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**ARTICLE** *in* ENVIRONMENTAL SCIENCE AND TECHNOLOGY · JUNE 2008

Impact Factor: 5.33 · DOI: 10.1021/es702748q · Source: PubMed



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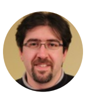

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# Arsenic in Rice: II. Arsenic Speciation in USA Grain and Implications for Human Health

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*Received November 1, 2007. Revised manuscript received February 24, 2008. Accepted March 8, 2008.*

Rice is a potentially important route of human exposure to arsenic, especially in populations with rice-based diets. However, arsenic toxicity varies greatly with species. The initial purpose of the present study was to evaluate arsenic speciation in U.S. rice. Twenty-four samples containing high levels of arsenic and produced in different regions of the U.S were selected from a previous market-basket survey. Arsenite and dimethyl arsinic acid (DMA) were the major species detected. DMA increased linearly with increasing total As but arsenite remained fairly constant at ~0.1 mg $kg^{-1}$, showing that rice high in As was dominated by DMA. A similar result was obtained when our data was combined with other published speciation studies for U.S. rice. However, when all published speciation data for rice was analyzed a second population dominated by inorganic As and lower levels of DMA was found. We thus categorized rice into DMA and Inorganic As types. Rice from the U.S. was predominantly the DMA type, as were single samples from Australia and China, whereas rice from Asia and Europe was the Inorganic As type. We suggest that methylation of As occurs within rice and that genetic differences lead to the two rice types. Insufficient understanding of DMA toxicity precludes a firm assessment of the relative health risks associated with the two rice types but, based on current knowledge, we suggest that the DMA rice type is likely to be less of a health risk than the Inorganic As rice type and, on this basis, rice from the U.S. may be safer than rice from Asia and Europe.

## Introduction

The WHO standard for As in drinking water of 10 $\mu$g $L^{-1}$ has been adopted by many countries. Arsenic in water is generally inorganic and can be a mixture of arsenite (As(III)) and arsenate (As(V)). The U.S. Environmental Protection Agency risk assessment for As in drinking water is based on carcinogenicity risk from inorganic As (*1*). No intake of inorganic As from food was considered in setting the drinking water standard, and it is now evident that significant amounts can be ingested this way. Arsenic in rice is of special concern because of the much higher levels of As in rice grain compared to other staple cereal crops (*2*), coupled with high levels of rice consumption in Asian populations. Adult daily rice intakes as high as 750 g uncooked wt have been reported in West Bengal, India (*3*) and between 400−650 g uncooked wt in Bangladesh (*4*). Rice grain As concentrations in Bangladesh vary widely, but 50% (between the 25th and 75th percentiles of the overall distribution from 871 samples) fall within the range of 0.15−0.36 mg $kg^{-1}$ (*5*), and values as high as 1.8 mg $kg^{-1}$ have been reported (*6*). Daily consumption of 400 g dry wt of rice containing 0.25 mg As $kg^{-1}$ would provide 100 $\mu$g As or 5 times the 20 $\mu$g As from consumption of 2 L of water at the acceptable WHO limit of 10 $\mu$g $L^{-1}$.

Recent publications by Williams et al. (*7*, *8*) and scientific commentaries (*9*) have questioned the safety of rice produced in the U.S. However, their finding that U.S. rice has higher total As concentrations than rice grown in Bangladesh and Europe (*7*) does not hold up when all published data on arsenic concentration in rice is considered (*5*). Moreover, knowledge of speciation of As in rice is critical to understanding the potential toxicity of rice to humans as the toxicity of different arsenic containing compounds varies widely. For example, As concentrations in fish and shellfish can reach 10 mg $kg^{-1}$ (*2*, *10*) and are approximately 10−100 times the levels found in rice. However, most As in seafood is present in organic compounds such as arsenobetaine and arsenocholine that are considered to be nontoxic to humans (acute toxicity ~$10^3$ times less than inorganic arsenic). Four species of As are commonly reported in rice; arsenite, arsenate, monomethyarsonic acid (MMA), and dimethylarsenic acid (DMA). The dominant species are usually arsenite and DMA, although the sum of arsenite + arsenate is often reported (*7*). The inorganic As content in rice can vary from 10−90% of total As (*11*), but the reason for this variability has not been established.

Discussion of the health risk of As in rice has largely been based on its inorganic arsenic content because these species have generally been considered to be more toxic than MMA and DMA (*12*, *13*) and can be directly compared to As in drinking water, assuming equal bioavailability of inorganic As in the rice matrix and in water. Rice produced in the U.S. contained a mean of 42% inorganic As compared to 60 and 80% for European and Bangladesh/Indian rice, respectively (*7*), so that U.S. rice contains one-third to one-half less inorganic As than rice from other countries.

The purpose of our study was to assess As speciation in rice from the U.S. in order to improve understanding of the health risk posed by As in U.S. rice. The results prompted us evaluate As speciation in rice more globally and to consider whether altering As speciation in rice would be a useful strategy for mitigation of human health risk.

## Materials and Methods

Twenty-four samples of U.S. rice at the higher end of the range of observed total As concentration, and representing rice grown in Texas (n = 16), Arkansas (n = 3), and California (n = 5), were selected from the market-basket study of Zavala and Duxbury (*5*). Total As content in rice grain was determined by $HNO_3/H_2O_2$ digestion followed by inductively coupled plasma atomic emission spectroscopy (ICP-AES) and ranged from 0.160 to 0.710 mg $kg^{-1}$ (*5*). An additional five rice samples from Asia with high total As concentrations and one from the U.S. were obtained from Zia Ahmed (Cornell University), and seven samples of BRRI dhan 28 from a water management experiment (Zavala and Duxbury, unpublished data) were also included.

**Arsenic Speciation.** Arsenic speciation analyses were performed by Applied Speciation and Consulting, LLC laboratory in Tukwila, Washington state, U.S. using

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10.1021/es702748q CCC: $40.75  
Published on Web 04/16/2008

ion chromatography-inductively coupled plasma dynamic reaction cell mass spectrometry (IC-ICP-DRC-MS). Sample extraction was based on previous work by Heitkemper et al. (*14*). Approximately 1.0 g of each sample was transferred to 50 mL polypropylene centrifuge tubes. A 10 mL aliquot of 2.0 M trifluoroacetic acid (TFA) was added to each sample. All extractions were placed in a sonicated-heated bath maintained at a temperature of 75 °C and 1200 W for 6 hours. Each sample was removed from heating every 30 min, and was placed on a vortex mixer for 30 s at 1000 RPM. The samples were then centrifuged for 45 min at 4000*g*. The supernatant was decanted, filtered with a syringe filter (0.45$\mu$m), and injected directly into sealed autosampler vials.

Ion chromatographic separation of As species (arsenate As(V), arsenite As(III), dimethylarsenic acid (DMA), monomethylarsonic acid (MMA), and arsenobetaine (AsB)) followed a gradient separation method similar to Jackson et al. (*15*) using an AS16 anion exchange column (Dionex, Sunnyvale, CA). The ion chromatograph was directly interfaced to an ICP-DRC-MS (Perkin-Elmer, Shelton, CT) operated in DRC mode. The DRC was operated with an $O_2$ flow of 0.9 mL min$^{-1}$ while monitoring mass 91 ($^{75}As^{16}O$) for species detection. Monitoring of possible chromatographic interferences was accomplished by inclusion of $^{32}S^{16}O$, $^{35}Cl^{16}O$, and $^{31}P^{16}O$ into the ICP-MS method. It should be noted that identification of arsenobetaine is not conclusive because other organic As species may coelute with the chromatographic method used.

**Speciation Quality Control.** A six point calibration was performed daily spanning the entire concentration range of interest. Calibration standards included As(III) and As(V) which were formulated from pure solid source standards. By using the ICP-MS as the detection system the calibration is species independent; therefore, the average of the slopes for As(III) and As(V) was used to determine concentrations for dimethylarsenic acid (DMA), monomethylarsonic acid (MMA), and arsenobetaine (AsB). Every extraction batch included preparation blanks, laboratory control samples, matrix duplicates, and matrix spikes at two levels or in duplicate. All laboratory control samples and matrix spikes were amended with all target arsenic species prior to extraction to monitor species conversion.

**Statistical Analysis.** Statistical analyses were done using the General Linear Models procedure of SAS 8.2 to test for As species differences. When a significant $F$ value was detected ($P < 0.005$), mean comparisons were separated using Duncan's multiple range test. Sigma Plot (v9.0) and Minitab (v11) were used to fit curves and for descriptive statistical analysis of As species, respectively.

## Results and Discussion

**Arsenic Species Recovery and Quality Control.** The mean detection limits for As(III), As(V), MMA, DMA, and AsB in rice from two different analytical batches were 0.007, 0.025, 0.007, 0.017, and 0.007 mg kg$^{-1}$, respectively. All detection limits were calculated from replicate analysis of the lowest level standard in the calibration and extrapolated to the sample preparation. The recoveries for all target arsenic species associated with the laboratory control sample were within experimental error, although the recovery for DMA was elevated (129.0%). However, recoveries for the DMA matrix spike 1 and 2 were 107.4 and 91.2%, respectively, suggesting acceptable method performance. The relative percent difference for all matrix duplicates included in each extraction batch was less than 25% giving acceptable precision for the applied extraction and analytical methods. The recoveries for all arsenic species in the matrix spikes ranged from 83 to 120% with a single outlier for arsenobetaine at 150%. Since none of the samples yielded an arsenobetaine concentration above the detection limit, the elevated response is deemed to have negligible impact on the validity of the data. The recovery data showed that minimal species conversion and matrix interference occurred during extraction. Additional quality control information is giving in the Supporting Information.

**Arsenic Speciation in U.S. Rice.** Arsenic total and species concentrations in market rice classified by color, commercial type, and U.S. state of production are presented in Table 1. Arsenite and DMA were the dominant species in all samples. Arsenate was present in most samples but at very low levels, and MMA was only detected in three rice samples from Texas. A low amount of an unidentified As species, eluting between MMA and DMA, was found in the brown basmati rice from Texas containing the highest total As level. Mean recovery of As measured as sum of species compared well with total As measured independently (range of 72−123% and a mean of 96 ± 12%), supporting the reliability of the speciation data.

A striking pattern for As speciation emerged when individual species data were plotted against the sum of species measure of total As (Figure 1). The absolute concentration of DMA increased linearly ($R^2 = 0.92$) with increasing total As concentration, whereas the concentrations of arsenite and arsenate remained relatively constant. Thus, an increasing concentration of As in U.S. rice, regardless of type, color, variety (mostly unknown), and location of production is primarily associated with increasing levels of DMA. We then plotted additional data for DMA in U.S. rice from studies by Williams et al. (*7*) and Heitkamper et al. (*14*), both separately and together with our data (Figure 2). The additional data followed the same pattern that we found (strong positive correlation) and the overall regression was very similar suggesting that our results are robust.

The distribution of inorganic As concentrations in U.S. rice from our data set and other studies (*7, 14, 16*) was also similar (Figure 3), which is consistent with our conclusion that the inorganic As in U.S. rice (presumably dominated by arsenite) varies relatively little compared to DMA. The combination of the studies provides information on the overall distribution of inorganic As in U.S. rice, showing that 75% of the samples are <0.138 mg kg$^{-1}$ with average and median values of 0.103 ± 0.045 and 0.110 mg kg$^{-1}$, respectively, and with 95% of the samples containing <0.181 mg kg$^{-1}$. Outliers above the 95th percentile may belong to the inorganic arsenic rice type (see discussion in next section).

**Arsenic Speciation in Global Rice.** To explore speciation of As in rice at the global level, we combined our results with all reported speciation data where the total sum of species recovery was higher than 70% of total As measured independently, giving a total of 105 samples (*2, 7, 14, 17−19*). In general, MMA is only occasionally found so this species was not considered. The inorganic species (arsenite and arsenate) are not always reported separately, due to concerns that some arsenate may be reduced to arsenite during TFA extraction (*20*) so we plotted total inorganic arsenic and DMA against total arsenic measured as the sum of species (Figure 4). This analysis showed that there were two populations of rice, one where increasing total arsenic is mostly associated with increasing DMA and the second where it is mostly associated with increasing inorganic As. The groups were separated by placing all samples where inorganic As (III + V) was > DMA into one group and remaining samples into a second group.

This produced the relationships shown in Figures 5a and 5b for what we term the DMA and Inorganic As rice types, respectively. The dominant As species in the two types of rice were highly and linearly correlated with total As ($R^2 =$ 0.94 and 0.98; Figure 5a and 5b). The inorganic As concentration in the DMA rice type increased only slightly as total As increased (Figure 5a). The regressions suggest that DMA will not be present in this rice when total As is <0.07 mg kg$^{-1}$, that equal amounts of DMA and inorganic As will be found when total As is 0.16 mg kg$^{-1}$ and that DMA becomes

**TABLE 1. Speciation of Arsenic in U.S. Commercial Rice by State of Production**

| color[a] | type[b] | total As ($HNO_3/H_2O2$ | species (TFA extraction) (mg $kg^{-1}$) DMA | AsIII | AsV | sum | species recovery % tot. As |
|---|---|---|---|---|---|---|---|
| | | | **Arkansas** | | | | |
| B | medium | 0.253 | 0.068 | 0.133 | 0.012 | 0.212 | 84 |
| W | long | 0.287 | 0.142 | 0.081 | 0.008 | 0.231 | 80 |
| W | jasmine | 0.356 ± 0.008 | 0.190 | 0.066 | <0.005 | 0.256 | 72 |
| | | | **California** | | | | |
| B | short | 0.201 ± 0.005 | 0.036 | 0.115 | 0.013 | 0.164 | 81 |
| B | long | 0.236 | 0.067 | 0.145 | 0.009 | 0.221 | 94 |
| B | basmati | 0.354 | 0.186 | 0.097 | 0.006 | 0.289 | 82 |
| B | long | 0.273 | 0.171 | 0.102 | <0.005 | 0.273 | 100 |
| W | arborio | 0.162 ± 0.006 | 0.040 | 0.112 | 0.017 | 0.169 | 104[e] |
| | | | **Texas** | | | | |
| B[c] | T−basmati | 0.710 ± 0.028 | 0.572 | 0.168 | <0.005 | 0.769 | 108 |
| B | T−basmati | 0.450 ± 0.021 | 0.320 | 0.116 | <0.005 | 0.437 | 97 |
| B | long | 0.241 ± 0.003 | 0.068 | 0.157 | 0.011 | 0.236 | 98 |
| B | long | 0.258 | 0.069 | 0.142 | 0.008 | 0.218 | 85 |
| W | arborio | 0.242 | 0.171 | 0.049 | 0.023 | 0.242 | 100 |
| W[d] | T−jasmine | 0.253 ± 0.002 | 0.138 | 0.076 | 0.095 | 0.312 | 123 |
| W[e] | arborio | 0.383 ± 0.003 | 0.302 | 0.071 | 0.003 | 0.382 | 100 |
| W | jasmine | 0.369 ± 0.008 | 0.221 | 0.069 | 0.013 | 0.302 | 82 |
| W | sushi | 0.190 ± 0.002 | 0.061 | 0.122 | 0.008 | 0.192 | 101 |
| W | T−basmati | 0.203 ± 0.005 | 0.095 | 0.094 | 0.013 | 0.201 | 99 |
| W | kalijira | 0.195 ± 0.017 | 0.106 | 0.086 | 0.014 | 0.207 | 106 |
| W | medium | 0.270 ± 0.020 | 0.179 | 0.098 | 0.008 | 0.285 | 106 |
| W | basmati | 0.256 | 0.128 | 0.118 | 0.014 | 0.259 | 101 |
| W | T−basmati | 0.351 | 0.239 | 0.078 | 0.007 | 0.323 | 92 |
| W | T−basmati | 0.240 ± 0.014 | 0.171 | 0.081 | 0.013 | 0.265 | 111 |
| W | T−basmati | 0.222 | 0.143 | 0.084 | 0.003 | 0.230 | 104 |

[a] Color: B = brown, W = white. [b] Commercial type. [c] Contained MMA at 0.013 and an unidentified As species at 0.017 mg $kg^{-1}$. [d,e] Contained MMA at 0.003 and 0.006 mg $kg^{-1}$, respectively. [f] Values > 100% represent experimental error between two different analytical methods.

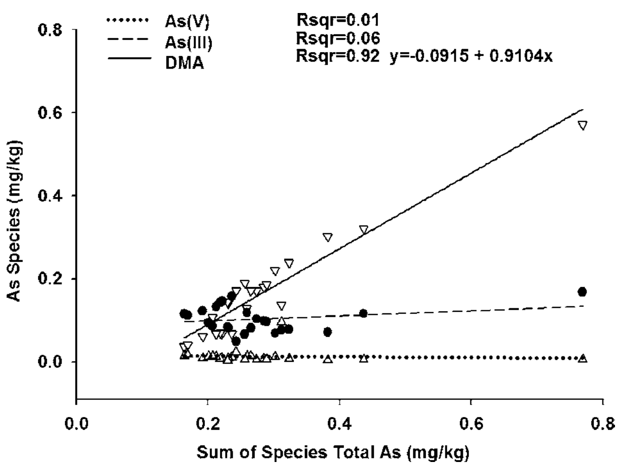


**FIGURE 1. Arsenic species relationship to sum of species total As for 24 U.S. rice grain samples.**

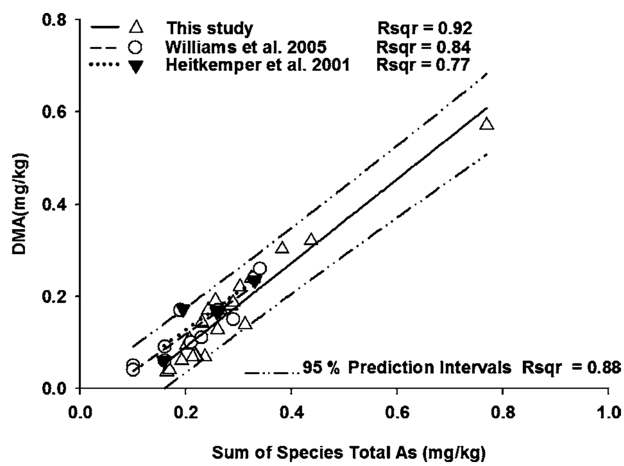


**FIGURE 2. Relationship of DMA to sum of species total As for U.S. rice grain; 95% prediction interval for combined data.**

progressively more dominant as total As concentration rises above 0.16 mg $kg^{-1}$. An upward trend of DMA with increasing total As is also seen for the inorganic As rice type (Figure 5b), although the data are more variable than that for inorganic As in the DMA rice type. The regression lines for inorganic As and DMA on total As essentially go through zero indicating that both inorganic and organic As forms will be present at low total As levels. The difference in As speciation between the two rice types at total As concentrations <0.2 mg $kg^{-1}$, provide evidence that the simple criterion we used to separate them is appropriate.

The occurrence of DMA in rice grain can be explained by methylation of inorganic As within the plant or by uptake of DMA from soil. The ability of terrestrial plants, and rice in particular, to methylate inorganic As has not been conclusively documented (*21*). However, metabolism of inorganic As by humans and animals through alternating reduction and methylation steps is well established (*22*−*24*):

$$H_3As(V)O_4 \rightarrow H_3As(III)O_3 \rightarrow CH_3As(V)O(OH)_2 \rightarrow CH_3As(III)(OH)_2 \rightarrow (CH_3)_2As(V)OOH \rightarrow (CH_3)_2As(III)OH$$

Several plant species (*21*, *25*), including rice (*26*), can reduce arsenate to arsenite but the ability to methylate As has only been found in tomato plants under nutrient deficiency stress (*27*) and in bent grass (*Agrostis tenuis*), an arsenic accumulator (*28*). In the latter case, strong induction of methylation of arsenite in extracts of leaves but not roots and the formation of DMA as the major product were found when the plant was exposed to arsenate.

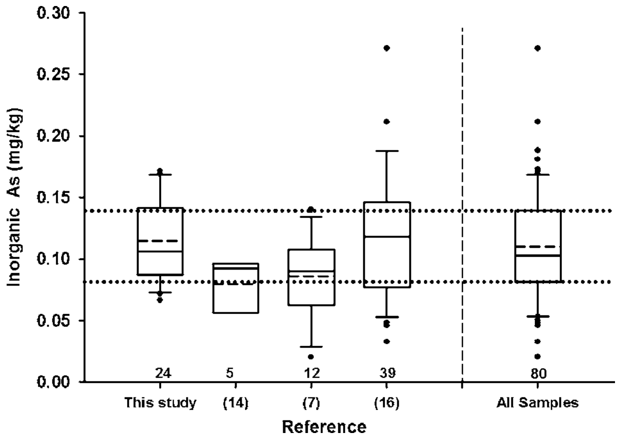


**FIGURE 3. Distribution of inorganic As concentrations reported for U.S. rice grain. The box represents data between the 25th and 75th percentiles. The whiskers (error bars) above and below the box indicate the 95th and 5th percentiles and dots above and below them represent outliers. Lines inside the box represent the mean (−−) and the median (−). Mean and Median for ref *16* were similar. Numbers above and below the *x* axis are the number of samples and the reference, respectively.**

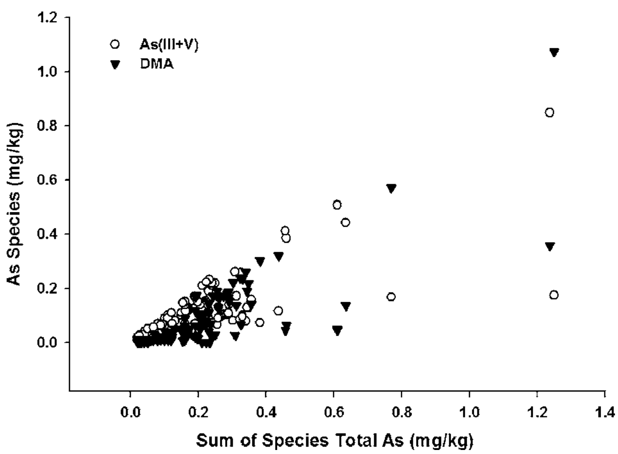


**FIGURE 4. Relationship between total arsenic measured as the sum of species and either inorganic arsenic (III+V) or DMA in rice grain.**

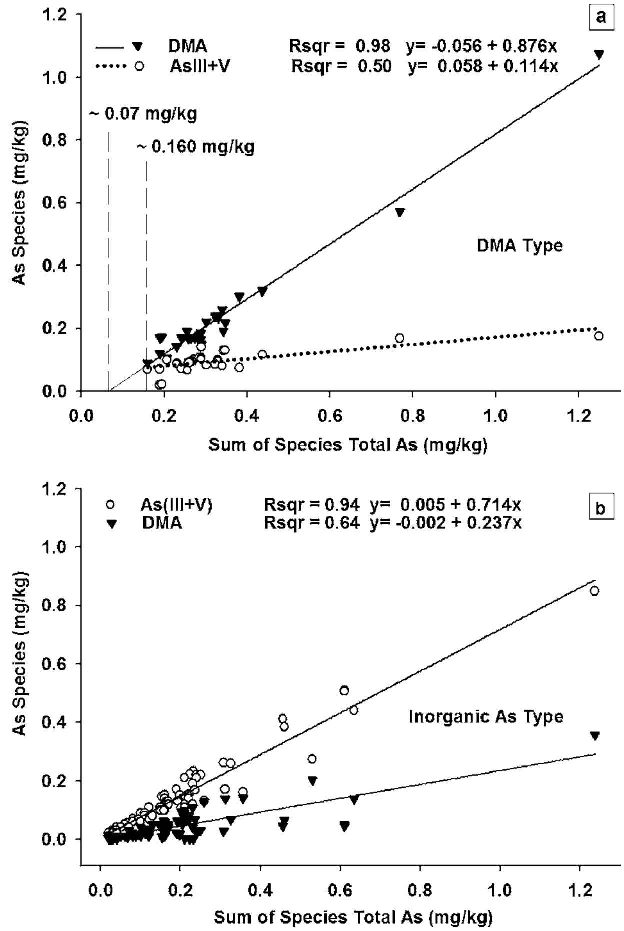


**FIGURE 5. a−b. Arsenic species concentration in rice grain as a function of sum of species total As for samples characterized as (a) the "DMA" type and (b) the "inorganic As" type.**

Microbial methylation of As in soil, which can be significant in flooded soil (*20, 29*), leads to the possibility of direct uptake of methylated As species by rice. However, the prevailing evidence is that inorganic As species are the major As forms in flooded soils (*20, 30*), and the rate of their uptake by rice is approximately 10 and 20−25 times faster than that of MMA and DMA, respectively (*20*). Consequently, it seems unlikely that DMA can be found at much higher levels in rice than inorganic As species without plant methylation of As. It is noteworthy that the highest DMA level for rice in Figure 5a (1.08 mg $kg^{-1}$, 86% of total As) was found for an Australian rice (cv. Quest) grown in sand culture with As applied as arsenate (*18*).

Induction of methylation of As in the DMA rice type would explain the linearity of the relationship between DMA and total arsenic, as well as the relatively low and constant level of inorganic As (Figure 5a), whereas this would not be expected for uptake of DMA from soil unless almost all of the As in soil solution was in this form. On the other hand, the low, but variable, levels of DMA found in grain of the inorganic-As rice type (Figure 5b) might reflect uptake of DMA from soil solution, a low methylation capacity, or a combination of these two processes. The differences in DMA content between the two rice types could also be due to differences in capacity to reduce arsenate to arsenite as a required step before methylation, although our results indicate that arsenite is the dominant inorganic As species in both rice types.

The majority of the rice from the U.S. was the DMA type, although 10 of the 24 samples in this study, 4 of 11 samples from Williams et al. (*7*) and 1 of 5 samples from Heitkamper (*14*) were categorized as the Inorganic As type (Table 2). In contrast, only 1 of 55 and 1 of 6 rice samples from Asia and Europe, respectively were the DMA rice type (Table 2). Assuming that speciation of arsenic in rice is under genetic, rather than environmental, control we expect that plant breeding programs could interconvert the two rice types.

**Human Health Implications for DMA and Inorganic As Rice types.** It is well-known that the speciation of As plays an important role in determining As toxicity to humans. Inorganic As in drinking water has been widely studied and is linked to human carcinogenesis, primarily bladder and lung cancer (*31*). A comparison of inorganic As levels in the two rice types (Figure 6) shows that the inorganic As rice type will have a higher level of inorganic As than the DMA rice type when total As concentration is greater than 0.09 mg $kg^{-1}$. Based on the classification of rice from different countries (Table 2) and a normal range for As in rice of 0.08−0.20 mg $kg^{-1}$ (*5*) most rice from Asia and Europe will have a higher inorganic As concentration than most rice from the U.S.

Inorganic As is metabolized by consecutive reduction and oxidative methylation in the liver and is largely excreted via urine (*32, 33*). These processes were considered to be a detoxification mechanism (*34, 35*) because the major me-

**TABLE 2. Classification of Global Rice by Arsenic Type**

| | | no. of samples of rice type | |
|---|---|---|---|
| country of origin | data source | DMA | inorganic As |
| Australia | *18* | 1 | 1 |
| Bangladesh | this study | | 10 |
| | *7* | | 12 |
| | *17* | | 7 |
| China | *17* | 1 | |
| India | this study | | 2 |
| | *7* | | 11 |
| Italy | this study | 1 | |
| | *19* | | 1 |
| | *7* | | 3 |
| Spain | *7* | | 1 |
| Taiwan | *7* | | 3 |
| | *2* | | 8 |
| Thailand | *7* | | 1 |
| U.S. | this study | 15 | 10 |
| | *7* | 7 | 4 |
| | *14* | 4 | 1 |
| NIST-1568a | *19* | 1 | |
| total | | 30 | 75 |

thylated metabolites MMA and DMA are easily excreted and are less acutely toxic than the inorganic species (*22, 32, 36*). More recently, methylation of As has been reported to be a bioactivation process because of the toxicity of the trivalent As metabolites MMA(III) and DMA(III) which were found to be more mutagenic, cytotoxic, and carcinogenic than inorganic As species (*37, 38*). Petrick et al. (*38*), found that As species toxicity followed the order MMA(III) > arsenite > arsenate> MMA(V) = DMA(V) in human hepatocyte cells. Dimethylarsinic acid has also been reported to be a tumor promoter for skin, lung, and bladder cancer in mice (for a review on the metabolism and toxicity of DMA see Kenyon and Hughes (*39*)) and a promoter of skin and lung cancer in mice via oxidative stress generated by formation of DMA(III) (*40*).

Humans exposed to inorganic As in drinking water generally excrete fairly constant levels of a mixture of As metabolites in urine, i.e. 10−30% inorganic As, 10−20% MMA, and 60−70% DMA (*41*). The incidence of skin lesions associated with chronic ingestion of inorganic As from drinking water in Southwestern Taiwan and Mexico has been reported to be strongly associated with patients excreting more MMA and/or inorganic As and less DMA in urine relative to their control (*42−44*). Valenzuela et al. (*45*) showed that a substantial portion of the methylated As species in urine contained trivalent As, i.e. DMA(III) 49% > DMA(V) 23.7%

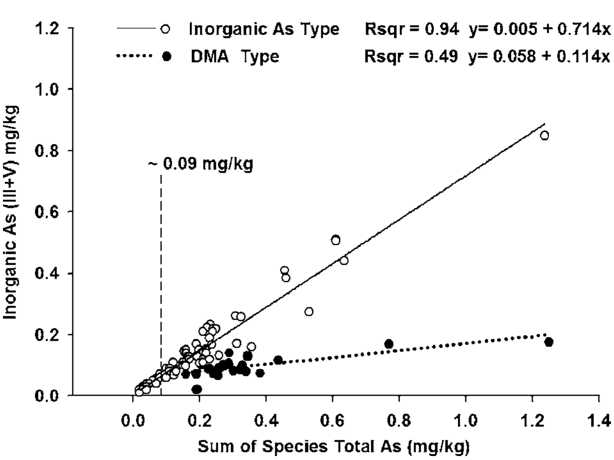


**FIGURE 6. Inorganic As levels in the DMA and inorganic As rice types as a function of sum of species total As.**

> As(V) 8.6% > As(III) 8.5% > MMA(III) 7.4% > MMA(V) 2.8%. Skin lesions were positively correlated with MMA(III) suggesting that this might be the toxic species reported in earlier studies.

There is very limited data on the human bioavailability of inorganic As and DMA in food. However, a study with swine showed that inorganic As in rice was highly bioavailable (89.4 ± 9%) compared to DMA (33.1 ± 3.2%) (*18*). Two human volunteer studies where a single dose of DMA was ingested gave similar results (*32, 46*). One study reported that 80−85% of the 8 mg DMA ingested was eliminated in urine and feces as unmetabolized DMA in a period of 48 h (*46*).

It can be inferred from these studies that As in the DMA rice type will be absorbed less and excreted more rapidly than As in the inorganic As rice type. When the latter rice is consumed, the time of As exposure will be longer and its metabolism will generate highly toxic MMA(III) as well as more oxidative stress. At present it is impossible to fully assess the health risk of As in rice but it seems likely that the DMA rice type will prove to be less of a health risk than the inorganic As rice type. In this case, plant breeding to convert currently popular Inorganic As rice type varieties around the world to the DMA type would be an important risk reduction strategy, especially for countries like Bangladesh and India with As contaminated environments and high rice consumption rates. Currently, at moderate to high total As levels, rice from the U.S. containing predominantly DMA would pose less of a health risk than rice from Asia and Europe containing higher levels of inorganic As.


## Acknowledgments

This research was supported in part by a grant from US-AID through the Soil Management Collaborative Research Support Program (SM-CRSP) and pro bono analysis by Applied Speciation and Consulting LLC, Tukwila, WA.


## Supporting Information Available

Arsenic speciation quality control. Tables of quality control summary for control samples (Table S1 and duplicates and matrix spikes (Table S2). This material is available free of charge via the Internet at http://pubs.acs.org.

## Literature Cited


(1) Environmental Protection Agency. National Primary drinking water regulations: Arsenic and clarifications to compliance and new source contaminants monitoring *Fed. Reg.* **2001**, *66*, 6975−7066, http://www.epa.gov/safewater/arsenic/history.html.

(2) Schoof, R. A.; Yost, L. J.; Eickhoff, J.; Crecelius, E. A.; Meacher, D. M.; Menzel, D. B. A. Market basket survey of inorganic arsenic in food. *Food Chem. Toxicol.* **1999**, *37*, 839–836.

(3) Roychowdhury, T.; Uchino, T.; Tokunaga, H.; Ando, M. Survey of arsenic in food composites from an arsenic affected area of West Bengal, India. *Food Chem. Toxicol.* **2002**, *40*, 1611–1621.

(4) Duxbury, J. M.; Mayer, A. B.; Lauren, J. G.; Hassan, N. Food chain aspects of arsenic contamination in Bangladesh: Effects on quality and productivity of rice. *J. Environ. Sci. Health.* **2003**, *38*, 61–69.

(5) Zavala, Y.; Duxbury, J. M. Arsenic in rice: I. Estimating normal levels of total arsenic in rice grain. *Environ. Sci. Technol.* **2008**, *42*, xxxx–xxxx.

(6) Meharg, A. A.; Rahman, M. M. Arsenic contamination of Bangladesh paddy field soils: implications for rice contribution to arsenic consumption. *Environ. Sci. Technol.* **2003**, *37*, 229–234.

(7) Williams, P. N.; Prince, A. H.; Raab, A.; Hossain, S. A.; Feldmann, J.; Meharg, A. A. Variation in arsenic speciation and concentration in paddy rice related to dietary exposure. *Environ. Sci. Technol.* **2005**, *39*, 5531–5540.

(8) Williams, P. N.; Raab, A; Feldmann, J.; Meharg, A. A. Market basket survey shows elevated levels of As in South Central U.S. processed rice compared to California: Consequences for human dietary exposure. *Environ. Sci. Technol.* **2007**, *41*, 2178–2183.

(9) Portera, C. U.S. rice serves up arsenic. *Environ. Health Perspect.* **2007**, *115*, A296.
(10) Tao, S.S.-H.; Bolger, P. M. Dietary arsenic intakes in the United States: FDA total diet study September 1991-December 1996. *Food Addit. Contam.* **1998**, *16*, 465–472.
(11) Heikens, A.; Panaullah, G. M.; Meharg, A. A. Review of arsenic behaviour from groundwater and soil to crops and potential impacts on agriculture and food safety. *Rev. Environ. Contam. Toxicol.* **2007**, *189*, 43–87.
(12) National Research Council. Arsenic in Drinking Water; National Academies Press: Washington, DC, 1999.
(13) Yamauchi, H.; Fowler, B. A. *Arsenic in the Environment. Part II: Human Health and Ecosystem Effects*; Nriagu, J. O., Ed.; Wiley: New York, 1984; p 35.
(14) Heitkemper, D. T.; Vela, N. P.; Stewart, K. R. Determination of total and speciated arsenic in rice by ion chromatography and inductively coupled plasma mass spectrometry. *J. Anal. Atom. Spectrom.* **2001**, *16*, 299–306.
(15) Jackson, B. P.; Bertch, P. M.; Cabrera, M. L. Trace element speciation in poultry litter. *J. Environ. Qual.* **2003**, *32*, 535–540.
(16) Lamont, H. W. Concentration of inorganic arsenic in samples of white rice from United States. *J. Food Comp. Anal.* **2003**, *16*, 687–695.
(17) Williams, P. N.; Islam, M. R.; Asomako, E. E.; Raab, A.; Hossain, S. A.; Zhu, Y. G.; Feldmann, J.; Meharg, A. A. Increase in rice grain arsenic for regions of Bangladesh irrigating paddies with elevated arsenic in groundwaters. *Environ. Sci. Technol.* **2006**, *40*, 4903–4908.
(18) Juhasz, A. L.; Smith, E.; Weber, J.; Rees, M.; Rofe, A.; Kuchel, T.; Sansom, L.; Naidu, R. *In Vivo* assessment of arsenic bioavailability in rice and its significance for human health risk assessment. *Environ. Health Perspect.* **2006**, *114*, 1826–1931.
(19) D'Amato, M.; Forte, G.; Caroli, S. Identification of quantification of major species of arsenic in rice. *J. AOAC Int.* **2004**, *87*, 238–243.
(20) Abedin, M. J.; Cresser, M. S.; Meharg, A. A.; Feldmann, J.; Cotter-Howells, J. Arsenic accumulation and metabolism in rice (*Oryza sativa* L.). *Environ. Sci. Technol.* **2002**, *36*, 962–968.
(21) Meharg, A. A.; Hartley-Whitaker, J. Arsenic uptake and metabolism in arsenic resistant and non-resistant plant species. *New Phytol.* **2002**, *154*, 29–43.
(22) Gebel, T. W. Arsenic methylation is a process of detoxification through accelerated excretion. *Int. J. Hyg. Environ. Health.* **2002**, *205*, 505–508.
(23) Butchet, J. P.; Lauwerys, R.; Roels, H. Comparison of the urinary excretion of arsenic metabolites after a single dose of sodium arsenite, monomethylarsenate or dimethylarsenate in man. *Int. Arch. Occup. Environ. Health* **1980**, *48*, 71–79.
(24) Marafante, E.; Vahter, M. The effect of methyltransferase inhibition on the metabolism of [74 As] arsenite in mice and rabbits. *Chem. Biol. Interact.* **1984**, *50*, 4–57.
(25) Bleeker, P. M.; Hakvoort, H. W. J.; Bliek, M.; Souer, E.; Schat, H. Enhanced arsenate reduction by a CDC25-like tyrosine phosphatese explains increased phytochelatin accumulation in arsenate-tolerant *Holcus lanatus*. *Plant J.* **2006**, *45*, 917–929.
(26) Duan, G. L; Zhou, Y.; Tong, Y. P.; Mukhopadhyay, R.; Rosen, B. P.; Zhu, Y. G. A CDC25 homologue from rice functions as an arsenate reductase. *New Phytol.* **2007**, *174*, 311–321.
(27) Nissen, P.; Benson, A. A. Arsenic metabolism in Freshwater and terrestrial plants. *Physiol. Plant.* **1982**, *54*, 446–450.
(28) Wu, J. H.; Zhang, R.; Lilley, R. M. Methylation of arsenic in vitro by cell extracts from bentgrass (*Agrostis tenuis*): Effect of acute exposure of plants to arsenate. *Funct. Biol.* **2002**, *29*, 73–80.
(29) Huey, C. C.; Chen, L. G.; Chung, Y. C.; Yeu, C. R. A study on the transformation of arsenite in soils after poultry compost and poultry manure application. *J. Chin. Agric. Chem. Soc.* **1998**, *36*, 380–393.
(30) Marin, A. R.; Masscheleyn, P. H.; Patrick, W. H. The Influence of chemical form and concentration of arsenic on rice growth and tissue arsenic concentration. *Plant Soil* **1992**, *139*, 175–183.
(31) Guo, H. R.; Chiang, H. S.; Hu, H.; Lipstits, S. R.; Monson, R. R. Arsenic in drinking water and incidence of urinary cancers. *Epidemiology* **1997**, *8*, 545–550.
(32) Buchet, J. P.; Lauwerys, R.; Roels, H. Urinary excretion of inorganic arsenic and its metabolites after repeated ingestion of sodium meta arsenite by volunteers. *Int. Arch. Occup. Environ. Health* **1981**, *48*, 11–118.
(33) Yamauchi, H.; Takahashi, K.; Mashiko, M.; Yamamura, Y. Biological monitoring of arsenic-exposed gallium arsenide and inorganic arsenic-exposed workers in urine and hair. *J. Hyg. Assoc.* **1989**, *50*, 602–612.
(34) Marafante, E.; Valther, M.; Envall, J. The role of the methylation in the detoxication of arsenate in the rabbit. *Chem. Biol. Interact.* **1985**, *56*, 225–238.
(35) Hughes, M. F.; Kenyon, E. M. Dose-dependent effect on the disposition of monomethylarsonic acid and dimethylarsinic acid in the mouse after intravenous administration. *J. Toxicol. Environ. Health A* **1998**, *53*, 95–112.
(36) Thomas, D. J.; Styblo, M.; Lin, S. The cellular metabolism and systematic toxicity of arsenic. *Toxicol. Appl. Pharmacol.* **2001**, *176*, 127–144.
(37) Styblo, M.; Del Razo, L. M.; Vega, L.; Germolec, D. R.; LeCluyse, E. L.; Hamilton, G. A.; Reed, W.; Wang, C.; Cullen, W. R.; Thomas, D. J. Comparative toxicity of trivalent and pentavalent inorganic and methylated arsenicals in rat and human cells. *Arch. Toxicol.* **2000**, *74*, 289–299.
(38) Petrick, J. S.; Ayala-Fierro, F.; Cullen, W. R.; Carter, D. E.; Aposhian, H. V. Monomethylarsonous acid (MMA(III)) is more toxic than arsenic in chang human hepatocytes. *Toxicol. Appl. Pharmacol.* **2000**, *163*, 203–207.
(39) Kenyon, E. M.; Hughes, M. F. A concise review of the toxicity and carginogenicity of dimethylarsinic acid. *Toxicology.* **2001**, *160*, 227–236.
(40) Yamanaka, K.; Mizoi, M.; Takabayashi, F.; Nakano, M.; An, Y.; Sagesaka, Y.; Kato, K.; Okada, S. The role of trivalent dimethylated arsenic in dimethylarsinic acid-promoted skin and lung tumorigenesis in mice: Tumor-promoting action through the induction of oxidative stress. *Toxicol. Lett.* **2005**, *158*, 87–94.
(41) Vahter, M. Methylation of inorganic As in different mammalian species and population groups. *Sci. Prog.* **1999**, *82*, 69–88.
(42) Froines, J. R.; Yu, C. R.; Hsu, K. H.; Chen, C. J. Arsenic methylation capacity and skin cancer. *Short Comunication: Cancer Epidemiol., Biomarkers Prev.* **2000**, *9*, 1259–1262.
(43) Hsuesh, Y. M.; Chiou, H. Y.; Huang, Y. L.; Wu, W. L.; Huang, C. C.; Yang, M. H.; Lue, L. C.; Chen, G. S.; Chen, C. J. Serum $\beta$-caroene level, arsenic methylation capability and incidence of skin cancer. *Cancer Epidemiol. Biomark. Prev.* **1997**, *6*, 589–596.
(44) Del Razo, L. M.; Garcia-Vargas, G. G.; Vargas, H.; Albores, A.; Gonsebatt, M. E.; Montero, R.; Ostrosky-Wegman, P.; Kelsh, M.; Cebrian, M. E. Altered profile of urinary arsenic metabolites in adults with chronic arsenicism. A pilot study. *Arch. Toxicol.* **1997**, *71*, 211–217.
(45) Valenzuela, O. L; Borja-Aburto, V. H.; Garcia-Vargas, G. G; Cruz-Gonzalez, M. B.; Garcia-Montalvo, E. A.; Calderon-Aranda, E. S.; Del Razo, L. M. Urinary trivalent methylated arsenic species in a population chronically exposed to inorganic arsenic. *Environ. Health Perspect.* **2005**, *113*, 250–254.
(46) Marafante, E.; Vahter, M.; Norin, H.; Envall, J.; Sandstriim, M.; Christakopoulos, A.; Ryhage, R. Biotransformation of dimethylarsinic acid in mouse, hamster and man. *J. Appl. Toxicol.* **1987**, *7*, 111–117.

ES702748Q