Occurrence and Profiles of Phthalates in Foodstuffs from China and Their Implications for Human Exposure

Ying Guo,[†] Zifeng Zhang,[‡] Liyan Liu,[‡] Yifan Li,[‡] Nanqi Ren,[‡] and Kurunthachalam Kannan*,[‡,†]

[‡]International Joint Research Center for Persistent Toxic Substances (IJRC-PTS), State Key Laboratory of Urban Water Resource and Environment, Harbin Institute of Technology, Harbin 150090, China

[†]Wadsworth Center, New York State Department of Health, and Department of Environmental Health Sciences, School of Public Health, State University of New York at Albany, Empire State Plaza, P.O. Box 509, Albany, New York 12201-0509, United States

S *Supporting Information*

ABSTRACT: Phthalate esters are used in a wide variety of consumer products, and human exposure to this class of compounds is widespread. Nevertheless, studies on dietary exposure of humans to phthalates are limited. In this study, nine phthalate esters were analyzed in eight categories of foodstuffs ($n = 78$) collected from Harbin and Shanghai, China, in 2011. Dimethyl phthalate (DMP), diethyl phthalate (DEP), dibutyl phthalate (DBP), diisobutyl phthalate (DIBP), benzyl butyl phthalate (BzBP), and diethylhexyl phthalate (DEHP) were frequently detected in food samples. DEHP was the major compound found in most of the food samples, with concentrations that ranged from below the limit of quantification (LOQ) to 762 ng/g wet weight (wt). The concentrations of phthalates in food samples from China were comparable to concentrations reported for several other countries, but the profiles were different; DMP was found more frequently in Chinese foods than in foods from other countries. The estimated daily dietary intake of phthalates (EDI$_{diet}$) was calculated based on the concentrations measured and the daily ingestion rates of food items. The EDI$_{diet}$ values for DMP, DEP, DIBP, DBP, BzBP, and DEHP (based on mean concentrations) were 0.092, 0.051, 0.505, 0.703, 0.022, and 1.60 μg/kg-bw/d, respectively, for Chinese adults. The EDI$_{diet}$ values calculated for phthalates were below the reference doses suggested by the United States Environmental Protection Agency (EPA). Comparison of total daily intakes, reported previously based on a biomonitoring study, with the current dietary intake estimates suggests that diet is the main source of DEHP exposure in China. Nevertheless, diet accounted for only <10% of the total exposure to DMP, DEP, DBP, and DIBP, which suggested the existence of other sources of exposure to these phthalates.

KEYWORDS: phthalate esters, dietary intake, DEHP, foodstuffs, total diet survey

■ INTRODUCTION

Phthalic acid esters or phthalates were introduced in the 1920s as plasticizers to soften plastics. Because phthalates make products flexible, durable, and long lasting, they are widely used in commercial and personal care products, such as electronics, building materials, medical devices, toys, detergents, and perfumes.[1] The global production of phthalates is estimated to be ∼5 million tons in 2010. Phthalates have been categorized as "chemicals of concern" by the United States Environmental Protection Agency (EPA)[2] due to their potential to elicit reproductive toxicities in laboratory animal studies.[3−6] Diethylhexyl phthalate (DEHP), dibutyl phthalate (DBP), and benzyl butyl phthalate (BzBP) have been well studied for their reproductive toxicities. Further, several human biomonitoring studies using urine specimens have reported widespread exposure to phthalates.[7−12]

A major source of human exposure to phthalates is diet.[13−15] Nevertheless, previous studies have suggested that, depending on the physicochemical properties of phthalates, the routes of human exposure to individual phthalates can vary. For example, diet is thought to be the main source of human exposure to DEHP,[13,16−19] whereas inhalation is the predominant route of exposure to dimethyl phthalate (DMP),[13] and inhalation and dermal absorption are important sources of exposure to DBP and diethyl phthalate (DEP).[13,16] A study from Korea showed that, after the study participants followed a strict vegetarian

dietary regimen for five consecutive days, urinary levels of DEP, DBP, and DEHP decreased significantly,[20] which suggested that dietary intervention can alleviate human exposure to certain phthalates.

As plasticizers, phthalates are not chemically bound to products and, therefore, can leach easily from the products into the environment. Contamination of foodstuffs with phthalates can occur through food-contact packaging materials and during processing, storage, and transport.[21] A recent study indicated that DEHP exposures were substantially reduced when individuals' diets were restricted to those that have limited contact with packaging materials.[22] Further, foodstuffs can be contaminated with phthalates during production or food chain transfer of these compounds. Despite the significance of foodstuffs as an important source of human exposure to phthalates, very few earlier studies have determined phthalates in foodstuffs, primarily due to the challenges associated with high background levels of contamination encountered in laboratory settings and from the analytical methods.[21,23] A recent report,[21] based on a review of the limited publications available on phthalates in various foodstuffs, indicated that the

concentrations and profiles of phthalates in foodstuffs vary considerably among different categories of food items and among geographic locations.

In our earlier studies, we reported widespread occurrence of phthalates in urine and house dust samples from China.[9,16,24] The phthalate exposure profile reported for the Chinese population was different from that reported for the population in the United States.[16] No previous studies have reported the occurrence of phthalates in foodstuffs from China. In this study, we analyzed 78 food samples collected from Harbin and Shanghai, China, in 2011. To our knowledge, this is the first study to report the occurrence and profile of phthalates in food samples from China. We estimated the daily dietary intake of phthalates based on the ingestion rate of foodstuffs by adults and the measured concentration of phthalates in the corresponding food item. Coupled with the data from a previous urinary biomonitoring study on phthalates in China,[24] in which we reported total exposure doses to phthalates by the Chinese population, we examined sources and pathways of phthalate exposure among the Chinese population.

■ MATERIALS AND METHODS

Standards and Solvents. Analytical standards of phthalate esters, DMP, DEP, DBP, diisobutyl phthalate (DIBP), BzBP, DEHP, di-*n*-hexyl phthalate (DNHP), dicyclohexyl phthalate (DCHP), and di-*n*-octyl phthalate (DNOP), and their corresponding d_4 (deuterated) internal standards (except for BzBP), were purchased from AccuStandard, Inc. (New Haven, CT), with a purity of >99%. Analytical grade acetone and acetonitrile were purchased from Macron Chemicals (Nashville, TN), and hexane and HPLC-grade water were purchased from J. T. Baker (Phillipsburg, NJ).

Sample Collection and Preparation. A total of 78 food samples were collected from local markets in Harbin (*n* = 64), northeastern China, and Shanghai (*n* = 14), eastern China, from August to November 2011. Samples were sorted into 8 categories, as cereals (*n* = 21), beverages (*n* = 17), condiments (*n* = 10), milk and milk products (*n* = 11), cooking oil (*n* = 3), seafood (*n* = 3), meat and meat products (*n* = 6), and others (*n* = 7). Further details of the samples are provided in the Supporting Information (Table S1). The food samples collected in this study were popular brands that were consumed widely by the Chinese population.

All the food samples were homogenized and spiked with deuterated phthalates as internal standards. For beverages and liquid samples (except for milk), 10−20 g of samples were extracted with hexane (10 mL) by shaking in a mechanical shaker (Eberbach, Ann Arbor, MI) at 250 oscillations/min for 30 min. After centrifugation at 4500*g* for 10 min, the hexane layer was transferred into a clean glass flask. The residue was extracted three times with hexane (10 mL each time), and the hexane extract was combined, concentrated using a rotary evaporator, and transferred into a gas chromatographic (GC) vial. For solid food samples, as well as milk and milk products, 3−20 g of samples were freeze-dried (Freezone6; Labconco, Kansas City, MO), homogenized, and extracted three times with hexane:acetone (1:1 v/v, 25 mL) by shaking in an orbital shaker for 30 min each time, as noted above. After centrifugation at 4500*g* for 10 min, the solvent layer was combined and then concentrated using a rotary evaporator, to 3 mL. The extract was then transferred into a separatory funnel containing 40 mL of hexane-saturated acetonitrile and shaken for 15 min; the hexane layer containing lipids was then discarded. Three milliliters of hexane was added to the separatory funnel, and the procedure was repeated twice for the removal of lipids. The sample extract was then concentrated to 5 mL and transferred into a glass tube containing 25 mL of high performance liquid chromatography (HPLC) grade water. Phthalates were extracted three times from the solution with hexane (7 mL) by shaking for 30 min, as noted above. After centrifugation for 10 min, the hexane layer was combined, concentrated using a rotary evaporator, and transferred into a GC

vial. For cooking oils, samples were transferred into a separatory funnel containing hexane-saturated acetonitrile and extracted, as noted above. All extracts were concentrated to 0.5 mL under a gentle stream of nitrogen prior to analysis by gas chromatography−mass spectrometry (GC−MS).

Instrumental Analysis. Nine phthalates were analyzed using GC (Agilent Technologies 6890) coupled with MS (Agilent Technologies 5973) in the selected ion monitoring (SIM) mode. A fused-silica capillary column (DB-5; 30 m × 0.25 mm i.d.; 0.25 μm film thickness) was used for separation. Ions m/z 163, 279, and 149 were monitored for the identification and quantification of DMP, DNOP, and seven other phthalates, respectively. The fragment ion m/z 177 was monitored for the confirmation of DEP, m/z 223 for DIBP and DBP, m/z 223 and 206 for BzBP, 167 for DCHP, m/z 167 and 279 for DEHP, and m/z 279 for DNHP. The responses of individual d_4-labeled internal standards of the corresponding phthalate esters were used for the quantification, and the response of d_4-DNHP was used for quantification of BzBP. The GC−MS conditions and column oven-temperature program were similar to those described earlier.[16] The limits of quantification (LOQ) were calculated from the lowest concentration of the calibration curve and a nominal sample weight of 1.0 g. The LOQ of DNOP was 10 ng/g wet wt, and, for eight other phthalate esters, it was 2 ng/g wet wt.

Quality Assurance and Quality Control. One of the major challenges associated with the low level analysis of phthalates in foods is the high background levels of contamination, especially for DBP and DEHP, often encountered in the analytical procedures. Prior to the analysis of samples, considerable effort was made to reduce the background levels of contamination in the analytical procedure. We found that many solvents, chemicals (including sorbents such as silica gel), glassware, and reagents contain phthalates, especially DBP and DEHP (the contamination of the solvents and chemicals with phthalates is expected to arise mainly during production, when they are stored in PVC storage tanks or containers). It was found that minimizing the use of glassware and other items that come in contact with samples during pretreatment, reducing sample preparation time, and minimizing the solvent volume enabled reduction in the background levels significantly. In other words, the analytical procedure was kept simple. All samples were processed using glass separatory funnels, flasks, or tubes. All glassware was washed with soap and Milli-Q water and baked at 450 °C overnight. The baked glassware was covered in clean aluminum foil and kept in a furnace until use. Sodium sulfate was baked at 450 °C overnight. HPLC-grade water (used in cleaning the sample extracts) was extracted with hexane before its use. All solvents were tested for background levels of phthalates after concentration and GC−MS analysis. The batches of solvents that contained the lowest levels of phthalates were used throughout the analysis.

For every batch of eight samples analyzed, three procedural blanks and a pair of matrix-spike samples (3.0 g mixture of 5 kinds of cooking oils) were processed. Procedural blanks were processed exactly similarly to samples, except that they did not contain the sample matrix (but contained equal amount/volume of all solvents, reagents, chemicals, glassware that come in contact with the samples). Trace levels of DMP, DEP, DIBP, and BzBP (1−5 ng) were found in procedural blanks, whereas the levels of DBP (2−20 ng) and DEHP (3−500 ng) were high (Table S2 and Table S3 in the Supporting Information). If the concentration of DEHP in three procedural blanks varied widely, and if the difference in concentrations between the blanks exceeded 50 ng, then all the samples analyzed in that batch were discarded, and a new set of samples was analyzed. The reported concentrations in food samples were subtracted by the average of the three blanks from each batch. Quantification was based on the isotopic dilution method. The average recoveries of 9 target compounds spiked into sample matrixes were between 56 ± 25% and 101 ± 3% (mean ± standard deviation). The average recovery ranges of 8 internal standards spiked into blanks and samples were 66 ± 24% to 83 ± 17%, and 59 ± 26% to 94 ± 20%, respectively. Concentrations below the LOQ were assigned a value of zero for statistical analysis. All data are reported as nanogram per gram, on a wet weight basis. Liquid samples

Table 1. Phthalate Concentrations in Various Foodstuffs from China (ng/g, wet weight)

sample (N)	concentration [ng/g range (mean/median)]								
	DMP	DEP	DIBP	DBP	DNHP	BzBP	DCHP	DEHP	DNOP
beverages (17)									
bottled water (1)	nd	nd	0.011	0.046	nd	nd	nd	0.15	nd
soft drinks (12)	nd–3.51 (0.43/0.14)	nd–13.3 (1.15/0.030)	0.032–3.82 (0.92/0.56)	nd–18.5 (2.06/0.41)	nd–0.020 (0.002/nd)	nd–0.43 (0.069/nd)	nd–0.15 (0.013/nd)	nd–73.1 (7.96/0.80)	nd
wine and beer (4)	0.25–97.0 (26.0/3.34)	0.016–0.33 (0.12/0.07)	0.37–107 (39.8/26.0)	2.03–557 (156/31.8)	nd–0.21 (0.052/nd)	nd	nd	0.20–7.03 (3.58/3.56)	—
condiments (10)	nd–14.5 (2.91/0.043)	nd–10.6 (1.88/0.25)	0.62–111 (18.8/5.05)	nd–236 (38.0/9.47)	nd–0.084 (0.009/nd)	nd–1.21 (0.28/0.14)	nd	nd–14.4 (2.88/0.14)	nd
milk or milk products (11)									
cheese (infant) (1)	6.82	1.92	59.1	39.6	0.075	1.49	nd	134	nd
milk or beverage (10)	0.17–25.0 (6.18/2.92)	0.066–1.30 (0.50/0.41)	1.18–38.9 (11.9/8.24)	2.38–226 (41.2/14.0)	nd–0.051 (0.005/nd)	nd–0.23 (0.044/nd)	nd	nd–88.3 (28.5/19.2)	nd–0.51 (0.079/nd)
cooking oil (3)	0.13–3.26 (1.72/1.76)	nd–0.018 (0.006/nd)	3.45–13.3 (7.20/4.70)	4.00–17.9 (9.40/6.20)	nd	1.66–18.0 (10.7/12.5)	nd	47.1–70.9 (60.1/62.4)	nd–1.88 (1.05/1.28)
meat or meat products (6)									
sausage (infant) (1)	nd	2.50	9.90	5.24	nd	nd	nd	53.9	2.39
fresh meat (3)	0.36–2.54 (1.20/0.71)	0.67–2.33 (1.72/2.17)	0.37–42.6 (17.9/10.8)	0.73–13.2 (6.91/6.84)	nd	nd	nd–0.88 (0.47/0.53)	36.8–184 (108/104)	nd–4.38 (2.61/3.45)
sausage (2)	nd–1.25 (0.62)	0.74–2.43 (1.58)	4.68–12.8 (8.72)	6.99–14.6 (10.8)	nd–0.90 (0.45)	nd–2.26 (1.13)	nd	82.3–98.3 (90.3)	—
seafood (3)	0.22–1.43 (0.71/0.47)	1.27–5.20 (3.23/3.23)	nd–64.9 (24.8/9.59)	1.57–11.9 (5.96/4.41)	nd–42.1 (14.0/nd)	nd	nd	26.9–111 (78.0/96.0)	nd
cereals or soy (21)									
bean powder (1)	1.20	0.97	2.71	21.2	0.029	13.0	nd	nd	nd
rice (3)	nd–0.41 (0.18/0.12)	0.02–1.45 (0.77/0.83)	1.82–70.8 (26.3/6.21)	1.48–99.0 (35.3/5.53)	nd	nd–0.64 (0.21/nd)	nd	14.0–378 (137/19.2)	nd
flour or noodle (6)	nd–5.80 (1.03/nd)	nd–4.86 (1.51/0.72)	5.64–326 (68.7/19.1)	5.94–258 (54.5/12.2)	nd	nd–0.56 (0.093/nd)	nd	nd–762 (135/9.22)	—
instant noodle (5)	1.83–90.8 (22.7/6.60)	nd–22.4 (5.60/1.89)	3.74–225 (76.6/3.92)	3.72–76.4 (23.9/7.17)	nd–0.11 (0.023/nd)	nd–2.07 (0.41/nd)	nd	26.9–487 (118/nd)	nd–0.19 (0.037/nd)
cookies, cakes (6)	3.27–58.9 (23.5/12.9)	0.35–1.97 (1.17/1.32)	24.5–142 (71.2/55.6)	13.7–572 (138/58.0)	nd	nd–17.0 (3.75/1.13)	nd	45.7–750 (189/86.4)	—
others (7)									
green tea (1)	0.22	2.96	107	79.3	nd	3.58	nd	452	nd
coffee powder (1)	0.29	nd	8.49	14.4	nd	nd	nd	nd	nd
salted egg (2)	3.10–13.6 (8.33)	nd–1.59 (0.79)	1.01–4.46 (2.74)	0.59–3.66 (2.12)	nd	nd–1.15 (0.58)	nd	nd–4.48 (2.24)	—
candy (3)	0.23–20.5 (7.59/2.08)	0.31–3.14 (1.51/1.11)	nd–76.2 (25.6/0.50)	nd–83.3 (27.8/nd)	nd–0.083 (0.028/nd)	nd–2.58 (0.86/nd)	nd	nd–172 (57.3/nd)	nd

Table 2. Estimated Daily Intake (EDI$_{diet}$) of Phthalates from Foodstuffs in China (ng/kg-bw/day)

	beverages[a]	cereals	soy	meat	seafood	milk	cooking oil	eggs	condiments	total
				Estimated from Median Concentrations in Food						
DMP	4.15	3.21	0.15	0.91	0.36	3.76	1.14	2.78	0.01	16.5
DEP	0.89	5.52	0.12	3.86	2.42	0.45	–[b]	0.26	0.04	13.6
DIBP	14.8	188	0.35	17.8	7.20	12.4	3.06	0.91	0.75	245
DBP	13.3	189	2.72	11.9	3.31	17.2	4.03	0.71	1.40	243
BzBP	–	–	1.66	–	–	–	8.13	0.19	0.02	10.0
DEHP	24.5	304	–	155	72.0	21.2	41.7	0.75	0.02	620
				Estimated from Mean Concentrations in Food						
DMP	13.2	65.6	0.15	1.39	0.53	6.86	1.12	2.78	0.48	92.1
DEP	35.4	8.17	0.12	3.10	2.42	0.69	–	0.26	0.28	50.5
DIBP	28.2	408	0.35	23.2	18.6	17.8	4.68	0.91	3.34	505
DBP	63.5	561	2.72	13.6	4.47	45.1	6.11	0.71	5.65	703
BzBP	2.12	10.5	1.67	0.65	–	0.19	6.96	0.19	0.06	22.4
DEHP	245	1047	–	160	58.5	41.9	39.1	0.75	2.20	1595
				Estimated from the Highest Concentrations in Food						
DMP	117	605	0.15	1.39	1.07	27.5	2.12	4.52	2.16	761
DEP	443	150	0.12	4.31	3.90	2.11	0.01	0.53	1.57	606
DIBP	127	2170	0.35	73.1	48.7	65.1	8.65	1.49	16.5	2510
DBP	617	3810	2.72	25.0	8.93	249	11.6	1.22	35.0	4760
BzBP	14.4	113	1.66	3.89	–	1.63	11.7	0.38	0.18	147
DEHP	2430	5080	–	316	83.4	148	46.1	1.49	2.13	8108

			Phthalate Concentrations in Samples			
	data source		sample code		data source	sample code
beverages	bottle water and 12 soft drinks		beverages: 1–13	milk	11 milk or milk products	milk or milk products: 1–11
cereals	all 21 cereals except for soy		cereals or soy: 1–15, 17–21	cooking oil	3 cooking oil	cooking oil: 1–3
soy	bean powder		cereals or soy: 16	eggs	2 egg samples	others: 3–4
meat	6 meat and meat product		meat and meat products: 1–6	condiments	10 condiments	condiments: 1–10
seafood	3 seafood		seafood: 1–3			

[a]Phthalate concentrations in samples were from the bottom section of this table. [b]EDI was estimated as zero.

were weighed prior to extraction, and moisture contents of solid food samples were calculated for conversion of data to wet weight basis.

RESULTS AND DISCUSSION

Occurrence of Phthalates. DMP, DEP, DBP, DIBP, BzBP, and DEHP were frequently detected (>60%) in food samples from China, whereas DNHP, DCHP, and DNOP were found in fewer than 16% of the samples analyzed. This pattern is similar to what was reported for indoor dust[16] and human urine from China.[24] DMP was found in 82% of the food samples analyzed, at a frequency similar to its metabolite, monomethyl phthalate, found in urine from China (88%). High frequency of detection of DMP in Chinese foodstuffs is remarkably different from what was reported for other countries, where DMP was seldom found.[13,18,21] Concentrations of DMP ranged from below the LOQ (i.e., <0.04 ng/g in bottled water and sausage) to 97.0 ng/g (in wine) in our study (Table 1). In food samples from Europe, Asia, and North America,[13] DMP was detected only in yogurt, fish, and condiments.

DEP was found in 81% of the food samples analyzed, at concentrations ranging from <LOQ (i.e., <0.04 ng/g in bottled water and coffee powder) to 22.4 ng/g (in instant noodles) (Table 1). These concentrations were lower than those reported in Canada,[25] where DEP concentrations ranged from 40 to 5300 ng/g in cereals, fruits, and miscellaneous foods. The measured concentrations of DEP in foodstuffs in our study were similar to those reported in Japan (0.7–1.0 ng/g).[26] Concentrations of DEP in our milk or milk products were 0.066 to 1.92 ng/g, which were 1 to 2 orders of magnitude lower than the concentrations reported for infant formula and milk from certain European countries (36.5–85.3 ng/g).[27]

DBP and DIBP were found in >94% of the food samples analyzed (Table 1), and the concentrations ranged from 0.011 ng/g (in bottled water) to 572 ng/g (in cookies). The concentrations of DBP and DIBP were similar across several food groups. For example, the concentration ratios of median values of DBP to DIBP in all foodstuffs were 1.1 ± 0.5, except for bean powder, which contained 7.8-fold higher concentrations of DBP than DIBP. The ratio of 1.1 found in most foodstuffs was close to the ratio of their corresponding metabolites determined in human urine from China (1.6).[9] The concentrations of DBP (median: 31.8 ng/g) and DIBP (26 ng/g) in wine and beer were significantly higher than those found in other beverages. Studies from Japan also reported high concentrations of DBP in wine.[28,29] The concentrations of DBP (2.38–226 ng/g) and DIBP (1.18–59.1 ng/g) in milk and milk products, in our study, were similar to the concentrations reported elsewhere (3–50.3 ng/g).[21]

DEHP, the most widely used phthalate, was found in 82% of the food samples analyzed. Although 100% of the urine samples from China contained the metabolites of DEHP,[9,24] relatively lower frequency of detection of this compound in foodstuffs than in urine could be due to the low recovery of this compound from foodstuffs (63%, on average) and subtraction of concentrations of this compound from procedural blank values (which resulted in concentrations below the LOQ for several foods that contained concentrations at or near the LOQ value). The concentrations of DEHP varied from <LOQ (i.e., <0.2 ng/g in bean and coffee powder) to 762 ng/g (in instant

noodles). DEHP was the most abundant phthalate in all food categories, except for wine, beer, and condiments, in which DBP and DIBP were the predominant compounds. Generally, the concentrations of DEHP in Chinese food samples were within the ranges of values reported for several other countries (~10 to 100 ng/g).[21]

Dietary Exposure to Phthalates in China. The daily dietary intake of phthalates by the Chinese population was estimated by the following equation:

$$\text{EDI}_{\text{diet}} = \frac{\sum_{i=1}^{n} C_i Q_i}{\text{bw}} r_{\text{uptake}}$$

where EDI_{diet} (μg/kg-bw/d) is the estimated daily intake from diet, C_i (ng/g) is phthalate concentration in food i, Q_i (g/day) is average amount of daily ingestion of the food i, r is gastrointestinal uptake factor, and bw (kg) is body weight. For bw, 60 kg was used as an average value for the Chinese adults; for r, a value of 100% was assumed, and for Q_i, the average intake values reported for adults from nine provinces in China (both rural and urban), including Harbin and Shanghai in 2006,[30] were used. The Q_i values for beverages, cereals, soybean, meat, eggs, cooking oil, and salt (condiments) were 2000, 400, 7.7, 103, 20, 39, and 8.9 g/day, respectively.[30] The average intakes of milk, seafood, vegetables, and fruits in China were 66, 45, 252, and 69 g/day, respectively.[31] Phthalate concentrations were not measured in fruits and vegetables in this study. Because of the lack of data on vegetables and fruits, we did not include these categories of foods in the calculation of dietary intakes. Therefore, the EDI_{diet} values may be an underestimate of actual exposures. However, based on some published data, we also calculated EDI_{diet} by inclusion of vegetables and fruits from China[32] and European countries,[13] and the results are shown in the Supporting Information (Table S4).

The EDI_{diet} values for DMP, DEP, DIBP, DBP, BzBP, and DEHP from different food categories are shown in Table 2. The EDI_{diet} values, calculated based on mean concentrations in foods, for DMP, DEP, DIBP, DBP, BzBP, and DEHP, were 0.092, 0.051, 0.505, 0.703, 0.022, and 1.60 μg/kg-bw/d, respectively. The corresponding EDI_{diet} values, estimated based on median concentrations in foods, were 0.016, 0.014, 0.245, 0.243, 0.010, and 0.620 μg/kg-bw/d, respectively. It can be generalized that the EDI_{diet} values were on the order of 0.010 μg/kg-bw/d for DEP, DMP, and BzBP, 0.10 μg/kg-bw/d for DIBP and DBP, and 1.0 μg/kg-bw/day for DEHP. In comparison with the reference doses suggested by the US EPA,[33] which were 20, 100, 200, and 800 μg/kg-bw/d for DEHP, DBP, BzBP, and DEP, respectively, the daily dietary exposures to phthalates by the adult Chinese population were low, even when the highest phthalate concentrations in foods were used in the estimation of EDI_{diet}; for DEHP, DBP (sum of DIBP and DBP), BzBP, and DEP the highest dietary intake values were 8.1, 7.3, 0.15, and 0.61 μg/kg-bw/d, respectively.

It should be noted that this is a pilot study, as the sample size is small ($n = 78$) and only two locations in China were surveyed. Phthalate concentrations varied widely in some categories of foodstuffs. Furthermore, due to the lack of data on daily food consumption by different age groups in China, we did not calculate the EDI_{diet} for age groups other than adults. The EDI_{diet} values for BzBP (approximately 0.01 μg/kg-bw/d) estimated in the present study were 10 times lower than those reported in Europe (approximately 0.16 μg/kg-bw/d, estimated

from 50th percentile values),[13] whereas the values for DEHP and DBP (sum of DBP and DIBP) in our study (~1 μg/kg-bw/d) were comparable to those reported for Europe (~3.10 and 2.50 μg/kg-bw/d for DBP and DEHP). A recent study from Italy reported that the intakes of DBP and DEHP by children were in the ranges of 1.7 to 16.9 and 2.8 to 17.7 μg/kg-bw/d, respectively,[34] which were higher than the values calculated for Chinese adults.

Contribution of Foodstuffs to Total Phthalate Exposure. Human exposure to phthalates can be estimated by two approaches. First, phthalate concentrations are measured in each medium of human exposure (air, water, foodstuffs, and dust), and the rate of intake/ingestion of that medium is multiplied by the measured concentrations, which are then summed to obtain total daily intake. The second method is based on the data from biomonitoring studies (e.g., urine analysis) and employ a simple pharmacokinetic model to estimate daily exposure doses, and this method is expected to yield an integrated measure of "total" exposure dose from various sources.[18]

In an earlier study, we estimated the "total" daily exposure to phthalates by the Chinese population based on a biomonitoring study of urinary concentrations of phthalate metabolites.[16,24] The daily exposure dose, estimated based on urinary concentrations for DMP, DEP, DBP (sum of DIBP and DBP), and DEHP, were 0.6/1.2 (median/mean), 1.1/3.8, 8.5/12.2, and ~2/~5 μg/kg-bw/d, respectively.[24] Comparison of dietary intakes of phthalates estimated in the present study with the mean value reported based on biomonitoring[24] indicated that dietary exposures represent a small fraction of the total exposure doses (Figure 1), and contributed ~10% for DBP,
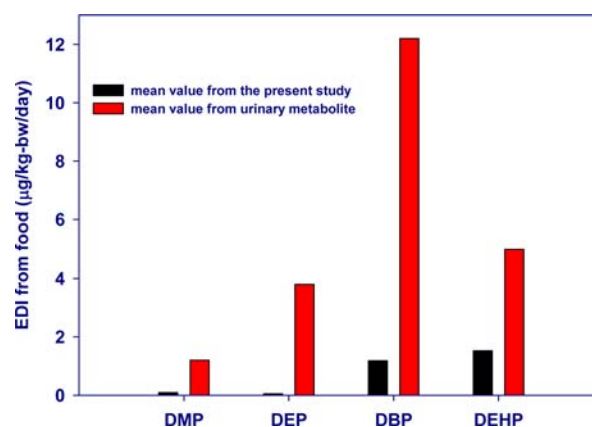
Figure 1. Comparison of estimated daily intakes (EDIs) of phthalates calculated from dietary sources and biomonitoring approach (μg/kg-bw/day). "Total" estimated daily intake (EDI) from urinary metabolites (mean) was from ref 24, and EDI from food consumption was based on the mean values calculated in the present study.

~10% for DMP, and ~2% for DEP to the total exposures. However, daily exposure doses to DEHP calculated by the two methods (biomonitoring versus food monitoring) were similar, and dietary intakes accounted for 30% (based on mean value of food) to 100% (based on maximum value of food) of the total exposures. These results confirm that diet is the major source of exposure to DEHP. In contrast, diet, particularly the food samples analyzed in this study, is not a major source of exposure to DMP, DEP, and DBP; these results were similar to those reported from Japan.[35]

We also reported daily exposure doses to phthalates from the ingestion of indoor dust by the Chinese population.[16] The daily intake values for DMP, DEP, DIBP, DBP, BzBP, and DEHP from dust ingestion were 0.0001, 0.0003, 0.012, 0.0141, 0.002, and 0.160 μg/kg-bw/d, respectively. These values are much lower than the dietary intake values calculated in the present study, indicating that indoor dust is not a major source of phthalate exposures in China.

The discrepancies in the magnitude of contribution of diet to DMP, DEP, and DBP exposures, estimated based on the two methods (foodstuffs versus biomonitoring study), offer some insight into the sources of human exposure to phthalates in China. A comparable contribution of DEHP exposures estimated in the current study (30–100%) with that estimated based on the previous biomonitoring study (>85%) confirms that the major source of DEHP exposure is diet. However, a much lower contribution of diet to DMP, DEP, and DBP exposures, as determined in this study, than those estimated through the biomonitoring study, suggests that several other sources contribute to exposures of these low molecular weight phthalates. DMP, DEP, and DBP are used in a variety of cosmetics and personal care products,[36] and it is probable that dermal exposure through the use of cosmetics and personal care products is significant for these phthalates. No earlier studies have measured the occurrence of phthalates in personal care products, including cosmetics, to assess dermal exposures.

A recent review compared phthalate exposures calculated based on food and environmental analysis with the biomonitoring approach,[18] and showed the existence of discrepancies in the estimates calculated by the two methods. Whereas these results indicate the existence of other sources of exposure, which were not accounted for, such discrepancies could also arise from the study design, particularly the lack of analysis of all types of food products, including processed, take-out (ready-to-eat), and fast food, as well as not taking into account the small sample size and locations of sampling. Further studies should assess dermal exposure pathways of phthalates from the use of personal care products in China.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Additional tables of experimental data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Wadsworth Center, Empire State Plaza, P.O. Box 509, Albany, NY 12201-0509. Tel: 1-518-474-0015. Fax: 1-518-473-2895. E-mail: kkannan@wadsworth.org.

Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) Antian, J. Toxicity and health threats of phthalate esters: Review of the literature. *Environ. Heal. Perspect.* 1973, 1–26.

(2) U.S. EPA. *EPA announces actions to address chemicals of concern, including phthalates: Agency continues efforts to work for comprehensive reform of toxic substance laws.* http://yosemite.epa.gov/opa/admpress.nsf/a543211f64e4d1998525735900404442/2852c60dc0f65c688525769c0068b219!OpenDocument (accessed December, 2011).

(3) Matsumoto, M.; Hirata-Koizumi, M.; Ema, M. Potential adverse effects of phthalic acid esters on human health: A review of recent studies on reproduction. *Regul. Toxicol. Pharmacol.* 2008, 50, 37–49.

(4) Martino-Andrade, A. J.; Chahoud, I. Reproductive toxicity of phthalate esters. *Mol. Nutr. Food Res.* 2010, 54, 148–157.

(5) Kamrin, M. A. Phthalate risks, phthalate regulation, and public health: A Review. *J. Toxicol. Environ. Health, Part B* 2009, 12, 157–174.

(6) Fisher, J. S. Environmental anti-androgens and male reproductive health: focus on phthalates and testicular dysgenesis syndrome. *Reproduction* 2004, 127, 305–315.

(7) Berman, T.; Hochner-Celnikier, D.; Calafat, A. M.; Needham, L. L.; Amitai, Y.; Wormser, U.; Richter, E. Phthalate exposure among pregnant women in Jerusalem, Israel: Results of a pilot study. *Environ. Int.* 2009, 35, 353–357.

(8) Becker, K.; Goen, T.; Seiwert, M.; Conrad, A.; Pick-Fuss, H.; Muller, J.; Wittassek, M.; Schulz, C.; Kolossa-Gehring, M. GerES IV: Phthalate metabolites and bisphenol A in urine of German children. *Int. J. Hyg. Environ. Health* 2009, 212, 685–692.

(9) Guo, Y.; Alomirah, H.; Cho, H.-S.; Minh, T. B.; Mohd, M. A.; Nakata, H.; Kannan, K. Occurrences of phthalate metabolites in human urine from several Asian countries. *Environ. Sci. Technol.* 2011, 45, 3138–3144.

(10) Itoh, H.; Iwasaki, M.; Hanaoka, T.; Sasaki, H.; Tanaka, T.; Tsugane, S. Urinary phthalate monoesters and endometriosis in infertile Japanese women. *Sci. Total Environ.* 2009, 408, 37–42.

(11) Silva, M. J.; Barr, D. B.; Reidy, J. A.; Malek, N. A.; Hodge, C. C.; Caudill, S. P.; Brock, J. W.; Needham, L. L.; Calafat, A. M. Urinary levels of seven phthalate metabolites in the US population from the National Health and Nutrition Examination Survey (NHANES) 1999–2000. *Environ. Health Perspect.* 2004, 112, 331–338.

(12) Latini, G.; Wittassek, M.; Del Vecchio, A.; Presta, G.; De Felice, C.; Angerer, J. Lactational exposure to phthalates in Southern Italy. *Environ. Int.* 2009, 35, 236–239.

(13) Wormuth, M.; Scheringer, M.; Vollenweider, M.; Hungerbuhler, K. What are the sources of exposure to eight frequently used phthalic acid esters in Europeans? *Risk Anal.* 2006, 26, 803–824.

(14) Schettler, T. Human exposure to phthalates via consumer products. *Int. J. Androl.* 2006, 29, 134–139.

(15) Clark, K.; Cousins, I. T.; Mackay, D. Assessment of critical exposure pathways. *Handb. Environ. Chem.* 2003, 3, 227–262.

(16) Guo, Y.; Kannan, K. Comparative assessment of human exposure to phthalate ethers from house dust in China and the United States. *Environ. Sci. Technol.* 2011, 45, 3788–3794.

(17) Itoh, H.; Yoshida, K.; Masunaga, S. Quantitative identification of unknown exposure pathways of phthalates based on measuring their metabolites in human urine. *Environ. Sci. Technol.* 2007, 41, 4542–4547.

(18) Clark, K. E.; David, R. M.; Guinn, R.; Kramarz, K. W.; Lampi, M. A.; Staples, C. A. Modeling human exposure to phthalate esters: A comparison of indirect and biomonitoring estimation methods. *Hum. Ecol. Risk Assess.* 2011, 17, 923–965.

(19) Spillmann-Dickson, M.; Siegrist, M.; Keller, C.; Wormuth, M. Phthalate exposure through food and consumers' risk perception of chemicals in food. *Risk Anal.* 2009, 29, 1170–1181.

(20) Ji, K.; Kho, Y. L.; Park, Y.; Choi, K. Influence of a five-day vegetarian diet on urinary levels of antibiotics and phthalate metabolites: A pilot study with "Temple Stay" participants. *Environ. Res.* 2010, 110, 375–382.

6918

dx.doi.org/10.1021/jf3021128 | *J. Agric. Food Chem.* 2012, 60, 6913–6919

(21) Cao, X. L. Phthalate esters in foods: Sources, occurrence, and analytical methods. *Compr. Rev. Food Sci. Food Saf.* **2010**, *9*, 21−43.

(22) Rudel, R. A.; Gray, J. M.; Engel, C. L.; Rawsthorne, T. W.; Dodson, R. E.; Ackerman, J. M.; Rizzo, J.; Nudelman, J. L.; Brody, J. G. Food packaging and bisphenol A and bis(2-ethyhexyl) phthalate exposure: Findings from a dietary intervention. *Environ. Health Perspect.* **2011**, *119*, 914−920.

(23) Wenzl, T.; JRC European Commission. *Methods for the determination of phthalates in food, outcome of a survey conducted among European food control laboratories*; European Commission, Joint Research Centre, Institute for Reference Materials and Measurements: Belgium, 2009.

(24) Guo, Y.; Wu, Q.; Kannan, K. Phthalate metabolites in urine from China, and implications for human exposures. *Environ. Int.* **2011**, *37*, 893−898.

(25) Page, B. D.; Lacroix, G. M. The occurrence of phthalate ester and di-2-ethylhexyl adipate plasticizers in Canadian packaging and food sampled in 1985−1989: A survey. *Food Addit. Contam.* **1995**, *12*, 129−151.

(26) Tsumura, Y.; Ishimitsu, S.; Saito, I.; Sakai, H.; Kobayashi, Y.; Tonogai, Y. Eleven phthalate esters and di(2-ethylhexyl)adipate in oneweek duplicate diet samples obtained from hospitals and their estimated daily intake. *Food Addit. Contam.* **2001**, *18*, 449−460.

(27) Casajuana, N.; Lacorte, S. New methodology for determination of phthalate esters, bisphenol A, bisphenol A diglycidyl ester, and nonylphenol in commercial whole milk samples. *J. Agric. Food Chem.* **2004**, *52*, 3702−3707.

(28) Tsumuta, Y.; Ishimitsu, S.; Kaihara, A.; Yoshii, K.; Tonogai, Y. Phthalates, adipates, citrate and some of the other plasticizers detected in Japanese retail food: A survey. *J. Health Sci.* **2002**, *48*, 493−502.

(29) Yano, K.; Hirokawa, N.; Katayama, H.; Moriguchi, T.; Joung, K. E.; Sheen, Y. Y.; Asaoka, K. Phthalate levels in beverages in Japan and Korea. *Bull. Environ. Contam. Toxicol.* **2002**, *68*, 463−469.

(30) Zhang, B.; Wang, H.; Du, W.; Zhang, J.; Wang, Z.; Su, C.; Ma, Y.; Zhai, F. Food consumption trend of Chinese adlults in nine province (autonomous region) from 1989 to 2006. *Chin. J. Prev. Med.* **2011**, *45*, 330−334.

(31) Zhai, F.; He, Y.; Ma, G.; Li, Y.; Wang, Z.; Hu, Y.; Zhao, L.; Zhai, C.; Li, Y.; Yang, X.-G. Study on the current status and trend of food consumption among Chinese population. *Chin. J. Epidemiol.* **2005**, *26*, 485−488.

(32) Mo, C. H.; Cai, Q. Y.; Tang, S. R.; Zeng, Q. Y.; Wu, Q. T. Polycyclic aromatic hydrocarbons and phthalic acid esters in vegetables from nine farms of the Pearl River Delta, South China. *Arch. Environ. Contam. Toxicol.* **2009**, *56*, 181−189.

(33) US EPA. *Phthalates, teach chemical summary.* http://www.epa.gov/teach/chem_summ/phthalates_summary.pdf (accessed March, 2012).

(34) Cirillo, T.; Fasano, E.; Castaldi, E.; Montuori, P.; Cocchieri, R. A. Children's exposure to di(2-ethylhexyl)phthalate and dibutylphthalate plasticizers from school meals. *J. Agric. Food Chem.* **2011**, *59*, 10532−10538.

(35) Wittassek, M.; Koch, H. M.; Angerer, J.; Brüning, T. Assessing exposure to phthalates—The human biomonitoring approach. *Mol. Nutr. Food Res.* **2011**, *55*, 7−31.

(36) Houlihan, J.; Brody, C.; Schwan, B. *Not too pretty, phthalates, beauty products and the FDA.* http://www.safecosmetics.org/downloads/NotTooPretty_report.pdf (accessed December 2010).