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Predicting Arsenic Relative Bioavailability in Contaminated Soils Using Meta Analysis and Relative Bioavailability−Bioaccessibility Regression Models

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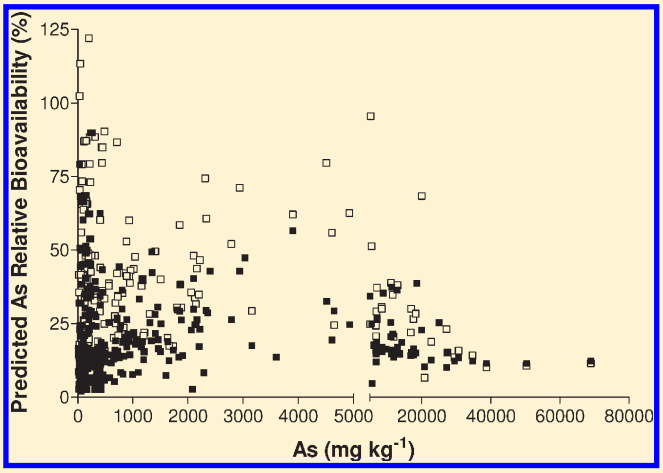
Supporting Information

ABSTRACT: A number of in vitro assays are available for the determination of arsenic (As) bioaccessibility and prediction of As relative bioavailability (RBA) to quantify exposure for site-specific risk assessment. These data are usually considered in isolation; however, meta analysis may provide predictive capabilities for source-specific As bioaccessibility and RBA. The objectives of this study were to predict As RBA using previously published in vivo/in vitro correlations and to assess the influence of As sources on As RBA independent of geographical location. Data representing 351 soils (classified based on As source) and 514 independent bioaccessibility values were retrieved from the literature for comparison. Arsenic RBA was predicted using published in vivo/in vitro regression models, and 90th and 95th percentiles were determined for each As source classification and in vitro methodology. Differences in predicted mean As RBA were observed among soils contaminated from different As sources and within source materials when various in vitro methodologies were utilized. However, when in vitro data were standardized by transforming SBRC intestinal, IVG, and PBET data to SBRC gastric phase values (through linear regression models), predicted As RBA values for As sources followed the order CCA posts ≥ herbicide/pesticide > mining/smelting > gossan soils with 95th percentiles for predicted As RBA of 78.0, 78.4, 67.0, and 23.7%, respectively.



INTRODUCTION

Arsenic (As) occurs naturally in soil and is the 20th most abundant element in the earth's crust. However, enrichment of soil As may occur as a result of anthropogenic processes, including (but not limited to) pesticide/herbicide manufacture and use, mining, smelting, and wood preservation. Where anthropogenic inputs have occurred, elevated As concentrations in soils may exceed regulatory guidelines, with potential impacts on human and environmental health.[1−4] Contamination of soil with As was ranked the most common inorganic constituent in the National Priority List of Sites in the United States.[5] Because of the effects associated with As exposure, such as the development of numerous health disorders in addition to carcinogenesis,[6,7] there is concern regarding the potential risk associated with soil-borne As to human and environmental health.

To define remediation goals for As-contaminated sites, site-specific data are required to ensure an accurate assessment of potential risk at the site. Site-specific data are also warranted to refine default risk variables that, as a result of their conservative nature, may result in unnecessarily low remediation goals, use of additional remediation resources, and deliver unwarranted remediation costs. A parameter that may be utilized to refine site-specific remediation goals is As relative bioavailability (RBA). Arsenic RBA is a measure of the amount of As that is absorbed into systemic circulation (with comparison to a reference dose) as a result of contaminated soil exposure. It is dependent on As mineralogy, the influence of soil properties (e.g., iron [Fe] content), and the residence time of As in the soil.[8] As a result of these factors, As RBA may be less than the conservative assumption of 100%, and this may have a significant influence on human exposure and risk assessment.

Adjustments to As RBA may be achieved by conducting in vivo bioavailability or in vitro bioaccessibility studies. Currently, in vivo assays (e.g., swine) are the method of choice; however, these assays are complicated, expensive, and time-consuming.[9] Because of their simplicity, speed, and affordability, in vitro assays (measuring bioaccessibility) that simulate conditions in the gastrointestinal tract may be an attractive alternative for predicting As RBA.[10] However, for in vitro assays to be used as

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Table 1. Linear Regression Models for Predicting in Vivo As RBA in Contaminated Soils Using SBRC, IVG, and PBET in Vitro Assays[a]

in vitro assay	phase	in vivo-in vitro predictive model	Pearson correlation
SBRC	gastric	in vivo relative As bioavailability (%) = 1.656 + (0.992) SBRC-gastric (%) R^2 = 0.754	0.868
	intestinal	in vivo relative As bioavailability (%) = 5.626 + (1.644) SBRC-intestinal (%) R^2 = 0.654	0.809
IVG	gastric	in vivo relative As bioavailability (%) = 14.323 + (0.853) IVG-gastric (%) R^2 = 0.573	0.757
	intestinal	in vivo relative As bioavailability (%) = 13.971 + (1.105) IVG-intestinal (%) R^2 = 0.567	0.753
PBET	gastric	in vivo relative As bioavailability (%) = 10.096 + (1.162) PBET-gastric (%) R^2 = 0.638	0.799
	intestinal	in vivo relative As bioavailability (%) = 5.682 + (1.762) PBET-intestinal (%) R^2 = 0.665	0.816

[a] Modified from Juhasz et al.[13]

a surrogate measurement of contaminant RBA, the correlation between bioaccessibility and RBA is a mandatory prerequisite for scientific as well as regulatory acceptance.

A limited number of studies have established the relationship between in vivo As RBA and in vitro As bioaccessibility.[11−14] Recently, Juhasz et al. [13] determined As bioaccessibility in contaminated soils (n = 12) using four commonly utilized in vitro assays (Solubility Bioaccessibility Research Consortium assay [SBRC], in vitro gastrointestinal extraction method [IVG], physiologically based extraction test [PBET], and German standardized in vitro assay [DIN]). In vitro results were compared to in vivo As RBA data (swine assay) to ascertain which methodologies best correlate with in vivo data. Comparison of in vitro and in vivo results demonstrated that the in vitro assay encompassing the SBRC gastric phase (SBRC-G) provided the best prediction of in vivo As RBA (R^2 = 0.75, Pearson correlation = 0.87). However, As RBA could also be predicted using gastric or intestinal phases of IVG, PBET, and DIN assays with varying degrees of confidence (R^2 = 0.53−0.67, Pearson correlation = 0.73−0.82).

Although in vivo As RBA studies are limited, a considerable amount of in vitro data has been published reporting As bioaccessibility in contaminated soils from varying geographical regions and As sources.[10,11,14−25] Although in vivo/in vitro correlations are not available for some of these studies, it may be possible to utilize other published in vivo/in vitro and in vitro/in vitro relationships to assess the variability in predicted As RBA for contaminated soils with different As sources. Consequently, the objectives of this study were to retrieve As bioaccessibility data from the literature, predict As RBA using previously published in vivo/in vitro correlations, and assess the influence of As sources on As RBA independent of geographical location.

MATERIALS AND METHODS

Data for As Bioaccessibility Meta Analysis. Arsenic bioaccessibility data was retrieved from the literature following key word searches in ISI Web of Knowledge (to March 2010), in addition to data from research and consultancy reports.[10,11,14−25] Only data utilizing SBRC, IVG, and PBET methodologies were retrieved because of the availability of As RBA−bioaccessibility regression models utilizing these in vitro assays (from Juhasz et al.[13]). Although Juhasz et al.[13] developed an As RBA−bioaccessibility regression model for the DIN assay, limited in vitro data were present in the literature utilizing this methodology, and therefore, they were not utilized for meta analysis. Available data were sorted into four categories (herbicide/pesticide, mining/smelting, copper chrome arsenate (CCA)-treated posts, geogenic) on the basis of the source of the As contamination. These source categories are representative of the common sources of As soil contamination reported in the literature.

Arsenic Relative Bioavailability−Bioaccessibility Regression Models. To transform bioaccessibility data from the literature into As RBA values, As RBA−bioaccessibility linear regression models, developed by Juhasz et al.[13] were utilized (Table 1). These models were developed following the assessment of As RBA in 12 As-contaminated soils using an in vivo swine assay with companion bioaccessibility analysis using gastric and intestinal phases of the SBRC, IVG, and PBET in vitro assays. Although other in vivo/in vitro data is available in the literature,[11,14,22] this information was not included in the development of linear regression models because of the lack of data that demonstrate that As RBA is congruent across rabbit,[22] monkey,[22] and swine models;[11,13,14] the difference in As RBA end points for swine data (urine[11,14] versus blood analysis[13]); and the difference in swine dosing matrix (dough[11,14] versus gavage[13]) and length of dosing. After consideration of the above, only the predictive models of Juhasz et al.[13] were utilized, although it is conceded that any model chosen may introduce some experimental bias into the analysis.

The relationship between in vitro bioaccessibility methods was also determined from data presented in Juhasz et al.[13] to transform As bioaccessibility values between methodologies. Because SBRC-G provided the best estimate for As RBA (see Table 1), linear regression models were developed for in vitro assays in order to predict SBRC-G As bioaccessibility from SBRC intestinal (SBRC-I), IVG, and PBET (gastric and intestinal) data (Table 2 and Supporting Information Figure S1). Incorporation of SBRC-G transformed data into the in vivo-SBRC-G linear regression model may propagate additional uncertainty, although with the application of two successive regression equations it provided a comparison of predicted As RBA for different As sources irrespective of bioaccessibility methodology.

Statistical Analysis. Linear regression models were developed using SPSS 16.0.1 (2007). Comparison of As bioaccessibility and RBA means were determined using unpaired t tests or one-way

Table 2. Linear Regression Models for Predicting SBRC-G As Bioaccessibility from SBRC-I, IVG and PBET (gastric and intestinal phase) Data

in vitro assay	phase	in vivo/in vitro predictive model	Pearson correlation
SBRC	intestinal	As bioaccessibility (SBRC gastric; %) = (1.670) SBRC-intestinal (%) + 3.771 R^2 = 0.882	0.939
IVG	gastric	As bioaccessibility (SBRC gastric; %) = (0.837) IVG-gastric (%) + 13.272 R^2 = 0.720	0.848
	intestinal	As bioaccessibility (SBRC gastric; %) = (1.102) IVG-intestinal (%) + 12.610 R^2 = 0.737	0.858
PBET	gastric	As bioaccessibility (SBRC gastric; %) = (1.137) PBET-gastric (%) + 9.172 R^2 = 0.800	0.894
	intestinal	As bioaccessibility (SBRC gastric; %) = (1.801) PBET-intestinal (%) + 3.660 R^2 = 0.908	0.953

Table 3. Summary of As Concentrations in Soil Used in the As RBA–Bioaccessibility Meta Analysis

		As (mg kg^{-1})[a]			
As source	no. of samples	minimum	maximum	mean	median
herbicide and pesticide	115	8.4	25 025	1124	270
CCA posts	32	23	319	164	163
mining and smelting	164	24	68 924	4771	911
geogenic	40	13	422	87	52
all soils	351	8.4	68 924	2663	327

[a] Concentration of As in the <250 μm soil particle size fraction.

ANOVA. The 90th and 95th percentiles for As RBA were generated in GraphPad Prism (version 5.0).

RESULTS AND DISCUSSION

Arsenic Contaminated Soil. Table 3 provides a summary of As contaminated soils used in the meta analysis. The 351 soils were divided into four categories on the basis of As source: As contamination arising from herbicide/pesticide application, use of CCA treated timber, mining/smelting activities, and naturally occurring elevated concentrations of As (geogenic). Minimum, maximum, mean, and median As concentrations are presented for each source category, in addition, for all soils (Table 3). Soil As concentrations ranged from 8.4 (herbicide/pesticide impacted) to 68 924 mg kg^{-1} (mining/smelting impacted), with mean and median As concentrations of 2663 and 327 mg kg^{-1}, respectively.

Arsenic Bioaccessibility. As highlighted in Table S1 and Figure S2 (Supporting Information), As bioaccessibility in the 351 soils varied considerably and was dependent on the As source and the methodology used for its assessment, including the in vitro phase. When SBRC-G was used to assess herbicide and pesticide impacted soils, As bioaccessibility ranged from <1 to 89.0%, with a mean of 15.8% (n = 103). In a much smaller data set (n = 12) assessed using IVG gastric (IVG-G) and intestinal (IVG-I) phases, the mean As bioaccessibility was significantly different from SBRC-G values ($p < 0.01$); however, there was no significant difference between As bioaccessibility when IVG-G or IVG-I were utilized (p = 0.83; Figure 1). Only the IVG methodology was utilized for the assessment of As bioaccessibility in soils surrounding CCA-treated posts (n = 32). Arsenic bioaccessibility ranged from 15.8 to 63.6% and from 17.0 to 66.3% following assessment using IVG-G and IVG-I, respectively, with no significant difference in the means for each in vitro phase (p = 0.23; Figure 1).

Mining- and smelting-impacted soils have attracted considerable attention in terms of As bioaccessibility research. Both gastric and intestinal phases of SBRC, IVG, and PBET methods have been utilized for assessing As bioaccessibility in contaminated soils ranging in concentration from 24 to 68 924 mg As kg^{-1}. Arsenic bioaccessibility ranged from 0.1 to 66.0% with mean values ranging from 7.9% (n = 105; PBET gastric [PBET-G] phase) to 23.1% (n = 6; SBRC-I). Significant differences between mean As bioaccessibility were observed between SBRC-G and IVG-I ($p < 0.05$), SBRC-G and PBET-G ($p < 0.001$), SBRC-I and PBET-G ($p < 0.05$), and PBET-I and PBET intestinal (PBET-I) phases ($p < 0.001$) (Figure 1). In gossan soils (n = 40), As bioaccessibility ranged from 1.0 to 21.0% with mean values <7.0%, irrespective of sample location and methodology utilized for its assessment (Figure 1). For SBRC and PBET (gastric and intestinal phases) methodologies, there was no significant difference (p = 0.67) between mean As bioaccessibility for gossan soils.

Due to the influence of soil properties and aging effects as a result of the dominance of surface adsorbed As (due to leaching or surface application), As bioaccessibility ranged considerably for CCA- and herbicide/pesticide-impacted soils. A number of researchers have identified the importance of soil Fe in controlling As sorption and bioaccessibility.[10,26−28] In spiked soil studies conducted by Yang et al.,[28] ∼75% of the variability in arsenate bioaccessibility was attributable to the soil's pH and Fe oxide content. Similarly, Juhasz et al.[10] showed that total As, Fe, and free Fe (dithionite citrate bicarbonate-extractable Fe) were variables best able to describe As bioaccessibility in herbicide/pesticide-impacted soils. Iron is an important variable controlling As bioaccessibility due to its marked influence on As sorption in pesticide/herbicide-contaminated soils.[29,30] In addition, Fendorf et al.[31] suggested that contaminant aging decreases bioaccessibility because of changes in surface phase complexes. A decrease in As bioaccessibility in CCA- and herbicide/pesticide-impacted soils may result from the development of inner sphere complexes, surface diffusion within micropores, or surface precipitates[32] with increasing As-soil residence time.

In mining and smelting-impacted soils and gossans, As bioaccessibility is influenced by mineralogical composition. Studies undertaken with pure minerals and impacted soils have shown decreasing As bioaccessibility with As sulfides (e.g., arsenopyrite,

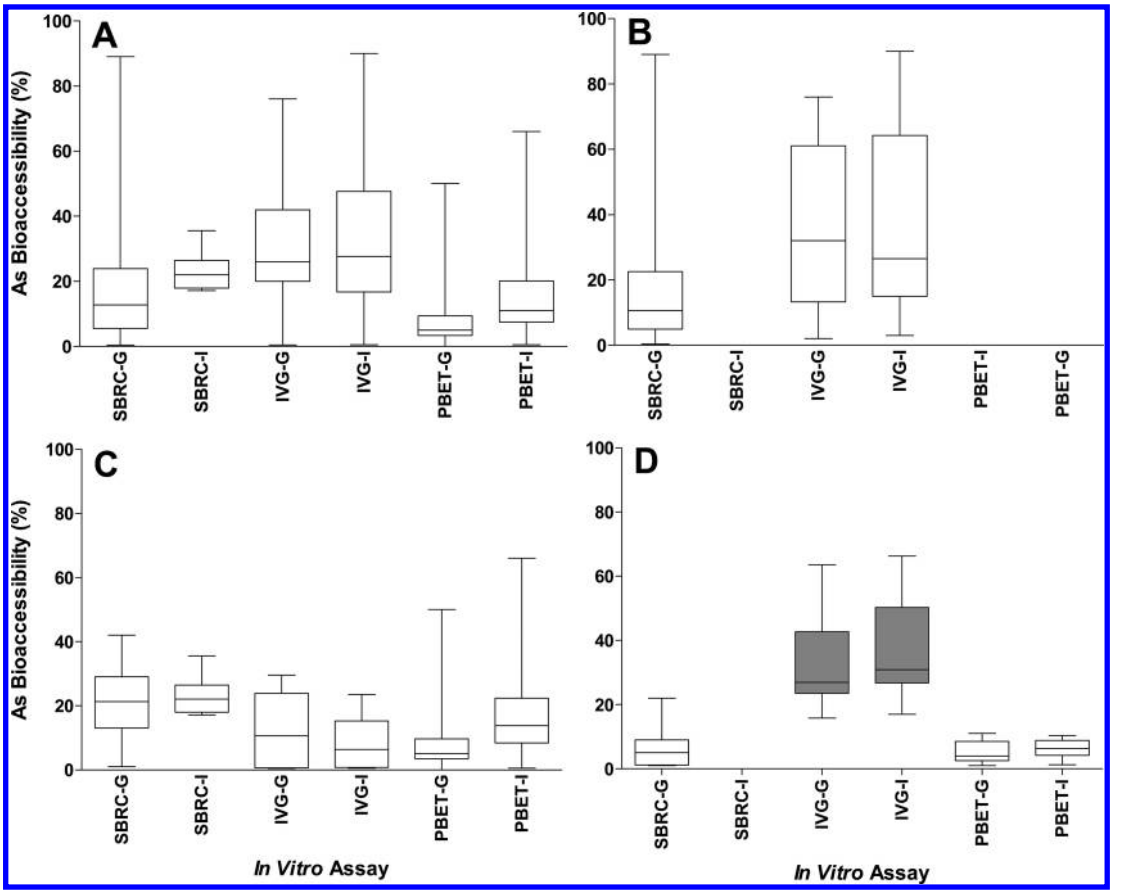

Figure 1. Box plot of As bioaccessibility determined using gastric and intestinal phases of SBRC, IVG, and PBET in vitro methods. Each box represents the lower and upper quartiles, and the band within the box represents the median As bioaccessibility value for the respective in vitro assay. Whiskers represent minimum and maximum values for data determined using each in vitro assay. Panels represent all soils used in the meta analysis (A), herbicide/pesticide (B), mining/smelting (C), and gossan (□) and CCA (■)-impacted soils (D).

realgar), iron arsenates (e.g., scorodite, kankite, pharmacosiderite), As-bearing Fe oxyhydroxides (e.g., goethite, lepidocrocite, akaganeite, roaster), iron oxides (e.g., hematite, maghemite), As sulfates (e.g., tooeleite, jarosite, schwertmannite), clay minerals, and calcium iron arsenates (e.g., yukonite).[33] Higher As bioaccessibility may be associated with calcinated samples in which As is associated with the more amorphous/less dense/more weathered Fe oxides.[3] Unlike discrete mineral phases, these weathered As−Fe oxide associations may undergo dissolution when exposed to pH conditions encountered during gastric phase extraction. Arsenic bioaccessibility may be <1% when As sulphides are the predominant As mineral phase.[8,33] In addition, As bioaccessibility may be influenced by the encapsulation or coating of grains due to a reduction in the dissolution of surface-bound As or the exterior portion of As-bearing grains.[8]

Arsenic Relative Bioavailability. When in vivo/in vitro regression equations developed by Juhasz et al.[13] were utilized to convert in vitro data from 351 soils (Supporting Information Table S1) into As RBA data (Supporting Information Figure S3 and Table S2), predicted values were higher than the corresponding As bioaccessibility values. This was particularly evident for soils assessed using SBRC-I, IVG and PBET methodologies because of the poorer fit of the in vivo/in vitro regression equations (i.e., the slope being >1 or due to large y intercepts) (Table 1). In some cases, predicted As RBA values were in excess of 100% because not all the variability was accounted for in the in vivo/in vitro linear regression models. However, as illustrated in Figure 2, some differences in predicted mean As RBA were observed between soils contaminated from different As sourced and within source materials when different in vitro methodologies were utilized.

For herbicide/pesticide-impacted soils assessed using the SBRC-G assay, the predicted mean As RBA was significantly lower ($p < 0.002$) compared with soils assessed using the IVG assay in which there was no significant difference in means when gastric or intestinal phase predictions were undertaken ($p = 0.33$). Similarly, for mining/smelting impacted soils, there was no significant difference ($p = 0.67$) in predicted mean As RBA when IVG-G and IVG-I were utilized. However, differences in SBRC and PBET predicted mean As RBA's were significant ($p < 0.005$) when gastric and intestinal phases of the respective assays were compared. In contrast, there was no significant difference ($p = 0.63$) between mean As RBA when either phase of the PBET assay was utilized for gossan soil predictions, although predicted mean As RBA was significantly lower ($p < 0.005$) when assessed using SBRC-G. For soils contaminated as a result of CCA post usage, As RBA was significantly higher ($p < 0.005$) when predictions utilized IVG-I data compared with IVG-G.

Table 4 shows the predicted As RBA 90th and 95th percentiles for herbicide/pesticide, mining/smelting, gossan, and CCA-impacted soils determined using in vivo/in vitro linear regression models outlined in Table 1 and the corresponding SBRC, IVG, or PBET in vitro data. For all in vitro assay predictions, As RBA

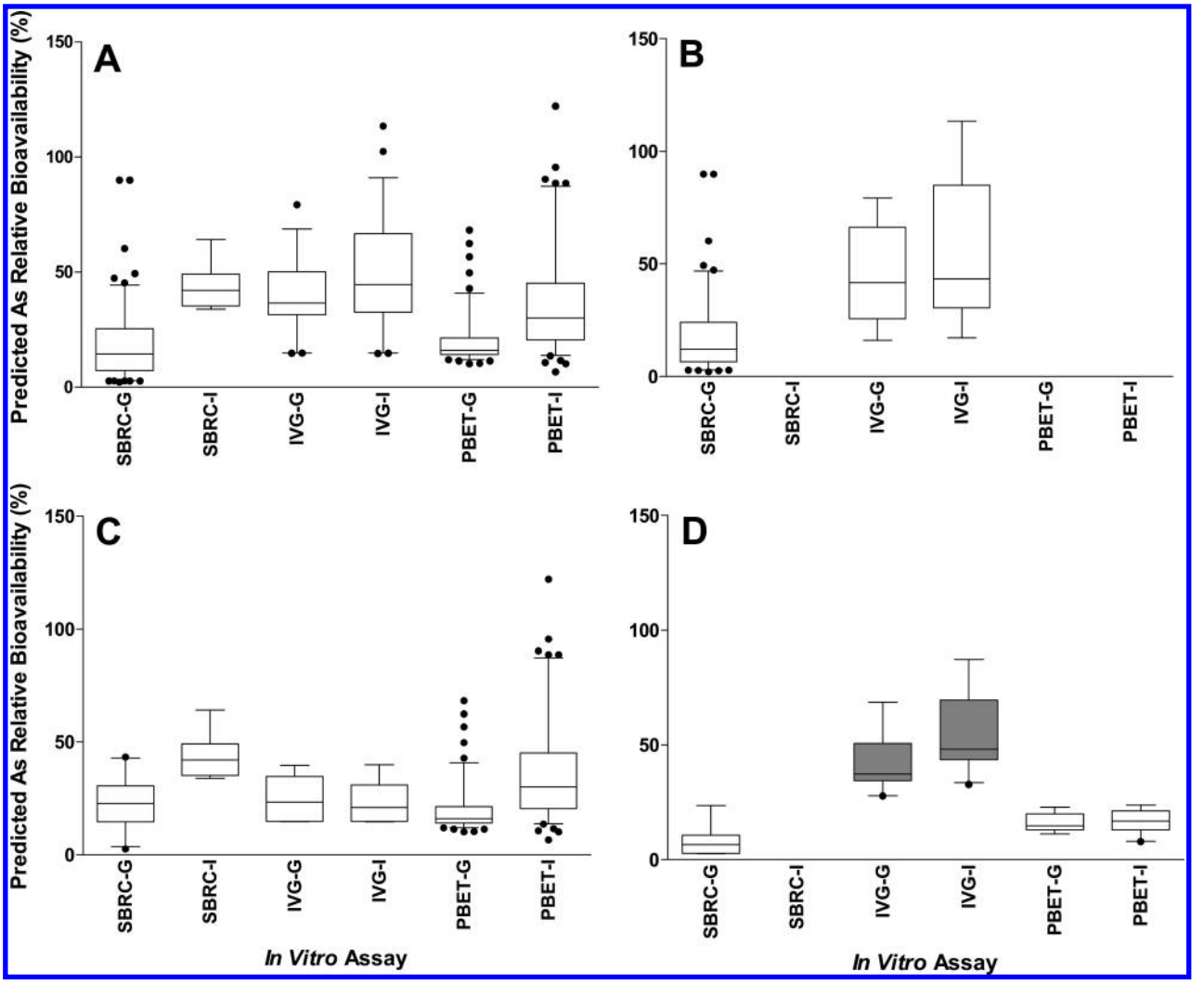

Figure 2. Box plot of predicted As RBA determined using gastric and intestinal phase data form SBRC, IVG, and PBET in vitro assays and in vivo/in vitro regression models of Juhasz et al.[13] Each box represents the lower and upper quartiles, and the band within the box represents the median predicted As relative bioavailability value for the respective in vitro assay. Whiskers represent the 95th percentile for predicted As RBA determined using each in vitro assay. Data above and below these percentiles are represented by a circle (●). Panels represent all soils used in the meta analysis (A), herbicide/pesticide (B), mining/smelting (C), and gossan (□) and CCA (■)-impacted soils (D).

90th and 95th percentiles were higher when intestinal phase data was utilized; however, the difference between calculated values using gastric and intestinal phase data was variable and was not specific to individual in vitro assays or As sources (Table 4). For example, when PBET data was utilized to calculate the 95th percentile for As RBA in gossan and mining/smelting-impacted soils, predicted values using gastric and intestinal phase data were similar for gossan soils, but values determined using intestinal phase data were 2.1-fold higher for mining/smelting soils compared with gastric phase predicted values. In contrast, predicted As RBA 95th percentile values for mining- and smelting-impacted soils were similar when calculated using IVG gastric and intestinal phase data; however, values generated using intestinal phase data were ~1.3-fold greater for CCA-impacted soils. For mining and smelting impacted soils, however, 95th percentile values for predicted As RBA were comparable across SBRC, IVG, and PBET assays for values calculated using gastric phase data (42.9, 39.6, and 40.8%, respectively) (Table 4).

Standardization of in Vitro Data and Predicted As Relative Bioavailability. In the study of Juhasz et al.,[13] the in vitro method incorporating SBRC-G was shown to be the best predictor of in vivo As RBA. To "standardize" As bioaccessibility data from the literature, in vitro data generated from SBRC-I, IVG, and PBET (gastric and intestinal phases) extractions were transformed to SBRC-G values using linear regression models outlined in Table 2. Linear regression models were developed using bioaccessibility data generated for the 12 As-contaminated soils in Juhasz et al.[13] For arsenic bioaccessibility for the 12 soils determined using SBRC-G yielded values that were 1.16−1.98 times higher than those generated using other in vitro methods or phases, however, in vitro/in vitro relationships were linear with variances of 0.720−0.908 compared with the model equations (Table 2).

When As bioaccessibility data was transformed to SBRC-G values, < 2% of data produced values in excess of 100% because not all the variability was accounted for in the model equations. For example, the maximum IVG-I bioaccessibility value for herbicide/pesticide-impacted soils (90.0%) produced a transformed SBRC-G bioaccessibility value of 111.8%. Although As

Table 4. Predicted As RBA for Herbicide/Pesticide, Mining/Smelting, Gossan and CCA-Impacted Soils Determined Using Linear Regression Models Outlined in Table *1* and SBRC, IVG, and PBET in Vitro Data[a]

		predicted as relative bioavailability (%)						
		SBRC assay		IVG assay		PBET assay		SBRC-G
As source	percentile	SBRC-G	SBRC-I	IVG-G	IVG-I	PBET-G	PBET-I	standardization
herbicide/pesticide	90th	39.9		75.9	110.0			50.6
	95th	46.9		79.2	113.4			78.4
CCA posts	90th			62.3	79.3			71.4
	95th			68.6	87.2			78.0
mining/smelting	90th	38.0	64.2	39.2	39.5	29.2	73.1	52.1
	95th	42.9	64.2	39.6	39.9	40.8	87.2	67.0
gossan	90th	21.9				22.9	23.7	23.0
	95th	23.5				22.9	23.9	23.7
all soils	90th	38.6	64.2	66.4	83.1	29.2	73.1	59.8
	95th	44.3	64.2	68.6	91.0	40.8	87.2	70.7

[a] 90th and 95th percentiles are shown for As source and in vitro assay. 90th and 95th percentiles are also shown for each As source following standardization of IVG and PBET data to SBRC-G values (according to Table 2) and recalculation of As RBA using the in vivo SBRC-G linear regression model.

bioaccessibility cannot exceed 100%, these values were retained (see Supporting Information Table S1) to illustrate the potential limitations of the model equations. The inclusion of data in excess of 100% had a modest impact on mean As bioaccessibility calculations, with little impact on 90th and 95th percentile values.

Table S1 (Supporting Information) provides an overview of transformed SBRC-G As bioaccessibility values for gossan soils in addition to herbicide/pesticide, CCA post, and mining/smelting impacted soils. Gossan soils ($n = 40$) yielded the lowest mean As bioaccessibility value (12.9 ± 6.2%), with an upper 95% confidence interval (CI) of the mean of 14.9%. In contrast, CCA-impacted soils yielded the highest As bioaccessibility value of 48.2%, with a standard deviation of 15.1% (upper 95% CI of the mean of 51.9%). For herbicide/pesticide- and mining/melting-impacted soils, there was no significant difference ($p > 0.05$) between mean As bioaccessibility values: 21.9 ± 22.8% (upper 95% CI of the mean of 25.9%) and 26.3 ± 18.4% (upper 95% CI of the mean of 28.5%), respectively, of the SBRC-G transformed As bioaccessibility data.

Figure 3 and Table S2 (Supporting Information) show predicted As RBA values for contaminated soils calculated using SBRC-G standardized in vitro data (from Table S2 of the Supporting Information) and the in vivo SBRC-G linear regression model (Table 1). Mean As RBA ranged from 14.4 ± 6.2% (gossan soils) to 49.4 ± 15.0% (CCA-impacted soils) but there was no significant difference ($p = 0.59$) between the means for herbicide/pesticide- and mining/smelting-impacted soils (~25%). The 90th and 95th percentiles for As RBA, calculated using SBRC-G standardized in vitro data, are presented in Table 4. Predicted As RBA percentiles for As sources followed the order CCA posts ≥ herbicide/pesticide > mining/smelting > gossan. However, for the majority of samples included in the study, the As source was not a good predictor of As RBA because of the wide range of values reported. For example, the relative standard deviation of predicted As RBA for herbicide/pesticide and mining/smelting sources (representing ~80% of the data) were 104 and 70%, respectively. In contrast, predicted As RBA for gossan soils was typically low because of the influence of As mineralogy,

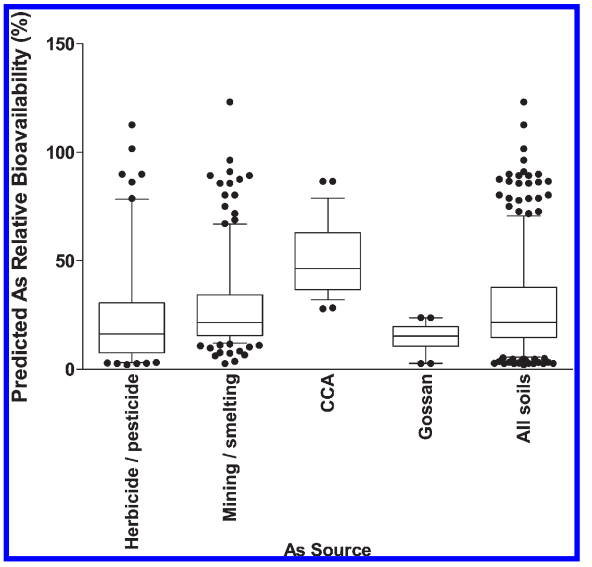

Figure 3. Box plot of predicted As RBA for each As source following conversion of SBRC-I, IVG and PBET data to SBRC-G values (according to Table 4) and calculation of As RBA using the in vivo SBRC-G linear regression model. Each box represents the lower and upper quartiles, and the band within the box represents the median predicted As RBA value. Whiskers represent the 95th percentile for predicted As RBA, and data above and below these percentiles are represented by a circle (●).

which controls As solubility in the gastric phase. In soils contaminated as a result of As pesticide/herbicide application or CCA post usage, As was mainly associated with amorphous Fe oxyhydroxide phases[1,34] which are more soluble in the gastric phase than As associated with mineral phases. Solubility in the gastric phase primarily determines the free ion concentration potentially available for absorption in the intestinal phase,[35] which was highlighted by the fact that predicted As RBA in gossan soils was low compared with the 90th and 95th percentiles for pesticide/herbicide, CCA post and mining/smelting impacted soils (Table 4).

When SBRC-G standardized predicted As RBA 95th percentiles were compared with values generated using in vitro-specific in vivo/in vitro regression models, similar values were observed for gossan soils. The 95th percentile for all SBRC-G standardized predictions was 23.7%, compared with 23.5, 22.9, and 23.9% for SRBC-G only, PBET-G, and PBET-I data, respectively. However, for herbicide/pesticide, CCA post, and mining/smelting impacted soils, standardized predicted 95th percentiles were generally more conservative than values generated using individual gastric phase data or less conservative than some individual intestinal phase data. The difference in predicted As RBA 95th percentiles (standardized versus in vitro method specific) is reflective of the model fit associated with in vivo/in vitro or in vitro/in vitro regressions. However, 95th percentiles for standardized predicted As RBA were 78.0, 78.4, 67.0, and 23.7% for CCA posts, herbicide/pesticide, mining/smelting, and gossan soils, respectively.

On the basis of the meta analysis, the As source may not provide useful predictions of As bioaccessibility or As RBA. Although predicted As RBA values (90th or 95th percentiles) for specific As sources could be used as a first screen to determine the impact of this parameter on human health risk assessment, for the majority of As sources, this may provide minimal impact when refining human health exposure. However, these values may provide further justification for additional site investigation to determine site-specific As bioaccessibility. In addition, for a number of sites, the source of As contamination may be unknown, or contamination may have arisen from multiple sources. In these situations, the assessment of site-specific As bioaccessibility is recommended.

Another factor that needs to be considered when predicting As RBA values (90th or 95th percentiles) for specific As sources is the influence of analytical methodologies on the determination of total As concentration, measurement and calculation of As bioaccessibility and their use for the prediction of As RBA. For example, the determination of total As concentration in soil may vary depending on the digestion matrix (e.g aqua-regia versus concentrated nitric acid versus hydrofluoric acid) and procedure used.[36] Arsenic bioaccessibility may also vary for a given in vitro methodology, depending on the laboratory where the analysis is undertaken. Round robin studies have identified considerable interlaboratory variability for As bioaccessibility with relative standard deviations ranging up to 46% (Koch Pers. comms.). These analytical factors will introduce variability when As bioaccessibility is determined and during As RBA predictions from data sourced from the literature. In addition, uncertainty in model predictions may be improved through the inclusion of additional As bioaccessibility data sets and by improvements in As in vivo/in vitro correlations; a worldwide bioavailability—bioaccessibility research priority.

■ ASSOCIATED CONTENT

Supporting Information. Graphs and tables showing the relationship between As bioaccessibility determined using SBRC-G and other in vitro methods (Figure S1); As bioaccessibility in herbicide/pesticide, CCA, mining/smelting, and gossan soils determined using gastric and intestinal phases of the SBRC, IVG, and PBET assays (Figure S2, Table S1); and predicted As RBA in herbicide/pesticide, CCA, mining/smelting, and gossan soils determined using gastric and intestinal phase in vitro data and bioaccessibility-RBA regression models (Figure S3, Table S2). This information is available free of charge via the Internet at http://pubs.acs.org.

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