score <2 and % of recovery within ±15%). There are only a few proficiency tests for iAs (FAPAS) for use as external quality controls. To date, the iAs method has been externally tested for rice, seafood, and seaweed with satisfactory results, independent of the matrix.

Throughout the routine sample analyses, quality controls for total As and iAs were performed by analyzing a reference material from FAPAS interlaboratory tests (Canned fish ref 07108, Rice ref 07134, Chili seasoning ref 07141, Crab meat ref 07112, Sugar ref 0796, Seaweed ref 07129) or a spiked sample with each batch of samples (with accepted range of recoveries of 80−120%), together with a process blank.

Risk Assessment. *Dietary Exposure Assessment.* To estimate the health risk associated with food consumption, the average daily dietary As and iAs intake for the adult Catalan population was estimated as the product between their mean concentration in each food group and the mean daily consumption[21] of these food groups. To provide a more realistic scenario of the risk posed by iAs in food, daily intake of iAs was also calculated by considering populations with higher consumptions than average (75th, 90th, 95th, and 99th percentiles).

For dietary exposure calculations the WHO suggests a conservative estimation (upper bound) considering samples below the quantification limit (LOQ) with a value. In contrast, when the percentage of samples without quantifiable results is high, a lower bound approach may be used, assuming the analyte content as zero.[27] In this study both approaches (upper and lower bound) were conducted. For the upper bound estimation samples below the LOQ were considered with a value of $^1/_2$ LOQ (LOQ for total As = 0.02 μg/g; LOQ for iAs = 0.04 μg/g). Food consumption data (g/day wet weight of uncooked food) and body weights of the population (kg) were obtained from the Catalan Nutrition Survey (ENCAT) of the Health Department of the Catalan Government,[21] in which dietary intake was assessed using two 24 h recalls on nonconsecutive days in a sample of 1613 individuals aged between 18 and 65 years from 83 cities. The weekly As and iAs intakes per body weight were also calculated using 70 kg as the average weight of the Catalan population.

Margins of Exposure (MOEs). MOEs have been adopted by the EFSA as the preferred approach for evaluating genotoxic carcinogens in food.[28] For genotoxic and carcinogenic substances, for which no dose can be considered free of a potential effect, the MOE is defined as a dimensionless ratio between a reference point on the observed dose range from experimental studies and the estimated dietary exposure in humans. This reference point (also called the point of departure) corresponds to the daily dose causing a low but measurable increase in the incidence of tumors. The CONTAM panel convened by the EFSA established a range of benchmark doses between 0.3 and 8 μg/kg bw/day as a reference point for risk characterization of iAs.[2] These values corresponded to the 95% lower confidence limit of the benchmark dose causing a 1% extra risk (BMDL01) for distinct end points (including lung and bladder cancer). In 2010, the JECFA recommended a narrower range of between 2 and 7 μg/kg bw/day, corresponding to the lower limit on the benchmark dose for a 0.5% increase in the incidence of lung cancer (BMDL0.5).[29] In the present study, an assessment of MOEs was made between the above-mentioned reference points[2] and the estimated dietary intake for iAs. This method does not quantify risk precisely but does indicate how much concern is warranted: a high estimated MOE corresponds to exposure of low potential risk.

RESULTS AND DISCUSSION

The satisfactory results consistently obtained with our method in the FAPAS interlaboratory proficiency tests for iAs demonstrate that our results are comparable with those obtained by other participants using LC-ICP-MS. In addition, we also analyzed a certified reference material for individual species (NMIJ CRM 7503-a rice), obtaining results that compared well with the certified values. Furthermore, a certified reference material (rice NIST 1568a) was analyzed, obtaining a mean value for iAs of 96 mg/kg, which is comparable with that published by other authors using LC-ICP-MS.[30] These results show that our analytical method provides feasible results without the need to couple LC to ICP-MS for iAs.

Total As and iAs Content in Food Groups. *Seafood.* Overall, total As was detected in 72% of the samples analyzed, with seafood having detectable levels in 100% of samples with values ranging from 1.29 μg/g in canned fish to 11.1 μg/g in crustaceans (Table 1). Seafood species with the highest total As levels were crab (22.9 μg/g), red shrimp (16.1 μg/g), octopus (12.4 μg/g), and clams (10.6 μg/g). Fish species with the highest total As levels were the benthic fish: tope shark (17.7 μg/g), monkfish (11.1 μg/g), and red mullet (9.90 μg/g), the latter being one of the species having the highest levels in other studies conducted in Catalonia.[31] Benthic fish species have been suggested to concentrate high levels of arsenic,[5] due to the As content of the constituents of their diet (i.e., sediments, benthic organisms, and algae),[32] which could explain the levels shown above. In comparison, iAs was detected in only 24% of seafood samples and in only 7% of fish samples. The highest iAs concentrations were found in bivalves and crustaceans: 0.04 and 0.02 μg/g, respectively. Seafood contained <1% of As as iAs. Marine species with greater contributions of iAs were bivalves: cockle and razor clams, which had 4 and 5% of iAs, and oyster, approximately 2%, whereas other seafood contained <1% iAs.

Rice Products. Although As was found in all samples of rice and rice crackers, total As levels were 1 or 2 orders of magnitude lower (0.24 and 0.09 μg/g ww, respectively) than those found in seafood (Table 2). For iAs, rice and spices had the highest levels (0.12 and 0.11 μg/g ww, respectively), as well as the highest proportions of inorganic content (52 and 43%), although a broad

Table 2. Mean Concentrations of Inorganic Arsenic (iAs) and Total Arsenic (As), iAs Contribution, Mean Consumption, and Estimated Daily Intake (Daily Consumption × Mean As or iAs Concentration) by Individual Foods and Food Groups of Terrestrial Origin

		mean concn (μg/g ww) (range given in parentheses)				As daily intake (μg/day)	
	N	iAs	total As	iAs (%)	daily consumption (g/day)	iAs	total As
spices	**29**	**0.11 (0−0.61)**	**0.26 (0−2.2)**	**43**	**0.31**[a]	**0.03**	**0.08**
cinnamon	3	0.05	0.06	67	0.13[c]	0.01	0.01
curry	1	0.10	0.26	40		0.01	0.03
dehydrated onion	1	<LQ[b]	<LQ[b]			0	0
garlic	1	<LQ[b]	<LQ[b]			0	0
mixed herbs	1	0.19	0.22	85		0.02	0.03
nutmeg	2	<LQ[b]	0.02			0	0
oregano	3	0.39	1.19	28		0.05	0.16
parsley	1	0.08	0.13	62	0.12	0.01	0.02
pepper	16	0.11	0.19	57	0.06	0.01	0.01
vegetables and fruits	**28**	**0.005 (0−0.09)**	**0.03 (0−0.2)**	**23**	**375**[a]	**1.97**	**7.51**
cabbage	4	0.02	0.06	44	2.90	0.07	0.16
leeks	5	<LQ[b]	<LQ[b]		1.72	0	0.02
lettuce	5	<LQ[b]	<LQ[b]		24.0	0	0.24
spinach	3	0.02	0.13	13	5.46	0.09	0.71
tomatoes	5	<LQ[b]	<LQ[b]		46.9	0	0.47
melon	2	<LQ[b]	<LQ[b]		8.26	0	0
orange	2	<LQ[b]	<LQ[b]		64.2	0	0
peach	2	<LQ[b]	<LQ[b]		8.85	0	0
meat	**9**	**0**	**0**		**73.3**[a]	**0**	**0**
chicken	3	<LQ[b]	<LQ[b]		34.8	0	0
beef	3	<LQ[b]	<LQ[b]		11.1	0	0
pork	3	<LQ[b]	<LQ[b]		18.3	0	0
oils and fats	**6**	**0**	**0**		**25.7**[a]	**0**	**0**
olive oil	2	<LQ[b]	<LQ[b]		16.0	0	0
sunflower oil	2	<LQ[b]	<LQ[b]		1.39	0	0
butter	2	<LQ[b]	<LQ[b]		0.92	0	0
rice and rice products	**27**	**0.11 (0−0.23)**	**0.22 (0.03−0.7)**	**50**	**33.9**[a]	**3.73**	**7.46**
rice	23	0.12	0.24	52	33.7	4.08	8.04
rice crackers	4	0.06	0.09	72	0.04	0	0
alcoholic drinks	**12**	**0**	**0**		**96.7**[a]	**0**	**0**
wine	6	<LQ[b]	<LQ[b]		43.5	0	0
beer	6	<LQ[b]	<LQ[b]		44.2	0	0
total samples of terrestrial origin (Lb/Ub)[d]	**111**					**5.7/17.0**	**15.1/20.7**

[a] These mean consumptions correspond to the total consumption for the Catalan population according to the Catalan Nutrition Survey (ENCAT) and not only to individual consumption of the individual products shown in the table. [b] <LQ, below the limit of quantification. [c] Individual consumption estimates of these spices were not available; the consumption of a generic group of condiments was used for all spices. [d] Lb, lower bound estimate (considering samples <LQ = 0); Ub, upper bound estimate (considering samples <LQ = $^1/_2$LQ).

Table 3. Total Arsenic (As) and Inorganic Arsenic (iAs) Concentrations in Rice Samples from Different Studies

origin of sample	type of rice	mean As concn (μg/g dw)	mean iAs concn (μg/g dw)	ref
Spain	white	0.22	0.11	present study
	brown	0.36	0.19	
Spain	white	0.21	0.09	34
	brown	0.20	0.15	
Spain	white	0.20		37
Spain	brown	0.29−0.30	0.13- 0.20	33
Spain	white	0.17	0.08	49
Spain	white	0.23−0.28	0.06	50
	brown	0.24		
worldwide	white	0.13		39
	brown	0.20		

range of iAs concentrations and contributions were found among samples. In rice, concentrations ranged from 0.04 to 0.23 μg/g ww and the iAs contribution ranged from 22 to 89%. These levels of variability are similar to previously reported values.[33,34]

The As level in food of terrestrial origin is highly dependent on the geographic area where the food is cultivated,[35] as well as on growing conditions and contamination of irrigation water. For this reason, As content can vary greatly among different rice-growing regions. Members of the European Union, jointly with the United States and Bangladesh, have been reported to be regions with high mean levels of As,[36,37] the parent rock and human activities being the main factors determining those levels. Factors such as climate, soil/water chemistry, the organic and inorganic components of the soils, and redox potential status also affect it. The samples analyzed in the present study were marketed in Barcelona, and most were produced along the Mediterranean coast, either in the Ebro river delta or the Valencia Albufera (19 of 23 samples). Spain is the second largest rice producer in Europe, after Italy, and these two rice-growing regions represent 30% of its annual rice production.[38]

The mean value of total As reported in the present study for white rice (0.22 μg/g dw; n = 17) is comparable to values obtained from previous studies for Spanish rice (Table 3). For brown rice, a slight difference can be seen, which could be due to the lower amount of data available. In our study, both total As and iAs were higher in brown rice than in white rice, which compares well with a review that analyzed a large number of samples worldwide.[39] The mean values of total As (0.36 μg/g dw) and iAs (0.19 μg/g dw) in brown rice (n = 6) were around 1.6 times higher than their mean concentrations in white rice, a proportion similar to that found by other authors.[34,39]

According to Meharg,[14] bran layers concentrate a high iAs content, which is around 10−20-fold higher than concentrations found in whole grain.[8] Therefore, some authors have highlighted the risk from consumption of products made from rice bran and germ such as rice milk.[13] In addition, rice bran may be added to products such as rice crackers or rice cereals to increase fiber content or can be used directly as a health food supplement (as it is high in antioxidants, vitamins, mineral nutrients, and soluble fiber).[9] Indeed, the iAs contribution to total As in rice crackers (72%) was much higher than that in rice, although levels were lower (from 0.03 to 0.1 μg/g). A similar iAs percentage has previously been found in rice products,[12] suggesting either that bran was added to the rice products or that raw rice processing alters iAs content.

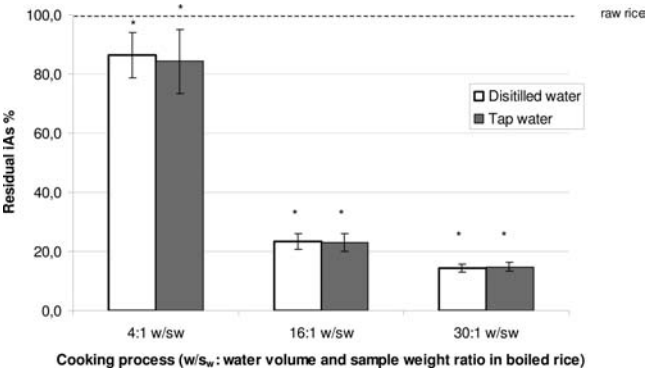

Figure 1. Amount of reduction (%) for inorganic arsenic (iAs) in rice after being boiled with different volumes of tap and distilled water. Standard deviation (±s) for n = 5 is shown on each cooking condition. ∗, statistical differences between raw and cooked samples (Student's t test, 95% confidence interval and 4 degrees of freedom).

Because rice is the main contributor to dietary iAs intake within the samples analyzed in this study, the effect of boiling with different volumes of distilled and tap water was studied for five different rice samples by comparing the reduction of iAs content in boiled rice with the initial result in the raw sample. The results (Figure 1) show a higher reduction of iAs content when larger volumes of water were used with no statistical differences (F test for variances and Student's t test) between tap and distilled water. Only 15% of iAs was reduced when rice was boiled under 4:1 w/s_w conditions, whereas under 16:1 and 30:1 w/s_w conditions, iAs reductions of 77 and 86%, respectively, were achieved. Statistical differences between raw and cooked samples (Student's t test, 95% confidence interval, and 4 degrees of freedom) were found between raw and cooked rice under all conditions.

The results show that iAs was leached from the samples to the water when boiled, confirming previously published results for rice[20] and other food samples.[15] When boiled under 4:1 w/s_w conditions, almost no water was left, avoiding iAs elimination during water draining as other authors have reported.[20,33] Nevertheless, with the higher proportions of water/rice described in the present study, higher percentages of iAs reduction were achieved compared with the 55% average reduction (6:1 w/s_w) found by Raab et al.,[20] who obtained this result performing an additional previous rinse step.

In view of these results, issuing a recommendation to the public to cook rice in high volumes of water (and to discard the drained water) could be useful in countries where water is As-free and boiling is the most frequent rice-cooking practice.

Wheat Products. None of the samples of wheat flour analyzed (n = 4) had detectable levels of As. This finding was not surprising as the As level in wheat grain is typically about 1 order of magnitude lower than that in rice,[6] although levels <0.024 μg/g have been reported in grain grown in soils not especially contaminated.[40] This level was within the limit of our LOQ (0.020 μg/g). In addition, as for rice, the As concentration in

wheat bran was 3.8−4.7-fold higher than that in white flour.[40] The percentage of iAs reported in wheat products varies greatly in the literature. Cubadda[41] found that 95% of the As in wheat grain was present in the inorganic form, whereas this percentage was 28% in flour[40] and 87% in bread in an area with endemic high As concentration in water, which may have contributed to the iAs content of processed food.[15] The available results on the contribution of iAs to wheat-derived products are limited, and further research on As speciation in these food products is required. In Catalonia, 80% of the cereals consumed by the average adult are wheat-based products,[21] and therefore wheat should not be ignored as a potential contributor to the dietary iAs intake of populations with a predominantly wheat-based diet, although it is also true that the iAs content of wheat is very low compared with that of other foods. Additional market basket surveys should evaluate the iAs in more wheat-based products in the region.

Baby Foods. None of our baby food samples had rice as the major ingredient; the As and iAs contents in baby rice have already been reported[14] in a similar concentration range as that in rice. Among the samples in our study (a mix of cereal formulas, vegetable and rice baby food, rice and chicken baby food), total As was detected in two of five samples (0.06 and 0.04 μg/g), whereas iAs was detected in only one sample (0.05 μg/g). Because the number of samples analyzed in the present study was so small, no clear conclusions can be drawn. However, exposure in children is higher when consumption is expressed on a body weight basis: according to the Spanish Agency of Food Safety, children aged 7−12 years consume 26 g of baby cereals and 33 g of rice daily[42] (or 1.8 g/day/kg bw versus the adult estimate of 0.6 g/day/kg bw). The dietary iAs exposure of European children under 3 years of age was estimated to be 2−3-fold higher than that for adults.[2] Cereal consumption starts on average at 4 months of life, and for this reason, there is long-term exposure to iAs with reported health effects[43] such as neurobehavioral effects or malignant and nonmalignant lung diseases. Nevertheless, the elimination of rice from the infant mix cereals formulas would reduce the iAs content from these baby foods and therefore the iAs risk of exposure.

A lower LOQ of the analytical method would be required to analyze these kinds of foods. Some methods of improvement could start with improving the extraction method with a higher amount of sample, optimizing instrumental conditions or even moving to LC-ICP-MS methods. Moreover, due to the higher iAs content in brown rice, organic baby food should be targeted in future studies, as these products are often based on nonpolished (brown) rice.

Other Foods. Arsenic was detected in 67% of spices and in 23% of vegetables with mean levels of 0.26 and 0.03 μg/g, respectively. As previously mentioned, spices had the second highest level and proportion of iAs and contained individual samples with the highest iAs contribution. However, their contribution to the estimated daily intake was negligible due to the small amounts usually consumed. In contrast, only 9% of vegetables had detectable iAs levels. No samples of meats, oils and fats, or alcoholic drinks had detectable levels of As.

Risk Assessment Estimations. Tables 1 and 2 summarize average daily As and iAs intake for each food group using the lower bound estimation. However, the overall result of each table is shown in both approaches (lower and upper bound estimations), because the WHO recommends showing both when possible.

The total average dietary intake was obtained by adding the overall result of each table (intake through seafood consumption + intake through samples of terrestrial origin). There was almost no effect on total As intake when the lower and upper bound estimations were compared (354 and 360 μg/day/person). However, for dietary iAs intake the upper bound estimation (18.5 μg/day/person) is 3 times the lower bound approach (6.1 μg/day/person). The reason for this clear upper estimation of dietary iAs intake was that the iAs content in highly consumed food groups such as vegetables was below the LOQ, and half of the LOQ is considered as the iAs content in samples for upper bound estimation.

Fresh fish was the highest contributor to total As intake (196 μg/day; 55% contribution) due to both its high As concentration and high consumption, mainly of demersal fish: monkfish (38 μg/day) and sole (29 μg/day). All together, seafood accounted for 96% of the total As intake. In terms of species, the most important seafood contributors to total As intake were red shrimp (26 μg/day) and cuttlefish (22 μg/day). In contrast, rice contributed only 2% of the dietary intake of total As. As previously reported,[3] only a relatively small proportion of dietary iAs intake came from seafood (5%), and the main contributor to iAs intake was rice (67%).

For total dietary As intake, our results are similar to those estimated in previous studies for the same population.[44,45] Compared with total As daily mean intakes in other countries,[46,47] our results are in the higher range of values reported, jointly with Japan, another country with a high consumption of seafood. For dietary iAs intake, previous estimations in the Catalan population and in the European Union[2] are higher than ours, but they are not comparable as they extrapolated iAs content considering fixed proportions of iAs from total As for each food category instead of considering analytical iAs results.

On a weekly basis and considering a mean body weight of 70 kg (the mean body weight of the Catalan population between 18 and 65 years old according to ENCAT), these intakes correspond to 35.4 and 0.61 μg/kg bw/week for total As and iAs, respectively. This latter value was clearly below the former recommended PTWI for iAs (15 μg iAs/week/kg bw). Even considering the individual with the lowest body weight (37 kg) from the Catalan Survey ENCAT, the iAs intake of 1.2 μg/kg bw/week is still below the PTWI. In the same way, when high consumers (95th percentile) of rice (200 g/day) were considered (Table 4), the resulting weekly intake of 2.9 μg iAs/week/kg bw represented only 20% of the former PTWI.

Bearing in mind that the PTWI needs to be reconsidered, tolerable dietary iAs intake could be approached by using information from other sources. Because the maximum As content allowed in drinking water is 10 μg/L[48] based on the assumption of 1 L consumption, and considering that As in water mainly corresponds to iAs, a simplistic notion of tolerable iAs intake of 10 μg/day can be formulated. Considering iAs intake via rice, which has been proven to be highly bioaccessible,[25] and using the mean iAs content of 0.12 μg/g obtained from our results, rice consumption of >83 g/day (which corresponds to 20% of the adult Catalan population) would exceed an intake of 10 μg/day.

Nevertheless, considering our results on dietary iAs intakes in the same units as the BMDL01 values (0.3−8 μg/kg bw/day), identified by the CONTAM panel, it can be seen that the average Catalan consumer is subjected to an iAs exposure (0.08 μg/kg bw/day) slightly below the BMDL01 range. When adult Catalans among the highest consumers (95th percentile) are considered,

Table 4. 75th, 90th, 95th, and 99th Percentiles for Food Consumption by the Catalan Population and Estimated Inorganic Arsenic (iAs) Intake

	daily consumption (g/day wet weight)					iAs daily intake (μg/day)			
food group	P75	P90	P95	P99		P75	P90	P95	P99
fresh fish	75	147	167	250		0.32	0.62	0.71	1.06
canned fish	0	31	50	83		0.00	0.00	0.00	0.00
bivalves	0	0	15	60		0.00	0.00	0.56	2.26
cephalopods	0	25	50	150		0.00	0.00	0.00	0.00
crustaceans	0	13	30	80		0.00	0.29	0.67	1.78
spices	0	1	2	5		0.00	0.12	0.24	0.59
vegetables and fruits	335	521	719	860		1.68	2.41	3.01	4.16
meat	120	175	210	300		0	0	0	0
oils and fats	35	48	55	71		0	0	0	0
rice	28	135	200	299		3.39	16.3	24.2	36.2
rice crackers	0	0	0	0		0	0	0	0
alcoholic drinks	100	300	430	768		0	0	0	0
					Lb[a]	**5.39**	**19.8**	**29.4**	**46.0**
					Ub[a]	**18.1**	**44.1**	**63.0**	**96.0**

[a] Lb, lower bound estimate (considering samples <LQ = 0); Ub, upper bound estimate (considering samples <LQ = $^1/_2$LQ).

their iAs mean dietary exposure (0.42 μg/kg bw/day) is within the above range but could fall below the interval identified by the JECFA (2 and 7 μg/kg bw/day).

As previously mentioned the MOE is not a quantitative risk estimate but a ratio between a level associated with toxicity and the actual level of exposure in a particular situation or population. The definition of a particular MOE as an appropriate level of protection is a complex issue and was not the objective of this study. In addition, there are multiple uncertainties inherent in deterministic intake estimations. Some of these uncertainties have already been discussed, such as the influence of upper bound calculation for nondetectable samples or the lack of some foods (i.e., wheat-derived products). Other important issues are the uncertainty of analytical results, extrapolation of constant consumption from information derived from 24 h recalls, food categories that integrate distinct individual foods for information on consumption, and analysis or nonconsideration of food processing. Estimated MOEs for the average adult Catalan consumer ranged between 4 and 93 and ranged between 0.7 and 19 for adults with high consumptions (95th percentile). The lower end of these intervals is low enough to indicate that the possibility of a risk to some consumers cannot be excluded.[2]

In summary, in Spain, seafood is the main contributor to total dietary As intake, whereas rice is the main contributor for iAs. The estimated iAs intake was very low when compared with the former PTWI, but considering the ratio between iAs intake and some BMDL for distinct end points (MOEs), the possibility of a risk for high consumers of rice and rice-derived products cannot be excluded. However, this risk will vary depending on the cooking process. This study showed that a boiling process with large volumes of water (30:1 water/rice ratio) had a higher reduction of iAs content (up to 86%) than cooking processes by which almost no drained water is left. For this reason, to reduce substantially the iAs content, rice should be boiled with as much water as possible and the drained water should be discarded. The analytical method described could be used for different food products, obtained without the need to couple LC-ICP-MS for iAs. Wheat-derived products may also influence dietary iAs intake, although the iAs content is much lower than that in rice. Consequently, analytical methods with lower quantification limits will be needed for further investigations of wheat products.

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