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Article

Concentrations of Total As and As Speciation in Chinese Rice Wine and Associated Risk Assessment in Main Producing Provinces

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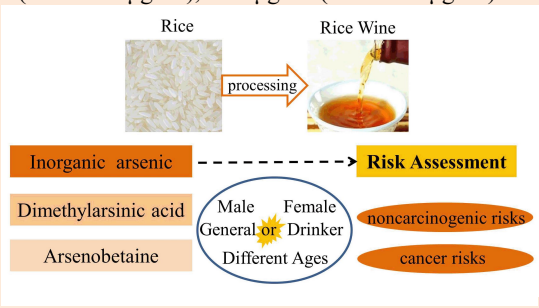
ABSTRACT: Rice and rice products have been identified as significant sources of As. Concerns have been raised about the presence of As in rice wine. This study collected 79 rice wine samples from China. High-performance liquid chromatography-inductively coupled plasma mass spectrometry was used to determine total As and As species concentrations. The average concentration of total As was 14.6 μg L^{-1}, and the concentration of As (III) (arsenite), As (V) (arsenate), dimethylarsinic acid (DMA), and arsenobetaine (AsB) were 2.86 μg L^{-1} (0.970–6.08 μg L^{-1}), 7.22 μg L^{-1} (2.24–22.9 μg L^{-1}), 3.92 μg L^{-1} (1.58–7.82 μg L^{-1}) and 0.620 μg L^{-1} (ND-0.950 μg L^{-1}), respectively. MMA (monomethylarsonic acid) and AsC (arsenocholine) were not detected. The THQs (target hazard quotients) for chronic noncarcinogenic risks (skin lesions as the point of departure) were below 1, suggesting that the Chinese population did not encounter a significant noncarcinogenic risk. However, the mean values of MOE (margin of exposure) for lung cancer were below 100 (62.1 to 75.1) for male drinkers, indicating a potential carcinogenic risk. By comparing the As species of rice wines and the main raw material, it was found that the methylation increased DMA during fermentation.



INTRODUCTION

Arsenic (As) is a carcinogenic and highly toxic metalloid found diffusely in the earth's crust, water, soil, plants, and food.[1,2] As can accumulate in the human body through food intake, which is a serious health risk to consumers. Inorganic arsenic (As_i), mainly arsenite and arsenate, is listed as a Group I carcinogen by the International Agency for Research on Cancer (IARC) and presents potential damage to the skin, lungs, kidneys, nervous system, respiratory system, and urinary system.[3] Minimizing the intake of As_i is essential to a healthy life. However, As contamination has become a severe environmental threat in some parts of the world. Apart from drinking water, food is the primary source of As for humans due to the exceedingly high ability of As to accumulate in organic tissue. Plants become a source of As because herbicides and insecticides are used heavily on crops.[4,5] In particular, rice is the staple food in East Asia and is affected by the As in soil and water. Rice products, such as rice wine, are also affected.[1,6]

The toxicity of As depends strongly on the compounds it forms with specific chemical structures, rather than merely the total content. As_i has proved to be more poisonous than the organic As species, including monomethylarsonic acid, dimethylasinic acid (DMA), arsenobetaine (AsB), arsenocholine (AsC), and arsenosugars.[7,8] Hence, a determination of the total As concentration cannot provide full, accurate information about As toxicity.

Research has shown that the concentrations of total As and As species change during grape and wine processing,[9-11] especially

during fermentation,[12] due to the microbes that metabolize As. Bertoldi et al.[13] assessed the risks associated with the ingestion of grape wines from 10 vineyards with soils rich in As. They found no difference in As content in 7 red wines before or after malolactic fermentation. As was higher in 7 white wines, suggesting that the biological As absorption by bacteria is negligible. However, Aguilar et al.[14] observed that As content decreased during fermentation and maceration in the wine-making process. They speculated that the physical and chemical changes (*i.e.* the existence of volatile compounds and the formation of colloidal substances as sediment) were predominant and caused As loss[15,16]—the chemical transformations of As species may occur during fermentation and influence the As species concentrations. Aguilar *et al.*[14] noted that the As(V) and DMA concentrations dropped in the red wine, whereas the As(III) concentration rose. In addition, they testified that 40 % of the spiked As(V) was converted to As(III), and no more than 1 % of the added organic As species were demethylated into inorganic forms. However, 7 % of the DMA was converted to MMA. The authors proved that DMA and MMA are the main As species that originated from inorganic As due to biomethylation of As. MMA(V) could be formed from As(III) combined with CH_3^+ undergoing oxidation. The reaction continued until the formation of DMA(V) and DMA(III).[10,16] Therefore, the biomethylation of As was regarded as an important way to enhance the As tolerance attributed to the lower toxicity of MMA (V) and DMA (V) when compared to As_i.

Rice wine is a traditional fermented wine in China and is known as the world's three ancient wines along with beer and grape wine.[17] It is produced from cereals (mainly rice) fermented with yeast and several bacteria. In the production of rice wine, starch is hydrolyzed and saccharified in the presence of microorganisms.[18] They are also the substrate for ethanol fermentation, which is the source of the flavor of the wine.[19] Rice wine contains many nutrients, such as proteins, amino acids, bioactive peptides, phenols, and oligosaccharides, which have antioxidant, hypotensive, and immunoregulatory qualities; they also help in lowering cholesterol.[17,20,21] Presently, customers and researchers are concerned about the nutritional value and safety of rice wine. According to the International Office of Vine and Wine (OIV), the maximum As concentration allowed in wines is 200 μg L^{-1}.[22] However, there is a risk associated with rice wine due to the accumulation of As in rice. Investigations have focused on the presence of As in beer,[23] red wine grapes,[24] and white wine grapes[9]; however, there is no risk assessment report on the presence of As in rice wine. This research aims to collect and analyze comprehensive data about As in rice wine to assess dietary exposure by determining the total As and As species concentrations using high-performance liquid chromatography-inductively coupled plasma mass spectrometry (HPLC-ICP-MS). Margin of exposure (MOE)[24] and target hazard quotient (THQ)[25] were used to assess the risks associated with As_i ingestion. MOE evaluates the carcinogenic risks of certain contaminants listed by the Expert Committee on Food Additives (JECFA)[26]; THQ is used to assess noncarcinogenic risks.[24] Furthermore, possible As species alterations in the wine processing were speculated to correspond with rice materials, which is aimed at providing support for understanding the risk level of rice wine.

EXPERIMENTAL

Sample collection and pretreatment. Seventy-nine bottles of rice wine were randomly collected as samples from the Zhejiang and Jiangsu provinces, considered the leading producers of rice wine. All wine samples were stored at 4 °C in a refrigerator before analysis, and aliquots of the samples were directly taken from the bottles. In addition, 203 rice samples were collected from the Zhejiang and Jiangsu provinces. Every rice sample (with hulls) was collected from five random, well-distributed points of one paddy field (>100 m^2). After harvesting, a quarter of every rice sample (at least 2 kg) was randomly separated for analysis. Then, all samples were transported to the laboratory as soon as possible to air-dry and to obtain a constant weight. To remain consistent with the rice wine-making process, hulls and bran layers were removed. The rice samples were then ground and sieved with a 0.45 mm mesh sieve and stored in bags at 4 °C before analysis.

Reagents and solutions. As standard (GBW08611) with 1000 μg mL^{-1} of As was purchased from the National Standard Material Center (Beijing, China) and used for calibration in total As determination. Other reagents were purchased from Sinopharm Chemical Reagent Co., Ltd, China. For As speciation, 5 μg mL^{-1} As (V), As (III), MMA, DMA, AsB, AsC standards were purchased from the National Standard Material Center (Beijing, China). These standard solutions were mixed with ultrapure water and diluted to 0.2, 0.4, 1.0, 4.0, and 10.0 μg L^{-1}. Ultrapure water (18 MΩ cm) was obtained from a Milli-Q water purification system (Millipore, Paris, France). The injection volume was 20 μL. Nitric acid (65–68%, GR) and other reagents used were purchased from Sinopharm Chemical Reagent Co., Ltd, China.

Instrumentation. The total As concentration was determined using inductively coupled plasma mass spectrometry (ICP-MS, iCAP RQ, Thermo Fisher scientific company, USA). The parameters used were according to Caruso *et al.*[27] with some modifications: incident RF power, 1550 W; plasma gas flow rate, 14 L min^{-1}; spray chamber temperature, 3 °C; intermediate Ar gas flow rate, 0.8 L min^{-1}; carrier Ar gas flow rate, 1.04 L min^{-1}. The collision mode with He gas (4.8 mL min^{-1}) was used to reduce interference by polyatomic ions. The ^{75}As isotope signal was measured.

For As speciation, a chromatograph (HPLC, Dionex UltiMate

3000, Thermo Fisher Scientific company, USA) was coupled with the ICP-MS instrument. A Dionex IonPac AS7 column (250 mm × i.d. 4 mm) was employed for As species separation. The mobile phase flow rate was 1.0 mL min^{-1} with solution A, $(NH_4)_2CO_3$ (100 mM) and solution B, $(NH_4)_2CO_3$ (5 mM). The elution gradient was: 0–3.5 min, 100 % solution B; 3.5–7.5 min, 20% solution B; 7.5–10 min, 100% solution B.[28]

The total As and As_i species concentrations in rice samples were determined using high performance liquid chromatography–hydride generation–atomic fluorescence spectrometry (HPLC-HG-AFS) (AFS 8220, Beijing Titan Instruments Co., Ltd., China). The mobile phase flow rate was 1.0 mL min^{-1} with 15 M $(NH_4)HPO_4$ (pH 6.0). 7% HCl solution and 20% KBH_4 dissolved in 5% KOH solution as the reducing reagent. The operational parameters were set according to Huang *et al.*[29]

Total As determination in rice wines by ICP-MS. A mixture of 2 mL rice wine, 8 mL HNO_3, and 2 mL H_2O_2 (30%, v/v) was prepared in 50 mL polypropylene tubes. The mixture was heated at 120 °C for 2 h on a heating block and then diluted with 2% HNO_3 (v/v) to 50 mL.[30]

As speciation in rice samples by HPLC-HG-AFS. A 1.0 g rice sample was blended with 10 mL of 0.02 M TFA, 50 % (v/v) methanol, and 0.02 M HNO_3. After uniform mixing, the mixture was heated at 90 °C for 1 h and centrifuged at 5000 rpm for 10 min. Then, 4 mL supernatant was concentrated to less than 1.5 mL with a controlled nitrogen flow, and 120 µL H_2O_2 was added to the concentrated solution heated at 70 °C for 0.5 h to oxidize As(III) to As(V). Then, the solution was filtered through a 0.45 µm polypropylene filter before analysis.[29]

As speciation in rice wine samples by HPLC-ICP-MS. The rice wine samples were prepared as described above, and then the extracts were diluted ten-fold by adding ultrapure water and filtered through 0.45 µm polypropylene filters before As determination.[31] A 100 µL filtrated sample was injected into the chromatographic column. Chromatograms for a standard (1.0 µg L^{-1}) with the investigated As species and a rice wine sample are shown in Fig. 1. The limit of detection (LOD) for As species by HPLC-HG-AFS and HPLC-ICP-MS were calculated based on 3 times the signal-to-noise ratios (Table 1)

Risk assessment of As_i through rice wine consumption. The estimated daily intake (EDI)[32] of As_i depended on its concentration and wine consumption. The EDI was calculated by equation (1):

$$EDI = (E_F \times E_D \times F_{IR} \times C)/(W_{AB} \times T_A) \quad (1)$$

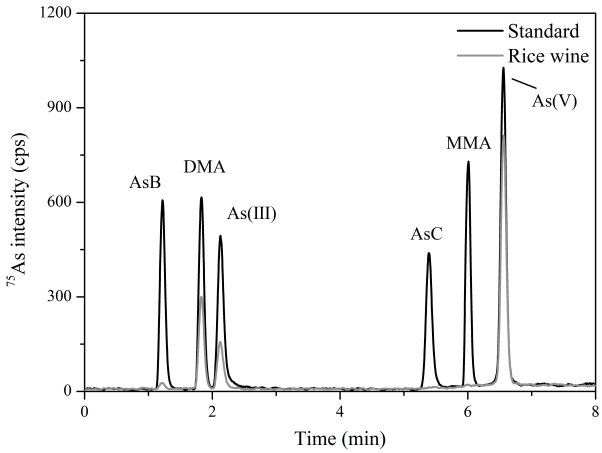


Fig. 1 Chromatograms for a Standard and a Rice Wine Sample.

E_F is the exposure frequency (365 days/year), E_D is the exposure duration (70 years), F_{IR} is the ingestion rate of rice wines is (g/person/d), C is the Asi concentration in rice wines (µg/kg), W_{AB} the average body weight (kg), and T_A is the average exposure time ($E_F \times E_D$). The average body weights of males and females are 60 kg and 55 kg, respectively.

Target hazard quotient. THQ was used to access noncarcinogenic risks for residents (pods are skin lesions) through the consumption of rice wines contaminated with As. THQ value >1 indicates risks for humans.[33] Otherwise, it is the opposite. The THQ was calculated using equation (2):

$$THQ = EDI/BMDL_{0.5} \text{ (skin lesions)} \quad (2)$$

MOE is an index applied to evaluate carcinogenic risk. $BMDL_{0.5}$ was primarily used instead of the provisional tolerance week intake (PTWI, 15 µg/kg bw/week) in the calculation due to the revocation of PTWI by JECFA in 2010.[34] $BMDL_{0.5}$, the benchmark dose levels (BMDL) for 0.5%, increased risk of lung cancer. According to JECFA, the lower limit of $BMDL_{0.5}$ induced by As_i was 3–5 µg/kg bw, whereas 3 µg/kg bw was adopted here. MOE $\geqslant$100 indicates no carcinogenic risk for humans and MOE $\leqslant$ 100 implies a lower exposure risk. The MOE was calculated following equation (3):

$$MOE = BMDL_{0.5} \text{ (lung cancer)}/EDI \quad (3)$$

Exposure assessment model. The dietary exposure to As_i was calculated depending on model construction theories and the Monte Carlo method and bootstrap values. The mean values and percentiles (P97.5) for individual samples were obtained in this study.

Table 1. Limits of Detection (LODs) of As Species for HPLC-HG-AFS and HPLC-ICP-MS

Methods	Unit	AsB	AsC	MMA	DMA	As(III)	As(V)	As_i
HPLC-HG-AFS	µg kg^{-1}	—	—	8.00	6.00	—	—	6.00
HPLC-ICP-MS	µg L^{-1}	0.230	0.440	0.230	0.310	0.540	0.340	—

Statistical analysis. Final experimental results were calculated using the statistical software SAS 9.2 (SAS, USA).

RESULTS AND DISCUSSION

Concentrations of As species in Rice and Rice Wine Samples.

Rice is the main material in rice wine production and contains starch, protein, fat, and cellulose. These basic components are responsible for the aroma and taste of rice wine. To better investigate the alteration of As concentration during the fermentation, 203 rice samples were analyzed from the same Chinese province from where the rice wine samples were collected. The total As concentration was 65.8 μg kg^{-1} (Table 2). MMA was not detected in any rice sample. The average concentrations of As_i and DMA were 52.6 and 13.5 μg kg^{-1}, respectively. The As_i and DMA contributed to 79.9% and 20.5% of total As concentration, respectively.

The average total As concentration in rice wine samples was 14.6 μg L^{-1} and MMA and AsC were not detected in any sample. The As_i (sum of As (III) and As(V)) contributed to 69.1% of total As concentration, and the average As_i in the rice wine was 10.1 μg L^{-1} (4.43–24.0 μg L^{-1}), reflecting the presence of As_i in rice grain. The average concentrations of As (III), As(V), DMA and AsB were 2.86 μg L^{-1} (0.970 – 6.08 μg L^{-1}), 7.22 μg L^{-1} (2.24–22.9 μg L^{-1}), 3.92 μg L^{-1} (1.58–7.82 μg L^{-1}), and 0.620 μg L^{-1} (ND-0.950 μg L^{-1}), respectively (Table 2). As(V) was the largest contributor to the total As concentration (49.5 % of total As), followed by DMA (27.4 % of total As), As (III) (19.6% of total As), and AsB (4.51 % of total As). In addition, DMA was the predominant organic As species and accounted for 86.3% of organic As.

As shown in Table 2, the average concentrations of total As and As_i in rice wine samples were lower than in rice samples, which may be due to the dilution during wine production. Aguilar *et al.*[14] found that the total As concentration in rosé and red wines declined during the fermentation and maceration stages. However, the proportion of organic As increased after fermentation. In particular, AsB was detected in rice wines, which accounted for 4.51% of the total As concentration. Although the DMA concentration in rice wine was less than that in rice, the proportion was the opposite. This suggests that As methylation occurred during fermentation, which might be due to As metabolism by microorganisms (*e.g.* yeasts, fungi, and bacteria) present in the medium. Lu *et al.*[19] found 10 bacterial genera in Shaoxing rice wine; *Bacillus* and *Lactobacillus* accounted for the largest proportion. Bacteria and fungi (28 genera of bacteria and 13 of fungi) were detected in Hong Qu glutinous rice wine, including *Bacillus ginsengihumi*, *Pantoea sp*., *Monascus purpureus*, and *Aspergillus niger*.[35] Besides, yeasts used to produce alcohol exists in rice wine diffusely, like *Saccharomyces cerevisiae*, *Pichia sp.* and *Trichosporon sp.* Yeast was found to be able to methylate inorganic As into organic As in soil environment.[7] Zeng *et al.*[36] found that As (III) might be oxidated and methylated by some fungi (*e.g. Trichoderma asperellum* SM-12F1, *Penicillium janthinellum* SM-12F4, and *Fusarium oxysporum* CZ-8F1) and generate As(V), MMA, and DMA. The conversion of As species is also related to temperature and pH during the fermentation process. Vriens *et al.*[37] testified that the methylation of As depends on the temperature. The production of rice wine is carried out in an open environment. As the temperature of surface water and air increases, the rate of methylation increases. At high pH, the organic mass, moderate moisture, and temperature contribute to biotransformation mediated by As. Meanwhile, the pH and redox potential are affected by the quantity of heat released from the microbial metabolism, which influences As speciation.[7]

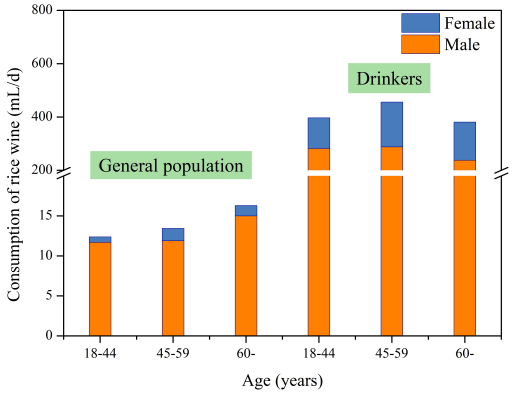


Fig. 2 Consumption of rice wine (mL/d) among population in five provinces. Day is abbreviated as d.

Exposure estimate

The study population was divided according to their habits of drinking rice wine: general population (all consumers ⩾18 years old) and drinking population. Each of these groups was further divided by gender (male/female) and further by age (18–44, 45–59, and >60). As seen from Fig. 2 and Table S1, the average

Table 2. Mean Concentration and Proportion of As species in 79 Rice Wine and 203 Rice Samples

Sample	Concentration and Proportion	AsB	AsC	MMA	DMA	As(III)	As(V)	As_i	Total
Rice wine	Concentration (μg L^{-1})	0.620	ND*	ND	3.92	2.86	7.22	10.1	14.6
	Proportion (%)	4.51	0.00	0.00	27.4	19.6	49.5	69.1	—
Rice	Concentration (μg kg^{-1})	—	—	ND	13.5	—	—	52.6	65.8
	Proportion (%)	—	—	0.00	20.5	—	—	79.9	—

* ND: not detected.

consumption of rice wine by all consumers and drinkers in five provinces were 7.40 and 250 mL day^{-1} (mL d^{-1}), respectively. Among the general population, the mean consumption by males was higher than that for females, which accounted for 14.4 and 1.10 mL d^{-1}, respectively. The group with the highest rice wine consumption was that of adults between 45 and 59 years of age, and the group with the lowest consumption consisted of adults between 18 and 44 years. The total average consumption by drinkers was 255 mL d^{-1}; an average of 273 mL d^{-1} for males and 142 mL d^{-1} for females. The highest consumption was by people between 45 and 59 years of age, and the minimum consumption was by the 60+ age group.

The average concentration of As_i was taken as the mean intake for dietary exposure assessment, and the estimated daily intakes per body weight of the different groups were obtained. The percentile (P97.5 in this study) was drawn to determine the intake by the population with higher exposure. Among the general population, the average daily exposure per body weight of males and females was approximately 2.42×10^{-3} and 2.02×10^{-4} μg/kg bw/d, respectively. For drinkers, the average daily consumption of rice wine resulted in a possible As_i intake dose of 0.0458 and 0.0260 μg/kg bw/d by males and females, respectively. In addition, P97.5 indicated that the estimated highest exposure intake dose by male and female consumers was 5.12×10^{-3} and 3.91×10^{-4} μg/kg bw/d, respectively. Among drinkers, the indices for males and females were 0.0970 and 0.0550 μg/kg bw/d, noticeably greater than those for all consumers.

Evaluation of noncarcinogenic and carcinogenic risk

THQ and MOE have been considered the main indices to assess the noncarcinogenic and carcinogenic risks of ingested As_i in daily rice wine consumption. For THQ calculation, it was assumed that the absorbed dose of Asi was equal to the intake dose. PTWI (15 μg/kg bw/week) was the denominator in the formula. In some studies[38] it has been found that skin lesions, lung cancer and urinary bladder cancer may rise when humans are exposed to As_i 15 μg/kg bw/week or less. These findings resulted in the withdraw of PTWI by JECFA in 2010[39]. Instead, $BMDL_{0.5}$ (5.4 μg/kg bw/d) for skin lesions was used to estimate the As_i toxicity. For MOE, the $BMDL_{0.5}$ of for lung cancer was lower than for urinary bladder cancer, so the $BMDL_{0.5}$ lung cancer (3.0-5.0 μg/kg bw/d) was considered to calculate MOE according to U.S. Environmental Protection Agency (USEPA)[40]. Thus, the lowest of daily dose (3.0 μg/kg bw/d) of As_i was adopted in this study.

As shown in Table 3, the THQs for the general population were less than that for drinkers of both genders and in all age groups. However, all THQ values were < 1, indicating no noncarcinogenic risk (skin lesions in this case) to people due to rice wine consumption.[41] However, because of the higher rice wine consumption, the THQ values for males were higher than those females in each gender group; P97.5 for any group did not exceed 1. These results indicated that the hazard of As_i exposure was permissible. The average MOE values for the general population, both males and females, were 1.24×10^3 (1.19×10^3–1.53×10^3) and 1.49×10^4 (1.06×10^4–2.41×10^4), respectively; they were 65.5 (62.1–75.1) and 115 (97.1–143) for male and female drinkers, respectively (Table 4). For the general population, all MOE values were > 100, demonstrating no carcinogenic risk for people in general. Nevertheless, among drinkers, the MOE values for males and those for females in the 45–59 age group were < 100, suggesting a potential carcinogenic risk (lung cancer) due to As_i intake. P97.5 for all age groups of female drinkers was lower than 100 (45.9–67.4), indicating a considerable proportion of females were exposed to the risk of lung cancer. From Table 4, it can be deduced that the exposure risk is related to the consumption of rice wine by drinkers; the higher the consumption of rice wine, the greater the carcinogenic risk. For the 45–59 age group, a higher carcinogenic risk was observed than for any other age group; this is related to Chinese drinking habits and features. The MOE values indicated that a large intake of rice wine might increase the carcinogenic risk; hence it should be noted by the people. To

Table 3. Dietary Exposures of As_i in Rice Wine for Different Age and Gender Groups (THQ for Noncarcinogenic Effects)

Age (years)	All people				Drinker			
	Male		Female		Male		Female	
	Mean	P97.5	Mean	P97.5	Mean	P97.5	Mean	P97.5
18-44	6.55×10^{-04}	1.39×10^{-03}	4.15×10^{-05}	8.06×10^{-05}	0.0158	0.0334	0.00700	0.0148
45-59	6.66×10^{-04}	1.41×10^{-03}	9.41×10^{-05}	1.82×10^{-04}	0.0161	0.0341	0.0103	0.0218
60-	8.40×10^{-04}	1.78×10^{-03}	7.94×10^{-05}	1.54×10^{-04}	0.0133	0.0282	0.00870	0.0185
Sum	8.06×10^{-04}	1.71×10^{-03}	6.72×10^{-05}	1.30×10^{-04}	0.0153	0.0323	0.00870	0.0183

Table 4. Dietary Exposures to As_i in Rice Wine for Different Age and Gender Groups (MOE for Lung Cancer)

Age (years)	General population				Drinker			
	Male		Female		Male		Female	
	Mean	P97.5	Mean	P97.5	Mean	P97.5	Mean	P97.5
18-44	1.53×10^3	721	2.41×10^4	1.24×10^4	63.3	29.9	143	67.4
45-59	1.50×10^3	709	1.06×10^4	5.48×10^3	62.1	29.3	97.1	45.9
60-	1.19×10^3	563	1.26×10^4	6.49×10^3	75.1	35.5	115	54.2
Sum	1.24×10^3	586	1.49×10^4	7.67×10^3	65.5	30.9	115	54.5

Table 5. Reported Concentrations of Total As and As Species in Wines from Different Countries

Country	Type	n	Total As, μg L^{-1} Mean (range)	Inorganic As (μg L^{-1}) Mean (range)	DMA (μg L^{-1}) Mean (range)	MMA (μg L^{-1}) Mean (range)	Ref
United States	Red wine	46	6.76 (0.520-23.2)	6.12 (0.400–20.5)	0.55 (0.02-2.66)	0.09 (0.08-0.17)	24
	White wine	26	22.6 (1.52-42.5)	9.50 (0.570–30.4)	0.82 (0.42-1.87)	0.17 (0.08-0.47)	
United States	Rosé	NA	16.7	16.0	0.72	ND [a]	43
	White wine	NA	12.1	11.4	0.72	ND	
	Red wine	NA	2.20	1.70	0.47	ND	
Spain	Grape juice wine	15	7.07 (4.00-11.3)	1.80 (0.60-8.80)	3.64 (1.3-8.3)	1.63 (1.50-2.50)	12
	White wine	15	9.71 (4.60-14.0)	1.81 (0.60-4.50)	4.82 (0.7-10.4)	3.08 (1.50-8.10)	
	Sherry wines	15	11.0 (2.00-15.1)	1.71 (0.60-4.00)	4.35 (0.70-15.1)	4.92 (1.50-9.60)	
China	Rice wine	79	14.6 (11.7-24.7)	10.1 (4.43-24.0)	3.92 (1.58-7.82)	ND	This study
Argentina/Brazil/ Chile	White wine	14	25.7 (ND)	ND (2.90-28.1)	NA [b] (< 0.450-1.07)	ND	11
Central Europe [c]	Grape juice wine	7	5.92 (3.74-7.32)	4.54 (1.10-6.76)	0.57 (2.08-3.90)	ND (ND-0.44)	44
	White wine	39	4.99 (0.83-21.0)	4.82 (ND-22.0)	0.16 (ND-0.600)	ND	
	Red wine	29	3.95 (0.46-15.7)	3.79 (ND-16.1)	ND (ND-3.95)	ND	
	Late harvest wine	6	9.59 (7.28-12.5)	8.99 (0.740-11.3)	0.17 (ND-1.20)	ND (ND-0.72)	
	Ice wine	6	11.1 (7.94-18.8)	10.22 (0.500-16.5)	0.14 (ND-0.55)	0.640 (ND-1.41)	
	Rice wine	9	1.88 (0.63-6.07)	1.10 (ND-6.21)	0.07 (ND-1.25)	ND	
13 countries [d]	Red wine	147	4.00 (< 0.1-56.0)	NA (< 0.200-10.7)	NA (< 0.150-2.52)	NA (< 0.30-1.01)	32

[a] ND: not detected; [b] NA: not analysis; [c] German, Austria, Switzerland; [d] Wine collected from France, Spain, Slovenia, Italy, Greece, Morocco, South Africa, Tunisia, China, Australia, Chile, Argentina, and the United States.

compare the risks due to As_i exposure, the total As and As species concentration in wines from different countries are summarized in Table 5, which shows that As_i was detected in wine. The As_i concentration in wines procured from the United States was higher than those from China and central Europe, indicating that the consumption of these wines could cause cancer. However, the total As concentration ($\leqslant$ 56.0 μg L^{-1}) in all wines was lower than the regulated limit of 100 and 200 μg L^{-1} in Canada and OIV, respectively.[30] The total As concentration and As species in different wine types varied from one country to another, and As_i was in general higher than organic As (Table 5).

CONCLUSIONS

The total As and As species concentration found in rice wine and rice samples varied. The concentration of As_i decreased after fermentation; AsB was detected in rice wine, while As_i was the predominant As species in all samples. The results of THQ showed no significant noncarcinogenic risk (skin lesions) to local rice wine-consumers. The MOE values < 100 demonstrated that local people might be exposed to carcinogenic risk (lung cancer) due to the consumption of rice wine. However, the amount of As_i ingested did not exceed 200 μg L^{-1}, as permitted by OIV. In addition, this study emphasized the risks of excessive rice wine consumption; the whole intake of As_i should be considered.

ASSOCIATED CONTENT

Please contact the corresponding author for the Supporting Information (Table S1).

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Notes

The authors declare no competing financial interest.

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REFERENCES

1. Y. Li, Y. Liu, X. Han, H. Jin, and S. Ma, *Front. Pharmacol.*, 2019, **10**, 1471. https://doi.org/10.3389/fphar.2019.01471
2. C. T. Markley and B. E. Herbert, *Water Air Soil Pollut.*, 2009, **204**, 385-398. https://doi.org/10.1007/s11270-009-0052-6
3. A. Biswas, A. Das, a. Deb, A. Ghose, and D. N. G. Mazumder, *Stoch. Environ. Res. Risk Assess.*, 2018, **32**, 1035-1050. https://doi.org/10.1007/s00477-018-1513-5
4. S. Chakraborty, M. O. Alam, T. Bhattacharya, and Y. N. Singh, *Water Qual. Expos. Health*, 2014, **6**, 233-246. https://doi.org/10.1007/s12403-014-0122-x
5. A. K. Chandrashekhar, D. Chandrasekharam, and S. H. Farooq, *Environ. Earth Sci.*, 2016, **75**, 142. https://doi.org/10.1007/s12665-015-5008-0

6. Y. Lu, F. Dong, C. Deacon, H.-j. Chen, A. Raab, and A. A. Meharg, *Environ. Pollut.*, 2010, **158**, 1536-1541. https://doi.org/10.1016/j.envpol.2009.12.022
7. W. Zhai, M. T. Wong, F. Luo, M. Z. Hashmi, X. Liu, E. A. Edwards, X. Tang, and J. Xu, *Sci Rep*, 2017, **7**, 42198. https://doi.org/10.1038/srep42198
8. V. A. Nguyen, S. Bang, V. Pham Hung, and K.-W. Kim, *Environ. Int.*, 2009, **35**, 466-472. https://doi.org/10.1016/j.envint.2008.07.014
9. C. K. Tanabe, H. Hopfer, G. Gilleland, A. Liba, S. E. Ebeler, and J. Nelson, *J. Anal. At. Spectrom.*, 2016, **31**, 1223-1227. https://doi.org/10.1039/c6ja00051g
10. C. K. Tanabe, J. Nelson, and S. E. Ebeler, *J. Agric. Food. Chem.*, 2019, **67**, 4154-4159. https://doi.org/10.1021/acs.jafc.9b00634
11. C. M. Moreira, F. A. Duarte, J. Lebherz, D. Pozebon, E. M. M. Flores, and V. L. Dressler, *Food Chem.*, 2011, **126**, 1406-1411. https://doi.org/10.1016/j.foodchem.2010.11.120
12. C. Herce-Pagliai, I. Moreno, G. Gonzalez, M. Repetto, and A. M. Camean, *Food Addit. Contam.*, 2002, **19**, 542-546. https://doi.org/10.1080/02652030110113762
13. D. Bertoldi, T. R. Villegas, R. Larcher, A. Santato, and G. Nicolini, *Environ. Toxicol. Chem.*, 2013, **32**, 773-779. https://doi.org/10.1002/etc.2119
14. M. V. Aguilar, M. C. Martinez, and T. A. Masoud, *Z. Lebensm.-Unters. Forsch.*, 1987, **185**, 185-187. https://doi.org/10.1007/bf01042044
15. J. Qin, B. P. Rosen, Y. Zhang, G. J. Wang, S. Franke, and C. Rensing, *Proc. Natl. Acad. Sci. U. S. A.*, 2006, **103**, 2075-2080. https://doi.org/10.1073/pnas.0506836103
16. Z. L. Gong, X. F. Lu, W. R. Cullen, and X. C. Le, *J. Anal. At. Spectrom.*, 2001, **16**, 1409-1413. https://doi.org/10.1039/b105834g
17. H. Cai, Q. Zhang, L. Shen, J. Luo, R. Zhu, J. Mao, M. Zhao, and C. Cai, *LWT-Food Sci. Technol.*, 2019, **111**, 226-234. https://doi.org/10.1016/j.lwt.2019.05.003
18. H. Li, A. Jiao, X. Xu, C. Wu, B. Wei, X. Hu, Z. Jin, and Y. Tian, *Bioprocess Biosystems Eng.*, 2013, **36**, 1141-1148. https://doi.org/10.1007/s00449-012-0868-0
19. Y. Lu, Y. Gong, Y. Li, Z. Pan, Y. Yao, N. Li, J. Guo, D. Gong, Y. Tian, and C. Peng, *J. Microbiol. Biotechnol.*, 2017, **27**, 1409-1418. https://doi.org/10.4014/jmb.1704.04029
20. S. Chen and Y. Xu, *J. Inst. Brew.*, 2010, **116**, 190-196. https://doi.org/10.1002/j.2050-0416.2010.tb00417.x
21. G. F. Xie, D. D. Yang, X. Q. Liu, X. X. Cheng, H. F. Rui, and H. J. Zhou, *J. Inst. Brew.*, 2016, **122**, 162-167. https://doi.org/10.1002/jib.304
22. L. B. Escudero, E. M. Martinis, R. A. Olsina, and R. G. Wuilloud, *Food Chem.*, 2013, **138**, 484-490. https://doi.org/10.1016/j.foodchem.2012.10.054
23. C. Herce-Pagliai, G. Gonzalez, A. M. Camean, and M. Repetto, *Food Addit. Contam.*, 1999, **16**, 267-271. https://doi.org/10.1080/026520399284037
24. A. D. Monnot, B. E. Tvermoes, R. Gerads, H. Gurleyuk, and D. J. Paustenbach, *Food Chem.*, 2016, **211**, 107-113. https://doi.org/10.1016/j.foodchem.2016.05.013
25. D. W. Lachenmeier and J. Rehm, *Sci Rep*, 2015, **5**, 8126. https://doi.org/10.1038/srep08126
26. W. W. K. Wong, S. W. C. Chung, B. T. P. Chan, Y. Y. Ho, and Y. Xiao, *Food Chem. Toxicol.*, 2013, **51**, 379-385. https://doi.org/10.1016/j.fct.2012.10.010
27. J. A. Caruso, D. T. Heitkemper, and C. B'Hymer, *Analyst*, 2001, **126**, 136-140. https://doi.org/10.1039/b009825f
28. Y. Zhang, G. Sun, Q. Huang, P. N. Williams, and Y. Zhu, *Environ. Int.*, 2011, **37**, 889-892. https://doi.org/10.1016/j.envint.2011.02.020
29. Y. Huang, M. Wang, X. Mao, Y. Qian, T. Chen, and Y. Zhang, *J. Agric. Food. Chem.*, 2015, **63**, 10838-10845. https://doi.org/10.1021/acs.jafc.5b04164
30. D. J. Paustenbach, A. L. Insley, J. R. Maskrey, J. L. Bare, K. M. Unice, V. B. Conrad, L. Iordanidis, D. W. Reynolds, K. S. DiNatale, and A. D. Monnot, *Am. J. Enol. Vitic.*, 2016, **67**, 179-187. https://doi.org/10.5344/ajev.2015.15041
31. A. C. rijalba, E. F. Fiorentini, L. D. Martinez, and R. G. Wuilloud, *J. Chromatogr. A*, 2016, **1462**, 44-54. https://doi.org/10.1016/j.chroma.2016.07.069
32. V. Vacchina, E. N. Epova, S. Berail, B. Medina, O. F. X. Donard, and F. Seby, *Food Addit. Contam., Part B*, 2018, **11**, 286-292. https://doi.org/10.1080/19393210.2018.1504823
33. Y. Fakhri, A. M. Khaneghah, M. R. Hadiani, H. Keramati, R. H. Pouya, B. Moradi, and B. S. da Silva, *Toxin Rev.*, 2017, **36**, 313-321. https://doi.org/10.1080/15569543.2017.1358747
34. N. Gonzalez, J. Calderon, A. Rubies, J. Bosch, I. Timoner, V. Castell, M. Marques, M. Nadal, and J. L. Domingo, *Food Chem. Toxicol.*, 2020, **141**, 111420. https://doi.org/10.1016/j.fct.2020.111420
35. Z. R. Huang, W. L. Guo, W. B. Zhou, L. Li, J. X. Xu, J. L. Hong, H. P. Liu, F. Zeng, W. D. Bai, B. Liu, L. Ni, P. F. Rao, and X. C. Lv, *Food Res. Int.*, 2019, **121**, 593-603. https://doi.org/10.1016/j.foodres.2018.12.024
36. X. Zeng, S. Su, Q. Feng, X. Wang, Y. Zhang, L. Zharig, S. Jiang, A. Li, L. Li, Y. Wang, C. Wu, L. Bai, and R. Duan, *Chemosphere*, 2015, **119**, 1163-1168. https://doi.org/10.1016/j.chemosphere.2014.10.034
37. B. Vriens, M. Lenz, L. Charlet, M. Berg, and L. H. E. Winkel, *Nat. Commun.*, 2014, **5**, 3035. https://doi.org/10.1038/ncomms4035
38. Scientific Opinion on Arsenic in Food, *EFSA Journal*, 2009, **7**, 1351. https://doi.org/10.2903/j.efsa.2009.1351
39. S. R. Yim, G. Y. Park, K. W. Lee, M.-S. Chung, and S.-M. Shim, *Food Sci. Biotechnol.*, 2017, **26**, 293-298. https://doi.org/10.1007/s10068-017-0039-9
40. V. S. T. Ciminelli, M. Gasparon, J. C. Ng, G. C. Silva, and C. L. Caldeira, *Chemosphere*, 2017, **168**, 996-1003. https://doi.org/10.1016/j.chemosphere.2016.10.111
41. D. P. Naughton, and A. Petroczi, *Chem. Cent. J.*, 2008, **2**, 22. https://doi.org/10.1186/1752-153x-2-22
42. A. D. Liu, D. G. Jiang, P. P. Zhou, X. F. Gao, J. W. Li, L. Zhang, Z. P. Liu, and D. J. Yang, *Chinese Journal of Food Hygiene*, 2015, **27**, 311-314. https://doi.org/10.13590/j.cjfh.2015.03.021
43. P. J. Gray, C. K. Tanabe, S. E. Ebeler, and J. Nelson, *J. Anal. At. Spectrom.*, 2017, **32**, 1031-1034. https://doi.org/10.1039/c7ja00041c
44. J. H. Huang, K. N. Hu, J. Ilgen, and G. Ilgen, *Food Addit. Contam., Part A*, 2012, **29**, 85-93. https://doi.org/10.1080/19440049.2011.615029