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Correlation of in Vivo Relative Bioavailability to in Vitro Bioaccessibility for Arsenic in Household Dust from China and Its Implication for Human Exposure Assessment

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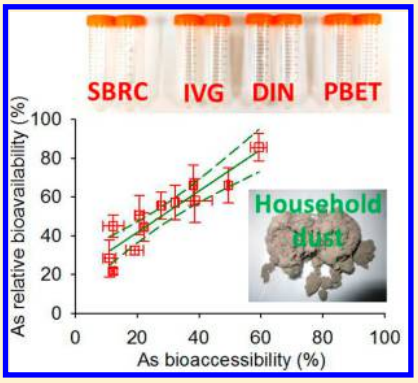
Supporting Information

ABSTRACT: Incidental ingestion of household dust is an important arsenic (As) exposure pathway for children. However, compared to soils, assessment of As relative bioavailability (RBA) in household dust is limited. In this study, As-RBA in 12 household dust samples (7−38 mg kg^{-1}) was measured using an in vivo mouse model and compared to As bioaccessibility determined using 4 assays [Solubility Bioaccessibility Research Consortium method (SBRC), in vitro gastrointestinal method (IVG), Deutsches Institut für Normunge.V. method (DIN), and physiologically based extraction test (PBET)]. Arsenic RBA ranged from 21.8 ± 1.6 to 85.6 ± 7.2% with samples containing low Fe and high total organic carbon content having higher As-RBA. Strong in vivo−in vitro correlations (IVIVC) were found between As-RBA and As bioaccessibility for SBRC and DIN (r^2 = 0.63−0.85), but weaker ones were obtained for IVG and PBET (r^2 = 0.29−0.55). The developed IVIVC for SBRC and DIN were used to calculate As-RBA based on As bioaccessibility for an additional 12 household dust samples. Although As bioaccessibility differed significantly (up to 7.7-fold) based on in vitro methods, predicted As-RBA was less variable (up to 3.0-fold) when calculated using As bioaccessibility data and the corresponding IVIVC. Our data suggested that both SBRC and DIN had potential to assess As bioavailability in household dust samples; however, additional research is needed.



INTRODUCTION

Chronic exposure to arsenic (As), a group-I human carcinogen, has been linked to various adverse health effects including cancers, skin disorders, vascular disease, and diabetes mellitus.[1−3] Arsenic exposure occurs via consumption of contaminated water and food,[4−6] and incidental ingestion of contaminated soil and dust.[7] In Asia, As exposure via drinking water and rice consumption are the predominant pathways.[8,9] However, for other locations where food and water quality are high, incidental ingestion of As-contaminated soil and dust may be important.

Assessment of soil As in environments has received considerable attention,[10−15] but limited information is available regarding As in household dust. Arsenic contamination in household dust is particularly pertinent for toddlers who spend substantial time indoors with their propensity for hand-to-mouth contact. Given the current debate regarding the impact of As exposure on human health at low dose,[2,16] assessing As in household dust is important to quantify early childhood As exposure. Recent studies have demonstrated that As concentrations in household dust vary considerably (0.10−636 mg kg^{-1}),[17−21] depending on anthropogenic As sources, household construction, outdoor soil As concentrations, and the cleaning practices of occupants.

Using total As concentration in household dust provides a worst case scenario for exposure assessment as all As is assumed to be absorbed into the systemic circulation (i.e., 100% bioavailability). However, absorption is influenced by As speciation, and properties of the matrix besides physiological parameters of the individual.[22,23] Although the influence of As speciation and matrix properties on As relative bioavailability (RBA, relative to the adsorption of soluble sodium arsenate) has been demonstrated in As-contaminated soils,[11,14] it is lacking for household dust due to the paucity of in vivo studies. Only one study measured As-RBA for a composite household dust based on monkeys.[24] Conceivably, As-RBA in household dust may differ from soils due to its higher organic carbon (OC) content and smaller particle size.[25]

Although the assessment of As-RBA in household dust is scarce, several studies have assessed As bioaccessibility in

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household dust (i.e., the soluble As fraction in gastrointestinal fluid, which is potentially available for absorption). For example, Dodd et al.[26] determined that As bioaccessibility in Canadian house dust samples is 34−52% using the gastric phase (GP) of the Solubility Bioaccessibility Research Consortium method (SBRC), whereas As bioaccessibility in household dust from a former mining area in southwest England is 10−19% and 31−43% based on GP and intestinal phases (IP) of the physiologically based extraction test (PBET), respectively.[18] Similarly, Huang et al.[27] reported that the mean As bioaccessibility in 10 household dust samples from air conditioner filters is 32−34% using PBET.

Compared to animal models, bioaccessibility methods offer a simple, inexpensive way to estimate As-RBA in household dust. However, it is important to establish the relationship between As bioaccessibility and As relative bioavailability (RBA) so that the assay is valid to predict As-RBA in household dust. The objectives of this study were: (1) to determine As-RBA in 12 household dust samples from 9 cities in China using a mouse blood model; (2) correlate As-RBA to As bioaccessibility determined using 4 in vitro assays; and (3) compare the in vivo−in vitro correlations (IVIVC) for household dust to those for As-contaminated soils to determine if the relationship holds true for different sample matrices. In addition, the derived IVIVC were used to predict As-RBA in an additional 12 household dust samples to assess the influence of As-RBA adjustment on daily As intake values from household dust ingestion. This is the first study to investigate the feasibility of in vitro assays to predict As-RBA in household dust. Our research helps to develop valid in vitro methods to assess As bioavailability in household dust.

MATERIALS AND METHODS

Household Dust Samples. The <150 μm particle size fractions of 24 dust samples collected using plastic brushes from indoor surfaces (e.g., floors, windowsills, and furniture) of 24 houses in 15 cities of 8 provinces in China were used. This fraction is most likely to adhere to children's hands and be ingested via hand-to-mouth contact.[28] Details on sample collection were provided in Supporting Information (SI). Total As and Fe concentrations in household dust were determined using inductively coupled plasma mass spectrometry (ICP−MS, NexION 300X, PerkinElmer, U.S.A.) and flame atomic absorption spectrophotometry (FAAS, PinAAcle 900T, PerkinElmer, U.S.A.) after digestion using USEPA Method 3050B on a heating block digestion system (Environmental Express, Mt. Pleasant, SC). Total organic carbon (TOC) content was determined using an element analyzer (vario TOC select, Elementar, Germany) after removing carbonate carbon with HCl.[29]

Arsenic Relative Bioavailability in Household Dust. Of the 24 household dust samples, samples 1−12 were assessed for As-RBA using an in vivo blood mouse model.[30,31] Female Balb/c mice of ∼20 g body weight (bw) were housed in cages on dry woodchips at 25 °C, 50% humidity, and 12/12 h light/dark cycle, with free access to rodent diet for mice (Qinglongshan Experimental Animal Breeding Farm, Nanjing, China) and Milli-Q water (Millipore, U.S.A.). Mouse care protocols were followed according to the Guide for the Care and Use of Laboratory Animals,[32] which were approved by the Ethics Committee of Animal Experiments of Nanjing University. Following acclimation for 1 week under animal house conditions, mice were randomly grouped (n = 3) into separate metabolic cages and fasted for 24 h prior to As exposure.

After fasting, mice were exposed to a single dose of sodium arsenate (0.5 mL of 5, 25, and 250 mg As L^{-1} in Milli-Q water) or household dust (0.5 mL of 0.1−0.3 g dust in Milli-Q water) via gavage. These doses were equivalent to 0.125, 0.625, and 6.25 mg As kg^{-1} bw (sodium arsenate) and 0.02−0.44 mg As kg^{-1} bw (household dust) (Table S3). For each dust and sodium arsenate exposure, 15 mice were gavaged. At each time interval (4, 8, 16, 24, and 48 h) after gavage, three mice were sacrificed by carbon dioxide anesthesia, and blood samples were collected in heparinized tubes. In addition, baseline blood As concentrations were determined in mice with no As exposure. Blood (∼0.5 mL) was digested using USEPA Method 3050B and analyzed using ICP−MS to establish As absorption kinetics.

Arsenic bioavailability was assessed using pharmacokinetic analysis encompassing area under the blood As concentration time curve (AUC) following zero correction and dose normalization. The AUC for Na_2HAsO_4 was used to calculate As-RBA in household dust (eq 1).

$$\text{As relative bioavailability (\%)} = \left(\frac{\frac{AUC_{\text{dust As}}}{DR_{\text{dust As}}}}{\frac{AUC_{\text{sodium arsenate}}}{DR_{\text{sodium arsenate}}}} \right) \times 100 \quad (1)$$

where $AUC_{\text{dust As}}$ and $AUC_{\text{sodium arsenate}}$ = area under the blood As concentration time curve following household dust and sodium arsenate administeration, respectively; $DR_{\text{dust As}}$ and $DR_{\text{sodium arsenate}}$= As dose of administered household dust and sodium arsenate, respectively (mg As kg^{-1} bw).

In Vitro Bioaccessibility in Household Dust. In vitro assays developed for contaminated soils were used to assess As bioaccessibility in household dust.[10,12,14,33] They included the Solubility Bioaccessibility Research Consortium method (SBRC), in vitro gastrointestinal method (IVG), Deutsches Institut für Normunge.V. method (DIN), and physiologically based extraction test (PBET). For all assays, both gastric (GP) and intestinal phase (IP) extractions were conducted according to Kelley et al.,[34] Rodriguez et al.,[10] DIN,[35] and Ruby et al.,[33] with details being provided in Table S1. Arsenic bioaccessibility was calculated by dividing As extracted in the GP or IP by total As (eq 2) (Table S2 and Figure S1).

$$\text{As bioaccessibility (\%)} = \frac{\text{Extractable dust As}}{\text{Total dust As}} \times 100 \quad (2)$$

Quality Assurance and Quality Control. Unless otherwise specified, three replicates were used for all experiments. A standard reference material (SRM NIST 2711a, National Institute of Standards and Technology) was included in the analyses. The accuracy of USEPA 3050B method was acceptable with As recovery in the SRM being 86.0 ± 0.8 mg kg^{-1} (n = 3) compared to the certified value of 107 ± 5.0 mg kg^{-1}, which was within 81−110 mg kg^{-1} measured by others.[36] Arsenic bioaccessibility in NIST 2711a by the SBRC-GP extraction was 54.4 ± 3.0 mg kg^{-1}, consistent with a previous result of 52.5 mg kg^{-1}.[37] Arsenic-RBA in SRM 2711a was 29.6 ± 6.2% based on the mice blood model, but there is no report of As-RBA for this SRM.

During ICP−MS measurement of As concentration in samples, a standard solution of 1 μg L^{-1} was included every 20 samples. Arsenic recovery (n = 40) was 94.9−107%,

Table 1. Total As and Fe Concentration, TOC Content, and Measured As Relative Bioavailability (RBA) in 12 Household Dust Samples Collected from China

dust sample	location (city, province)	total As (mg kg^{-1})[a]	Fe (g kg^{-1})[a]	TOC (%)[a]	As-RBA (%)[a]
1	Jieshou, Anhui	12.0 ± 0.2	27.0 ± 0.8	10.9 ± 0.6	45.0 ± 5.7
2	Nanjing, Jiangsu	11.9 ± 0.1	36.9 ± 0.3	5.7 ± 0.5	50.6 ± 10
3	Jining, Shandong	9.8 ± 1.5	48.7 ± 3.8	4.2 ± 0.0	28.4 ± 9.6
4	Wuhan, Hubei	34.2 ± 0.1	32.8 ± 0.4	3.7 ± 0.0	32.5 ± 2.3
5	Nanjing, Jiangsu	38.2 ± 1.0	25.6 ± 0.7	6.4 ± 1.0	21.8 ± 1.6
6	Taian, Shandong	8.8 ± 0.1	32.6 ± 0.5	9.6 ± 0.8	57.2 ± 8.9
7	Shenyang, Liaoning	13.9 ± 0.3	25.6 ± 0.4	24.1 ± 3.2	85.6 ± 7.2
8	Nantong, Jiangsu	7.0 ± 0.2	33.0 ± 0.6	4.6 ± 0.5	66.0 ± 9.0
9	Liaocheng, Shandong	13.4 ± 0.2	27.2 ± 1.2	9.1 ± 0.3	66.0 ± 10
10	Jining, Shandong	13.7 ± 0.3	21.0 ± 0.8	10.7 ± 0.3	55.6 ± 6.8
11	Nantong, Jiangsu	7.0 ± 0.2	24.1 ± 1.3	4.5 ± 0.5	58.2 ± 11
12	Nanjing, Jiangsu	10.3 ± 0.2	13.5 ± 0.6	5.5 ± 0.6	44.5 ± 7.3

[a]Values represent the mean and standard deviation of triplicate analyses; TOC = total organic carbon.

averaging 101%. Throughout ICP-MS analysis, ^{74}Ge was used as an internal standard with recovery of 94.5−105%. Each sample was measured in triplicate, with a mean relative standard deviation of 0.20−8.1%.

Statistical Analysis. Simple linear regression analysis between As-RBA and As bioaccessibility, and between As-RBA and concentrations of Fe and TOC was performed using SAS software (version 9.1.3, NC, U.S.A.). Significant differences in slopes and *y*-intercepts of IVIVC between household dust and soils were performed using GraphPad Prism (version 5.0, GraphPad Software, CA, U.S.A.). One-way ANOVA was performed to determine significant differences in As bioaccessibility and calculated As-RBA based on the Tukey's Post Hoc Test using SAS.

RESULTS AND DISCUSSION

Characterization of Household Dust. Total As concentrations in the 24 household dust samples from 15 cities in China varied greatly from 4.48 to 38.2 mg kg^{-1}, averaging 11.5 ± 8.20 mg kg^{-1} (Tables 1 and S2). The highest As concentrations (34.2 and 38.2 mg kg^{-1}) were detected in samples 4 and 5 from Nanjing and Wuhan. Lower As concentrations were detected in samples from smaller cities (e.g., 7 mg kg^{-1} for dust 8 and 11 from Nantong). Total As concentrations in household dust samples were similar to those for dust from Canadian urban houses (n = 1025; 0.10−153 mg kg^{-1}, averaging 13.1 ± 14.3 mg kg^{-1}).[20] Arsenic concentrations in 48 samples from nursery schools in Xi'an, China are 6.0−38.3 mg kg^{-1}, averaging 14.5 ± 6.60.[21] However, compared to household dust from mining areas, the samples in this study contained lower As concentrations. For example, Hysong et al.[17] reported As concentration of 25−192 mg kg^{-1} (averaging 62.4 ± 37.2 mg kg^{-1}) in 85 household dusts from a mining district of Arizona. Arsenic concentrations are 43.0−486 mg kg^{-1} (averaging 149 ± 120 mg kg^{-1}) in household dusts from a former mine site in southwest England (n = 20) and 12.9−636 mg kg^{-1} (averaging 143 ± 19.0 mg kg^{-1}) in a mining district of Bolivia (n = 57).[18,19]

Household dust is often rich in OC compared to outdoor dust and soils, resulting from enrichment of textile fibers, hairs, and skin cells. In this study, TOC in the 24 household dust samples varied from 2.70 to 24.1% (averaging 8.60 ± 5.80%). They were significantly higher than TOC in 80 Chinese soils (0.30−5.2%, averaging 1.8 ± 1.2%)[38] and comparable with those from Canada (18−37%)[25] and the UK dust (10−30%).[39] In addition, total Fe concentrations in household dust varied from 12.8 to 48.7 g kg^{-1} (averaging 24.0 ± 8.80 g kg^{-1}). Compared to Fe contents (24.0−51.5 g kg^{-1}, averaging 38.1 ± 5.90 g kg^{-1}) in 80 Chinese soils,[38] household dust samples contained significantly lower Fe concentrations. The difference in TOC and Fe concentrations between household dust and soils may influence As bioaccessibility. As detailed by Yang et al.[40] and Bradham et al.,[14] As sorption to Fe oxides reduces As solubilization and thereby decreases As bioaccessibility.

Arsenic Relative Bioavailability in Household Dust. In vivo experiments using a mouse blood model were conducted with sodium arsenate (Na_2HAsO_4) to establish the linear dose AUC response (Figure S2). Na_2HAsO_4 was gavaged to mice at As doses of 0.125, 0.625, and 6.25 mg kg^{-1} bw. Because of limited dust sample, the As dose levels for dust samples 2, 6, 7, 8, and 9 (0.02−0.06 mg As kg^{-1} bw) were lower than the lowest sodium arsenate level (0.125 mg As kg^{-1} bw) (Table S3). However, established relationship between sodium arsenate dose levels (0.125, 0.625, and 6.25 mg As kg^{-1} bw) and AUC values showed that As absorption in mice was linearly dose dependent (Figure S2). In addition, previous studies suggested that As concentration up to 50 mg L^{-1} in drinking water does not affect As uptake by mice.[41] So the linear response in this study suggested that As-RBA in dust was not affected by As dose levels.

The linear dose−response relationship confirmed that a single dose of Na_2HAsO_4 could be used to normalize As absolute bioavailability to obtain As-RBA in dust (eq 1). Because the As dose in dust samples administered to mice (0.02−0.44 mg kg^{-1} bw) was closest to the 0.125 mg kg^{-1} bw Na_2HAsO_4 dose (Table S3), it was used for As-RBA calculation. Because the As AUC was linearly dose-dependent (Figure S2), using AUC data for other two Na_2HAsO_4 doses resulted in only <3.0% variations in calculated As-RBA in dust.

Results from the in vivo mouse assay showed that As-RBA varied considerably among the 12 samples, ranging from 21.8 ± 1.60 (dust 5) to 85.6 ± 14.4% (dust 7) and averaging 51.0 ± 18.0% (Table 1). The large range in As-RBA of household dust samples provided a good base to correlate As-RBA to As bioaccessibility in this study.[42] As-RBA values in household dust were generally higher than those for soils from mining/smelting areas. For instance, As-RBA in mining/smelting contaminated soils were 11−53% (n = 11, 33 ± 17%),[14] 3.0−43% (n = 13, 21 ± 13%),[10] 7.0−75% (n = 12, 32 ± 25%.),[11] and 5.0−31% (n = 14, 17 ± 8%).[13] The lower total As

concentration but higher As-RBA in household dust than contaminated soils could be attributed to different As distribution in solid phases. As detailed by Meunier et al.[22] and Bradham et al.,[14] mining/smelting impacted soils contain a higher portion of insoluble As species, such as arsenopyrite, which decreases As-RBA. The household dusts in this study were probably not affected by mining/smelting activities, and therefore contained more soluble As species.[22]

Previous studies examined the impact of soil properties on As-RBA, finding an inverse correlation between As-RBA and total Fe concentration;[14,22] however, a poor correlation was found in household dust (Figure S3). Compared to soils, household dust contains significantly higher TOC,[25] thus As-RBA in household dust was more related to TOC (r^2 = 0.43) than Fe concentration (r^2 = 0.06), accounting for 43% of the variability in As-RBA. The data suggested TOC played a more important role in influencing As-RBA in household dust than Fe oxides, which have been hypothesized to control As-RBA in As-contaminated soils.[14]

Correlation between in Vivo As Relative Bioavailability and in Vitro As Bioaccessibility. For As-contaminated soils, a strong linear relationship between As-RBA and As bioaccessibility has been reported.[10,12,14,33,42−44] By establishing good in vivo−in vitro correlations (IVIVC), bioaccessibility assays can serve as surrogate to predict As-RBA to refine human health exposure. However, IVIVC have not been established for As in household dust due to the paucity of in vivo studies. For the 12 household dust samples, As bioaccessibility was determined using SBRC, IVG, DIN, and PBET (Figure S1). Arsenic bioaccessibility based on GP extraction varied with assays, being 46.1−89.4%, 45.6−83.4%, 34.6−63.7%, and 30.1−69.2% for SBRC, IVG, DIN, and PBET and following the order of SBRC > IVG > DIN > PBET. The difference in As bioaccessibility based on different methods was probably related to their differences in GP-pH (1.5, 1.8, 2.0, and 2.5 for SBRC, IVG, DIN, and PBET respectively).

Arsenic bioaccessibility also differed in the IP. For SBRC and IVG, As bioaccessibility was lower in the IP than GP, decreasing by 1.5−6.1 and 1.3−1.8 fold. However, with DIN and PBET, As bioaccessibility in most samples did not decrease. In the IP, As bioaccessibility was 12.2−59.3% for SBRC, being significantly lower (p < 0.05) than 29.1−62.9%, 30.5−63.8%, and 27.9−57.1% for IVG, DIN, and PBET. The lower As bioaccessibility using the SBRC-IP assay compared to other assays was probably related to the impacts of different gastric constituents (i.e., glycine for SBRC vs. pepsin and mucin for other assays, Table S1) on As adsorption onto newly formed Fe oxides during IP extractions.

Arsenic bioaccessibility determined using the four assays was compared to As-RBA in household dust (Figure 1). Table 2 details the correlation coefficient (r^2), slope, and y-intercept for IVIVC using data from the four assays and the mouse blood model. The strength of the predictive models varied from r^2 = 0.29 (PBET-GP) to r^2 = 0.85 (SBRC-IP). While the SBRC (r^2 = 0.76−0.85) and DIN (r^2 = 0.63−0.71) satisfied the benchmark of r^2 > 0.60,[45] the IVG and PBET did not (r^2 = 0.29−0.55). Although IVIVC have not been reported for household dust, they have for As-contaminated soils. Based on a swine AUC assay, Juhasz et al.[12] reported that the SBRC (r^2 = 0.75−0.65) and PBET (r^2 = 0.64−0.67) provide a better prediction of As-RBA in 12 contaminated soils than the IVG (r^2 = 0.57−0.57) and DIN (r^2 = 0.55−0.53). Bradham et al.[14] and Brattin et al.[43] reported that the SBRC-GP provides good

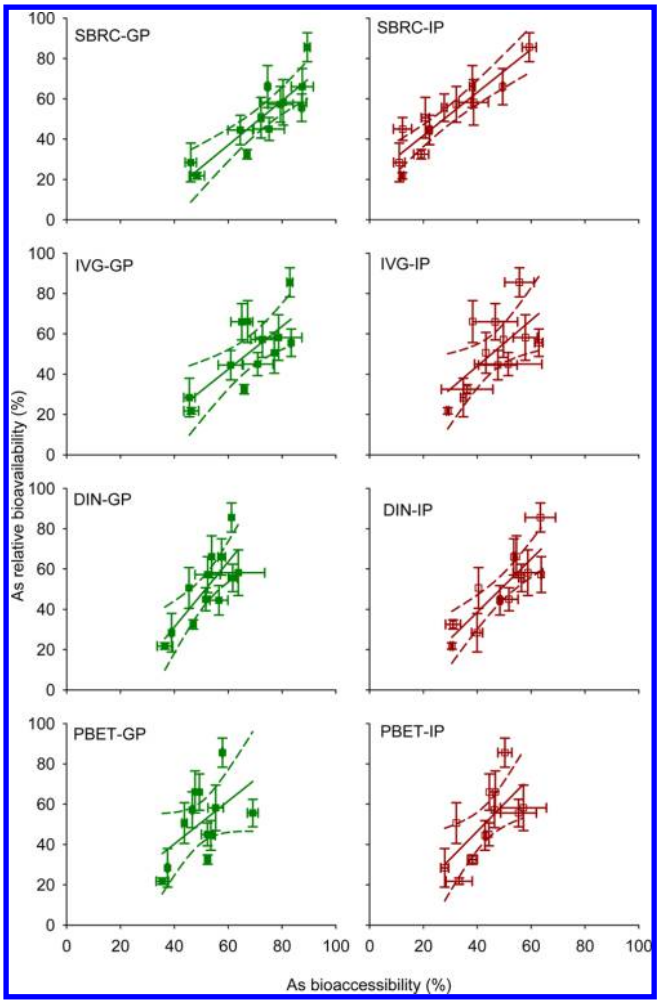

Figure 1. Correlation between As relative bioavailability measured using an in vivo mouse blood model and in vitro As bioaccessibility determined using gastric (GP) and intestinal phases (IP) of the SBRC, IVG, DIN, and PBET assays for 12 household dust samples (1−12). Best fit linear regression (solid lines) and 95% confidence interval (dashed lines) are shown. Each data point represents the mean and standard deviation of triplicate analyses.

Table 2. Linear Regression between in Vivo As Relative Bioavailability (RBA) and in Vitro As Bioaccessibility Determined Using Gastric (GP) and Intestinal Phases (IP) of SBRC, IVG, DIN, and PBET Assays for Household Dust Samples 1−12

in vitro assay	phase	in vivo−in vitro predictive model (IVIVC)	correlation coefficient (r^2)[a]
SBRC	gastric	As-RBA = −29.0 + 1.10 (SBRC-GP)	**0.76**
	intestinal	As-RBA = 20.4 + 1.07 (SBRC-IP)	**0.85**
IVG	gastric	As-RBA = −21.6 + 1.07 (IVG-GP)	0.55
	intestinal	As-RBA = −1.62 + 1.14 (IVG-IP)	0.42
DIN	gastric	As-RBA = −33.6 + 1.62 (DIN-GP)	**0.63**
	intestinal	As-RBA = −14.1 + 1.32 (DIN-IP)	**0.71**
PBET	gastric	As-RBA = −2.37 + 1.06 (PBET-GP)	0.29
	intestinal	As-RBA = −8.04 + 1.36 (PBET-IP)	0.47

[a] r^2 >0.60 are in bold.

prediction (r^2 = 0.92 and 0.72) of soil As-RBA based on mouse and swine steady state urinary excretion models. Using the same soils from Bradham et al.,[14] Juhasz et al.[44] showed that

Table 3. Comparison of in Vivo−in Vitro Correlations (IVIVC) for Gastric (GP) and Intestinal Phases (IP) of SBRC and DIN Assays between Contaminated Soils and Household Dust

			in vivo assay		parameters for IVIVC		
in vitro assay	previous study	number of samples	animal	biomarker	slope	intercept	r^2
SBRC−GP	Juhasz et al.[12]	12	swine	blood AUC	0.99	1.66***	0.75
	Juhasz et al.[44]	10	mouse	urinary excretion	0.62*	5.4*	0.90
	Bradham et al.[14]	11	mouse	urinary excretion	0.72	5.64*	0.92
	Brattin et al.[43]	20	swine	urinary excretion	0.62	19.7***	0.72
	this study[a]	**12**	**mouse**	**blood AUC**	**1.10**	**−29.0**	**0.76**
SBRC−IP	Juhasz et al.[12]	12	swine	blood AUC	1.64	5.62	0.65
	Juhasz et al.[44]	10	mouse	urinary excretion	0.51*	19.1	0.61
	Brattin et al.[43]	19	monkey	urinary excretion	0.43	17.1***	0.71
	this study	**12**	**mouse**	**blood AUC**	**1.07**	**20.4**	**0.85**
DIN−GP	Juhasz et al.[12]	12	swine	blood AUC	1.78	5.73***	0.55
	Juhasz et al.[44]	10	mouse	urinary excretion	0.60**	11.1***	0.90
	this study	**12**	**mouse**	**blood AUC**	**1.62**	**−33.6**	**0.63**
DIN−IP	Juhasz et al.[12]	12	swine	blood AUC	1.46	9.2**	0.53
	Juhasz et al.[44]	10	mouse	urinary excretion	0.61*	12.6**	0.88
	this study	**12**	**mouse**	**blood AUC**	**1.32**	**−14.1**	**0.71**

[a]IVIVC of this study are in bold. *, **, and ***indicate significant differences in slope or *y*-intercept between this study and previous study at $p <$ 0.05, <0.01, and <0.001 for each assay.

IVG, DIN, and PEBT also have strong predictive ability (r^2 = 0.67−0.90) of As-RBA.

In addition to r^2, the *y*-intercepts and slopes of IVIVC also influence their predictive ability. For most IVIVC in this study, the slope was close to 1,[45] but significant variability was observed in the *y*-intercept (−33.6 to 20.4) (Table 2). Wragg et al.[45] suggested that the *y*-intercept should be close to zero. Although the *y*-intercept was small for IVG-IP and PBET-GP, r^2 was poor at 0.29−0.42. In contrast, assays exhibiting a strong IVIVC (SBRC and DIN) had large *y*-intercepts (−33.6 to 20.4), which may introduce underestimation and overestimation of As-RBA at low values. For example, if the IVIVC for SBRC-GP and DIN assays were used to predict As-RBA, an underestimation would occur in samples with low As-RBA due to their negative *y*-intercepts (−33.6 to −14.1). The opposite would be true if SBRC-IP were used. With a view of being conservative when estimating As-RBA for exposure assessment, the SBRC-IP assay with positive *y*-intercept and strongest r^2 at 0.85 was the best predictor of As-RBA for the 12 household dusts. However, caution should be exercised for samples with low As-RBA due to the large *y*-intercept. For better prediction, additional research is needed to improve the IVIVC (e.g., smaller *y*-intercept). This may be accomplished by including more dust samples, especially those contaminated from other sources (e.g., mining, smelting, and arsenical pesticide), which increase the range of As RBA and bioaccessibility.

For SBRC and DIN with the strongest IVIVC, a comparison was made between household dust and As-contaminated soils.[12,14,43,44] Previous research on As-contaminated soils has found variability in the slopes and *y*-intercepts of the IVIVC (Table 3). Compared to IVIVC for As-contaminated soil, the IVIVC of the SBRC and DIN for household dust were not significantly different in slopes, but they were significantly different in *y*-intercepts. For example, the *y*-intercept of −29.0 for SBRC-GP IVIVC of household dust was significantly different from values (5.64−19.7) for soils reported by Juhasz et al.[12] ($p < 0.001$), Bradham et al.[14] ($p < 0.05$), and Brattin et al.[43] ($p < 0.001$). There were also significant ($p < 0.01$) differences in *y*-intercepts of DIN IVIVC between Juhasz et al.[12] and this study. When IVIVC were compared to that by Juhasz et al.,[44] significant differences were observed in both slope and *y*-intercept for SBRC and DIN assays. However, for the SBRC-IP, the slope and intercept (1.07 and 20.4) for household dust were not significantly (p = 0.10 and 0.74) different from those (1.64 and 5.62) reported by Juhasz et al.[12] for contaminated soils. Different IVIVC observed for household dust might be attributed to differences in physiological parameters of animals (i.e., mouse vs swine) and biomarker (blood AUC vs urinary excretion) besides differences in properties between dust and soils.

Estimation of Arsenic RBA Using Derived IVIVC to Refine Exposure Assessment. Although As-RBA may be used to refine exposure for the incidental dust ingestion pathway, the use of animal models en masse is not feasible due to ethical considerations besides cost and time constraints. However, as detailed above, strong IVIVC for some assays suggested that in vitro methods may be used as a surrogate measure to predict As-RBA. Hence, data derived from As bioaccessibility of household dust were put into appropriate linear regression models for risk assessment (Table 2).

Arsenic bioaccessibility determined using SBRC and DIN for an additional 12 household dust samples (13−24) were used to calculate As-RBA using their respective linear regression models. Arsenic bioaccessibility varied with assay used. For GP extraction, As bioaccessibility based on SBRC was significantly ($p < 0.05$) higher than those based on DIN (Figure S4). This may be attributed to the lower gastric pH of the SBRC-GP (1.5 vs 2.0), which influences As dissolution from the dust matrix.[12,46] However, during IP extraction, As bioaccessibility using SBRC was significantly ($p < 0.05$) lower than DIN. The decrease in As bioaccessibility from SBRC-GP to SBRC-IP has been reported for soils, corresponding to decreased Fe solubilization.[12,44] The higher pH in the IP (7.0) resulted in precipitation of dissolved Fe as amorphous Fe oxides, reducing soluble As via adsorption or coprecipitation. However, for DIN, the presence of different components (e.g., pepsin, mucin, and phosphate; Table S1) in the IP fluid may have inhibited the precipitation of dissolved Fe or adsorption of

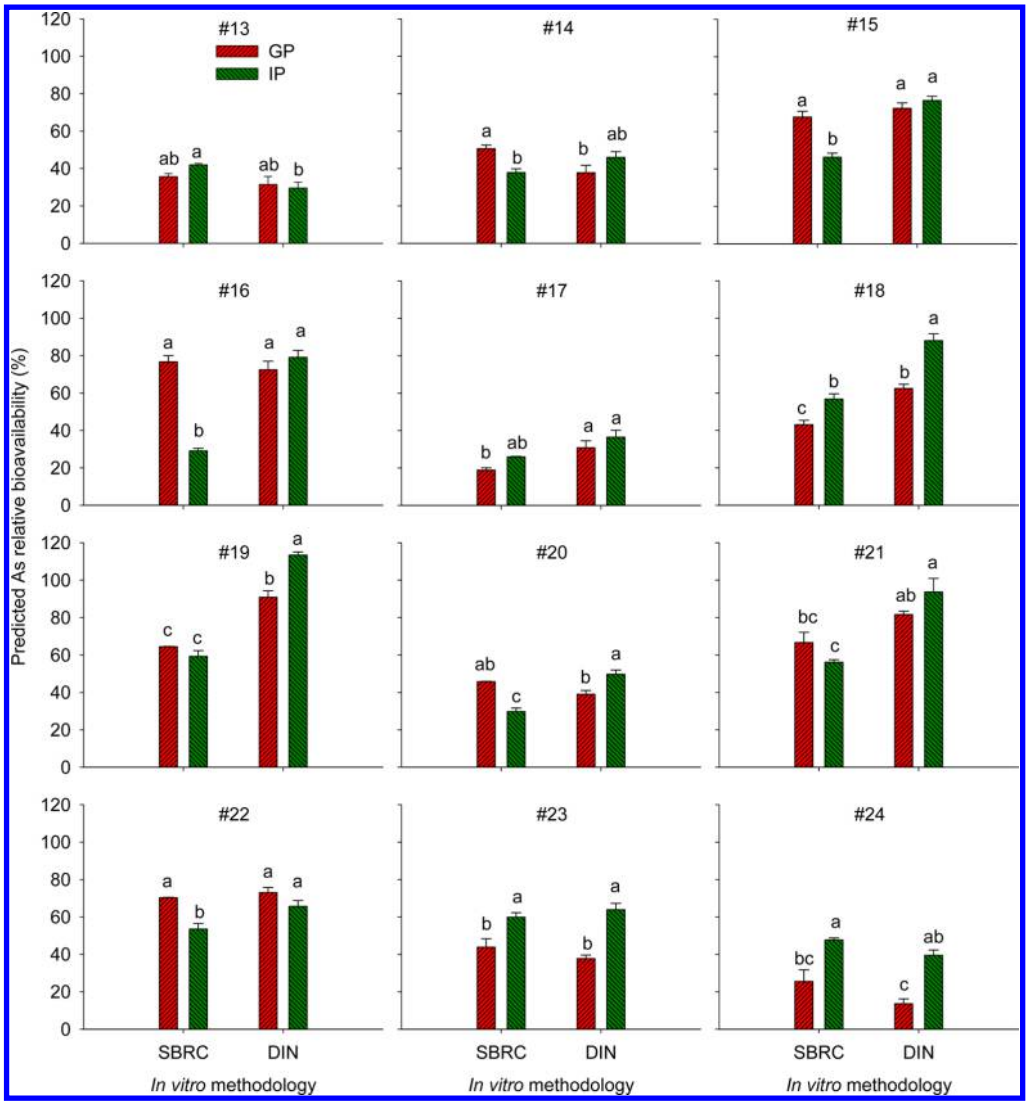

Figure 2. Predicted As relative bioavailability in the household dust samples 13−24 based on As bioaccessibility measured using the gastric (GP) and intestinal phases (IP) of SBRC and DIN assays and the constructed in vivo−in vitro correlations (Table 2). Means marked with different letters indicate significant ($p < 0.05$) differences in predicted As relative bioavailability for each soil.

dissolved As onto Fe oxides during IP extraction, resulting in higher As bioaccessibility in the IP than GP.[12]

Using As bioaccessibility based on SBRC and DIN and their respective IVIVC of household dust samples 1−12, As-RBA was predicted for household dust samples 13−24 (Figure 2). Arsenic bioaccessibility in household dust samples 13−24 differed significantly (up to 7.7-fold; Table S2) based on in vitro methods, but predicted As-RBA was less variable (up to 3.0-fold). Although predicted As-RBA from SBRC and DIN assays were incongruent for individual dust sample, there was no significant difference ($p > 0.05$) in calculated As-RBA values between SBRC-GP and DIN-GP for eight samples (Figure 2). Predictions of As-RBA based on the SBRC-GP were more conservative (higher) than SBRC-IP. In contrast, As-RBA predicted from DIN-IP results were higher than those obtained from SBRC results for five samples. Where significant variability was observed in predicted As-RBA (e.g., samples 18 and 19), DIN-IP provided the most conservative (highest) estimate of As-RBA.

Influence of As Relative Bioavailability on As Daily Intake Values. To determine the influence of As-RBA predictions on As exposure following incidental ingestion of household dust, daily As intake values were calculated for samples 13−24 on the basis of total As concentration or predicted As-RBA using SBRC and DIN. Assuming ingestion of household dust at 60 mg/d for a child of 18.6 kg body weight (bw; 3−6 years),[47] daily As intake via ingestion was calculated. Based on total As concentration, dust ingestion would represent 0.5−1.7% (0.01−0.05 μg As kg^{-1} bw d^{-1}) of the benchmark dose for 0.5% increased incidence of lung cancer (BMDL0.5) at 3 μg kg^{-1} bw d^{-1} by WHO.[48] However, after taking predicted As-RBA into consideration, the contribution of dust ingestion to the As BMDL0.5 was reduced to 0.1−0.6%. The greatest influence on As intake occurred for household dust having low As-RBA value (e.g., 17). Ingestion of dust 17 would contribute 1.7% of the BMDL0.5 value based on total As concentration; however, it was reduced to 0.3−0.6% using predicted As-RBA. As a result, As intake was comparable to dust 15 (0.3−0.5%) even though the total As concentration in sample 17 (16.2 mg kg^{-1}) was 3-fold greater than dust 15 (6.5 mg kg^{-1}). Determination of As intake based on total As concentration in household dust may overestimate As exposure

for this pathway. The low As exposure in the current study was primarily due to the low As concentrations in household dusts. However, for household dusts with high As concentrations (i.e., from mining and smelting impacted locations), adjustment of exposure through As-RBA predictions using As bioaccessibility data and the corresponding IVIVC may significantly impact exposure calculations and subsequently health risk assessment.

■ ASSOCIATED CONTENT

Supporting Information

Description of the in vitro assays used to assess As bioaccessibility (Table S1), As bioaccessibility and As-RBA data for household dust samples (Figures S1 and S4, Tables S2 and S3), mouse blood As concentration time curves (Figure S2), the relationship between As-RBA and total Fe/TOC (Figure S3), and daily As intake calculation can be found in the Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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