Occurrence of parabens in foodstuffs from China and its implications for human dietary exposure

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ABSTRACT

Parabens are alkyl esters of *p*-hydroxybenzoic acid and are used as antimicrobial preservatives in a range of consumer products, including cosmetics, pharmaceuticals, and foodstuffs. Despite their widespread use, prior to this study, paraben concentrations in foodstuffs from China and human dietary exposure to these chemicals have been unknown. In this study, concentrations of six parabens were determined in 13 categories of food samples ($n = 282$), including cereals and cereal products, meat, fish and seafood, eggs, dairy products, bean products, fruits, vegetables, cookies, beverages, cooking oils, condiments, and others, collected from nine cities in China. Almost all (detection rate: 99%) food samples contained at least one of the parabens analyzed, and the total concentrations (Σ Parabens; sum of six parabens) ranged from below limit of quantification (LOQ) to 2530 ng/g fresh weight, with an overall mean value of 39.3 ng/g. Methyl paraben (MeP), ethyl paraben (EtP), and propyl paraben (PrP) were the major paraben analogs found in foodstuffs, and these compounds accounted for 59%, 24%, and 10%, respectively, of Σ Paraben concentrations. Although the mean concentrations of Σ Parabens varied among different categories of food items (from 0.839 ng/g in beverages to 100 ng/g in vegetables), the concentrations were not statistically significant among the 13 food categories, including canned foodstuffs. Estimated daily intake (EDI) of parabens was based on the measured concentrations in foods and the corresponding daily food ingestion rates. The mean and 95th percentile values for EDI were 1010 and 3040 ng/kg body weight (bw)/day for adult men and 1060 and 3170 ng/kg bw/day for adult women, respectively.

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1. Introduction

Endocrine-disrupting compounds (EDCs) are substances that interfere with the synthesis, secretion, transport, action, or excretion of natural hormones in the body and result in developmental and reproductive abnormalities (Casals-Casas and Desvergne, 2011; Crisp et al., 1998; Schug et al., 2011). EDCs comprise a diverse group of chemicals of anthropogenic origin, including organochlorine pesticides, organotins, polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), phthalates, bisphenols, and parabens, among others. Although production and use of some EDCs have been regulated, many of these chemicals are still used in a wide range of consumer products. Assessment of sources and doses of human exposure to EDCs is of great public health significance.

Parabens are alkyl esters of *p*-hydroxybenzoic acid and are widely used as preservatives in cosmetics, pharmaceuticals, and foodstuffs (Andersen, 2008; Eriksson et al., 2008; NTP, 2005; Soni et al., 2005).

Parabens are popular preservatives due to their stability, high water solubility, broad spectrum antimicrobial activity, and low allergenicity (Andersen, 2008; NTP, 2005; Soni et al., 2005). The commonly used parabens are methyl paraben (MeP), ethyl paraben (EtP), propyl paraben (PrP), butyl paraben (BuP), benzyl paraben (BzP), and heptyl paraben (HepP). Concern in regard to the safety of parabens has been raised since the first report of the accumulation of MeP in human breast tumors (Darbre et al., 2004). Although controversy still surrounds the carcinogenic potential of parabens (Darbre et al., 2004; Golden et al., 2005), these compounds elicit weak estrogenic effects in animal studies (Byford et al., 2002; Darbre and Harvey, 2008; Lemini et al., 2003; Miller et al., 2001; Okubo et al., 2001; Pugazhendhi et al., 2005; Witorsch and Thomas, 2010). The estrogenic activity of parabens increases with the length of the alkyl chain; MeP, EtP, PrP, and BuP exhibit estrogenic potencies that are 2 500 000-, 150 000-, 30 000-, and 10 000-fold, respectively, less than that of 17 β -estradiol (Routledge et al., 1998). Laboratory studies have shown that dietary exposure to parabens (approximately 10–15 mg/kg to 1000–1500 mg/kg) for 4 to 10 weeks elicited a remarkable reduction in testosterone levels and sperm counts in rats (Kang et al., 2002; Oishi, 2001, 2002, 2004). One study showed that MeP activated transient receptor A1 channels and elicited pain sensation in

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mice (Fujita et al., 2007). Another study reported a positive association between urinary concentrations of MeP and BuP and sperm DNA damage in men (Meeker et al., 2011). In view of the potential for toxicity, an acceptable daily intake (ADI) for the sum of three parabens, MeP, EtP, and PrP, at 0–10 mg/kg body weight (bw)/day has been established by the Joint FAO/WHO Expert Committee on Food Additives in 1974 (JECFA, 1974). Denmark prohibited the use of two parabens, PrP and BuP, in children's products in March, 2011 (SCCS, 2011).

Parabens can be absorbed via skin and via the gastrointestinal tract (Akomeah et al., 2004; Janjua et al., 2007; Lobemeier et al., 1996) and are excreted in urine (Andersen, 2008; Soni et al., 2005). A few biomonitoring studies have reported the occurrence of parabens in human urine, plasma, serum, and milk (Calafat et al., 2010; Casas et al., 2011; Darbre and Harvey, 2008; Frederiksen et al., 2011; Janjua et al., 2007; Schlumpf et al., 2010; Ye et al., 2006a, 2006b, 2008). MeP and PrP were found in >96% of urine samples collected from the U.S. (Ye et al., 2006a). The 2005–2006 National Health and Nutrition Examination Survey (NHANES) report indicated the presence of MeP and PrP in >90% of urine samples collected from the U.S. (Calafat et al., 2010). The presence of parabens in urine samples from Spain and Denmark also was documented (Casas et al., 2011; Frederiksen et al., 2011). Studies have reported the occurrence of parabens in human plasma, serum, and milk at concentrations on the order of a few nanograms per milliliter (Frederiksen et al., 2011; Schlumpf et al., 2010; Wang et al., 2013; Ye et al., 2008). Nevertheless, information on the occurrence of parabens in foodstuffs and other source of human exposure is still scarce.

In the present study, a total of 282 food samples, representing 13 food categories (i.e., cereals, meat, fish and seafood, eggs, dairy products, bean products, fruits, vegetables, cookies, beverages, cooking oils, condiments, and others) were collected from nine cities in China for the determination of six paraben analogs, namely MeP, EtP, PrP, BuP, BzP, and HepP. The baseline concentrations of parabens were established, and geographic patterns and composition profiles of the six paraben analogs were determined. Based on the concentrations in foods, human dietary exposure doses to parabens were calculated.

2. Materials and methods

2.1. Reagents and chemicals

All solvents used in this study were of HPLC grade and were purchased from Mallinckrodt Baker (Phillipsburg, NJ). Standard solutions (100 µg/mL in methanol) of individual parabens (viz., MeP, EtP, PrP, BuP, BzP, and HepP) were purchased from AccuStandard, Inc (New Haven, CT). Internal standards, $^{13}\text{C}_6$ -MeP (99%) and $^{13}\text{C}_6$ -BuP (99%), were purchased from Cambridge Isotope Laboratories (Andover, MA). Formic acid (98.2%) was purchased from Sigma-Aldrich (St. Louis, MO). Ultrapure water was prepared with the milli-Q ultrapure system (Barnstead International, Dubuque, IA). All stock solutions were stored at $-20\text{ }^{\circ}\text{C}$.

2.2. Sample collection and preparation

Foodstuffs ($n = 282$) were collected from nine cities in China during the summer (July–September) of 2012 (Fig. S1; Supporting Information). The majority of food samples were purchased from large retail stores, and a few samples were purchased from local grocery stores. Brands were chosen to represent available varieties that are commonly consumed by the Chinese, including national brands, store brands, and specialty brands. The foodstuffs were divided into 13 categories on the basis of national or regional surveys on food consumption in China (Ma et al., 2007; Zhai, 2008; Zhang et al., 2011; Zhong et al., 2006): cereals and cereal products ($n = 52$; e.g., rice and rice products, wheat flour, bread, noodle, pasta, corn products), meat and meat products ($n = 21$; e.g., beef, pork, chicken, duck, sausages), fish and seafood ($n = 16$; e.g., freshwater and marine fish, shrimp, squid), eggs ($n = 11$; including salted eggs), dairy products

($n = 17$; e.g., milk, infant formula, yogurt, cheese), bean products ($n = 31$; e.g., red and green beans, soybeans, orchid beans, dried bean curd), fruits ($n = 25$; e.g., walnuts, chestnuts, jujubes, plums, hawthorns, raisins), vegetables ($n = 60$; e.g., mushrooms, peanuts, peppers, seaweed, bamboo shoots, potatoes, edible tree fungus, Chinese cabbage, salted mustard), cookies and snacks ($n = 56$; e.g., candy, chocolate, biscuits, potato chips, sachima, glutinous rice cakes, pancakes), beverages ($n = 4$; e.g., juice, liquor, coffee drink), cooking oils ($n = 11$; e.g., bean, peanut, corn, and sesame oils), condiments ($n = 55$; e.g., soy sauce, vinegar, cooking wine, ketchup, bean paste, aniseed, chili powder), and others ($n = 15$; e.g., jelly, black sesame powder, lotus root starch, milk tea powder, coffee powder). Details of foods grouped under various categories are shown in Table S1 (Supporting Information) fruits and vegetables include fresh and processed (canned) products. Grouping of foods into certain categories was challenging, especially for processed and mixed foods, but we selected the major ingredient present in such food types. All samples were stored at $-20\text{ }^{\circ}\text{C}$ until analysis.

For the purpose of extraction, food samples were classified into four broad categories: solid foods, beverages, dairy products, and oil samples. Solid food samples were homogenized and freeze-dried prior to analysis. Approximately 1.0–3.0 g of dry solid food samples were weighed, spiked with internal standards ($^{13}\text{C}_6$ -MeP and $^{13}\text{C}_6$ -BuP: 10 ng each), and equilibrated for 30 min at an ambient temperature. Acetonitrile (6 mL) was added, and the sample was extracted by shaking in a mechanical shaker for 60 min (Cao et al., 2010; Noonan et al., 2011). The sample was centrifuged at $4500 \times g$ for 5 min (Eppendorf 5804, Hamburg, Germany), and the supernatant was transferred into a glass tube. The extraction was repeated with an additional 6 mL of acetonitrile. The aliquots of acetonitrile were combined and concentrated to near-dryness under a gentle nitrogen stream.

The residue was dissolved in 2 mL of 10% dichloromethane/hexane (v/v) and purified by passage through a Strata® NH_2 cartridge (200 mg/3 cc, Phenomenex, Torrance, CA), using a RapidTrace® SPE workstation (Caliper Life Sciences, Inc., Hopkinton, MA). The cartridge was conditioned with 5 mL of 80% methanol/acetone (v/v) and then with 5 mL of hexane. The extract was loaded onto the cartridge and rinsed with 5 mL of hexane. Target analytes were eluted with 5 mL of 80% methanol/acetone (v/v). After being concentrated to 0.5 mL, the eluate was transferred into a GC vial for high performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS) analysis. The extraction procedure for oil samples was similar to that for solid food samples, except that the oil samples were not freeze-dried.

For beverage samples, ~5 g of each sample was weighed, spiked with internal standards ($^{13}\text{C}_6$ -MeP and $^{13}\text{C}_6$ -BuP: 10 ng each), and extracted twice with 6 mL of ethyl acetate in a mechanical shaker for 60 min. The extracts were combined and concentrated to near-dryness, dissolved in 2 mL of 10% dichloromethane/hexane (v/v), and purified by passage through a Strata® NH_2 cartridge, as described above. For dairy products, ~3 g of each sample was spiked with internal standards ($^{13}\text{C}_6$ -MeP and $^{13}\text{C}_6$ -BuP: 10 ng each) and extracted with ~6 mL of acetonitrile (sample:acetonitrile = 1:2, v/v) (Yan et al., 2009). The sample was shaken for 60 min, centrifuged at $4500 \times g$ for 15 min, and transferred into a glass tube. After being concentrated to ~4 mL, the sample was diluted to ~10 mL with 0.2% formic acid (pH 2.5), and purified by passage through an Oasis® MCX cartridge (60 mg/3 cc; Waters Corporation, Milford, MA). The cartridge was conditioned with 5 mL of methanol and then with 5 mL of water. The cartridge was washed with 15 mL of 25% methanol/water (v/v) and 5 mL of water. Target analytes were eluted with 5 mL of methanol, and the eluate was concentrated to 0.5 mL for HPLC–MS/MS analysis (Liao et al., 2012).

2.3. Instrumental analysis

HPLC–MS/MS analyses were performed using an Agilent 1100 Series HPLC system (Agilent Technologies, Inc., Santa Clara, CA) interfaced with an Applied Biosystems API 5500 electrospray triple quadrupole

mass spectrometer (ESI-MS/MS; Applied Biosystems, Foster City, CA). Chromatographic separation was conducted using a Betasil C18 column (2.1×100 mm, $5 \mu\text{m}$; Thermo Electron Corporation, Waltham, MA), which was connected to a Javelin guard column (Betasil C18, 2.1×20 mm, $5 \mu\text{m}$; Thermo Electron Corporation). The injection volume was $10 \mu\text{L}$, and the column temperature was maintained at 25°C . The mobile phase consisted of methanol (A) and water (B) at a flow rate of $300 \mu\text{L}/\text{min}$, and the gradient elution program of the mobile phase is shown in Table S2 (Supporting Information). The MS/MS was set in electrospray negative ionization mode, with a cone voltage of -30 V, collision energy of -28 eV, capillary voltage of -4500 V, and desolvation temperature of 700°C . Target compounds were monitored by multiple reaction monitoring (MRM), and the MRM transitions are shown in Table S3 (Supporting Information). Nitrogen was used as both a curtain and a collision gas.

2.4. Quality Assurance and Quality Control (QA/QC)

With every batch of 60 samples, procedural blanks ($n = 3$) were analyzed to monitor for contamination arising from laboratory materials and solvents used in sample extraction. Trace levels of MeP (0.09 ng/g), EtP (0.01 ng/g), and PrP (0.02 ng/g) were found in procedural blanks; BuP, BzP, and HepP were not found in procedural blanks. The concentrations measured in food samples were subtracted from the mean values of the target chemicals found in procedural blanks ($n = 3$). Recoveries of individual parabens through the entire analytical procedure were determined by spiking six target compounds (10 ng each) into procedural blanks ($n = 3$ for each batch) as well as into randomly selected samples ($n = 4$ for each batch) that represented different food categories. The average recoveries of parabens spiked into procedural blanks ranged from 92% to 115% (Table S4; Supporting Information), and those spiked into food matrices were in the ranges of 67%–109%, 66%–104%, 74%–106%, and 77%–98% for solid foods, beverages, dairy products, and oils, respectively. With every batch of samples, six samples were randomly selected for duplicate analysis, and the results showed a coefficient variation of $<20\%$ among the measured values for all target compounds. The limit of quantification (LOQ) was 0.01 ng/g for each analyte, which was calculated from the value of the lowest acceptable calibration standard and a nominal sample weight of 1.0 g (Table S3). Quantification of analytes was performed using linear regressions ($r > 0.99$) generated from a ten-point calibration standard at concentrations ranging from 0.01 to 100 ng/mL, and the concentrations were corrected for the recoveries of the internal standards, $^{13}\text{C}_6$ -MeP (for MeP and EtP) and $^{13}\text{C}_6$ -BuP (for PrP, BuP, BzP, and HepP). Methanol and a midpoint calibration check standard were injected after every 20 samples as a check for instrumental drift in sensitivity and carry-over of analytes between samples.

2.5. Data analysis

Liquid samples were weighed before extraction, and the moisture contents of solid food samples were calculated for conversion of data from a dry-weight to a wet-weight basis. All data are presented on a wet-weight (or fresh-weight) basis. For data analysis, concentrations below the LOQ were assigned a value equal to LOQ divided by 2 (LOQ/2). Differences between food groups were compared by one-way ANOVA with the Tukey test, and correlations among the concentrations of parabens in foodstuffs were assessed by Pearson correlation analysis, using SPSS (version 17.0). A value of $p < 0.05$ was considered significant.

3. Results and discussion

3.1. Paraben concentrations in foods

Of the 282 food samples analyzed, 279 samples (99%) contained parabens, and the total concentration of parabens (sum of six parabens):

$\sum$ Parabens) ranged from below LOQ to 2530 ng/g, with a mean value of 39.3 ng/g (Table 1 and Table S5 in Supporting Information). The highest $\sum$ Paraben concentration (mean: 219 , median: 40.0 ng/g) was found in food samples collected from Shanghai (Fig. S1), followed by samples from Baoding (86.9 , 70.0 ng/g), Jinan (61.0 , 4.29 ng/g), and Tianjin (47.3 , 22.3 ng/g). The foodstuffs collected from Jinchang (located in northwestern China), Harbin (northern China), and Liuzhou (southern China) had relatively lower $\sum$ Paraben concentrations, and the mean and median concentrations for these three cities were 8.38 and 1.36 ng/g, 9.35 and 0.352 ng/g, and 15.2 and 2.91 ng/g, respectively (Fig. S1). The mean concentrations of $\sum$ Parabens in foodstuffs varied by over two orders of magnitude (Tables 1 and S5), and the differences were statistically significant between locations ($p < 0.05$, one-way ANOVA). The overall concentration of $\sum$ Parabens in foodstuffs (median: 3.09 ng/g for the entire sample set; Table S5) from China was approximately three orders of magnitude lower than that reported for indoor dust (1560 ng/g) collected from Albany, New York (Wang et al., 2012).

MeP, EtP, and PrP were the predominant paraben analogs found in food samples, accounting for $59 \pm 29\%$ (mean $\pm$ SD), $24 \pm 29\%$, and $10 \pm 12\%$, respectively, of the total paraben concentrations. BzP, BuP, and HepP collectively accounted for $<5\%$ of the total concentrations (Fig. 1). MeP was found in almost all of the samples (99%) at concentrations ranging from $<\text{LOQ}$ to 2170 , with a mean value of 22.4 ng/g. EtP and PrP were detected in the majority of samples (EtP, 84%; PrP, 79%) and the concentrations were in ranges of $<\text{LOQ}$ – 1140 ng/g (mean: 11.0 ng/g) and $<\text{LOQ}$ – 547 ng/g (5.22 ng/g), respectively (Tables 1 and S5). BuP and BzP were detected less frequently (BuP, 55%; BzP, 37%) in food samples, and HepP was found in only 4 of the 282 samples analyzed (1%). This composition pattern of parabens in food samples is somewhat different from what was reported for human urine, blood, and breast milk from the U.S., in which the concentrations were generally on the order of $\text{MeP} \gg \text{PrP} > \text{EtP}$ (Calafat et al., 2010; Frederiksen et al., 2011; Sandanger et al., 2011; Schlumpf et al., 2010; Ye et al., 2006a, 2006b, 2008). Parabens with longer alkyl chain length possess higher antimicrobial activity, but lower water solubility (Elder, 1984). As microbial replication usually occurs in the water phase, parabens with shorter chain lengths are commonly used (Soni et al., 2005). In practice, parabens are often used in combination to increase the antimicrobial activity and the mixture of MeP and PrP is widely used in commerce (Andersen, 2008; CIR, 2009; Eriksson et al., 2008).

Relationships among the concentrations of individual parabens except for HepP in all food samples were determined by Pearson correlation analysis (Table 2). HepP was excluded from the correlation analysis due to low detection rate (1%) and concentration (mean: 0.005 ng/g; Table 1). There was a strong correlation between the concentrations of EtP and PrP ($r = 0.81$, $p < 0.01$) and of MeP and PrP ($r = 0.49$, $p < 0.01$). The correlation coefficients between concentrations of MeP or PrP and BuP were weak ($r = 0.25$ and 0.16 , respectively) but significant ($p < 0.01$). A similar positive correlation between MeP and PrP has been reported for human urine (Calafat et al., 2010; Ye et al., 2006a) and indoor dust (Wang et al., 2012). The correlations among paraben analogs suggest the existence of similar sources of parabens in foodstuffs from China (Calafat et al., 2010; Ye et al., 2006a). Parabens are used in various combinations as preservatives in certain types of food products, especially processed foods (Soni et al., 2005).

3.2. Comparisons among food categories

In the present study, we categorized food samples into 13 groups, namely cereals, meat, fish and seafood, eggs, dairy products, bean products, fruits, vegetables, cookies, beverages, cooking oils, condiments, and others. The concentrations of individual and total parabens were compared among the 13 categories of foods (Tables 1 and S5). The highest $\sum$ Paraben concentration (mean: 109 , median: 17.3 ng/g) was found in vegetables including processed vegetables, followed by condiments (75.4 , 10.0 ng/g) and cereals (25.2 , 2.59 ng/g), which was approximately

Table 1
Concentrations (ng/g) of parabens in several categories of food items from China.

		BzP	BuP	EtP	HepP	MeP	PrP	ΣParabens
Cereals (n = 39)	Mean	0.011	1.24	5.39	0.005	16.6	1.94	25.2
	95th percentile	0.025	4.77	34.2	0.005	57.6	7.81	122
	Frequency (%)	15	59	85	0	97	72	100
Meat (n = 19)	Mean	0.027	0.371	1.87	0.006	2.27	1.11	5.65
	95th percentile	0.132	0.751	10.8	0.006	6.46	8.53	21.0
	Frequency (%)	47	53	95	5	100	89	100
Fish and seafood (n = 10)	Mean	0.020	0.185	0.692	0.005	1.45	0.377	2.72
	95th percentile	0.081	0.951	3.27	0.005	3.85	1.32	7.13
	Frequency (%)	30	70	100	0	100	90	100
Eggs (n = 11)	Mean	0.011	0.155	0.275	0.005	1.17	0.173	1.79
	95th percentile	0.028	0.822	0.837	0.005	3.87	0.426	4.84
	Frequency (%)	36	27	91	0	100	82	100
Dairy products (n = 16)	Mean	0.005	0.288	0.715	0.005	17.7	1.57	20.2
	95th percentile	0.007	1.32	3.18	0.005	89.9	7.30	97.8
	Frequency (%)	6	25	25	0	88	38	88
Bean products (n = 27)	Mean	0.028	0.486	4.36	0.005	11.0	0.685	16.6
	95th percentile	0.126	3.09	29.4	0.005	57.2	2.58	76.5
	Frequency (%)	37	70	89	0	100	89	100
Fruits (n = 20)	Mean	0.074	0.384	6.89	0.005	9.68	3.36	20.4
	95th percentile	0.162	2.09	37.2	0.005	41.7	9.96	77.7
	Frequency (%)	40	40	90	0	100	80	100
Vegetables (n = 39)	Mean	0.107	1.75	10.9	0.006	81.1	14.7	109
	95th percentile	0.388	6.51	62.1	0.005	111	50.4	249
	Frequency (%)	51	82	100	3	100	92	100
Cookies/snacks (n = 26)	Mean	0.028	0.394	3.70	0.005	12.9	4.41	21.4
	95th percentile	0.065	2.43	10.9	0.005	54.9	24.6	84.0
	Frequency (%)	65	62	88	0	96	92	96
Beverages (n = 4)	Mean	0.011	0.009	0.283	0.005	0.524	0.007	0.839
	95th percentile	0.025	0.013	0.874	0.005	1.39	0.012	1.57
	Frequency (%)	25	50	50	0	100	25	100
Cooking oils (n = 11)	Mean	0.103	0.016	4.22	0.005	6.32	0.250	10.9
	95th percentile	0.420	0.047	22.7	0.005	28.4	1.06	40.0
	Frequency (%)	55	45	82	0	100	82	100
Condiments (n = 47)	Mean	0.309	0.168	42.8	0.006	20.0	12.1	75.4
	95th percentile	0.965	0.853	107	0.005	155	3.38	281
	Frequency (%)	32	57	87	4	100	79	100
Others (n = 13)	Mean	0.014	0.005	0.037	0.005	24.0	0.017	24.1
	95th percentile	0.053	0.005	0.117	0.005	139	0.045	139
	Frequency (%)	31	0	54	0	100	46	100
All (n = 282)	Mean	0.086	0.607	11.0	0.005	22.4	5.22	39.3
	95th percentile	0.165	2.70	42.0	0.005	93.8	12.7	140
	Frequency (%)	37	55	84	1	99	79	99

Vegetables and fruits include fresh and processed products; cereals include cereal products.

two orders of magnitude higher than the concentrations found for beverages (0.839, 0.843 ng/g) and eggs (1.79 and 1.32 ng/g) (Fig. 2). Although the Σ Paraben concentration for individual food samples within and between the categories varied widely (from 0.04 ng/g for noodles in the cereal category to 2530 ng/g for dried peppers in the vegetable category), there was no significant difference in concentrations among the food categories ($p > 0.05$; Fig. 2 and Table S5).

MeP was found in almost all samples in most food categories; it was not found in only 1 of the 39 samples in the cereal category, 2 of the 16 samples in the dairy product category, and 1 of the 26 samples in the cookie category (Tables 1 and S5). The highest concentration of MeP (2170 ng/g) was found in a dried pepper sample (processed sample) in the vegetable category. Samples of dried aniseed (291 ng/g) and chili powder (223 ng/g; both are processed samples) in the condiment category and oats (176 ng/g) in the “others” category contained notable concentrations of MeP (Table S5). The highest mean concentrations of MeP were found in vegetables (81.1 ng/g), “others” (24.0 ng/g), condiments (20.0 ng/g), dairy products (17.7 ng/g), and cereals (16.6 ng/g). The mean concentration of MeP varied by over two orders of magnitude (Table 1) among the food categories, but the difference was not statistically significant ($p > 0.05$). MeP was the most abundant paraben analog in each food category, which accounted for 42% (in condiments) to 75% (in “others”), of the total paraben concentrations (Fig. S2; Supporting Information).

The next two major parabens in food samples were EtP and PrP, which accounted for 8.5%–48% and 5.3%–20%, respectively, of the total concentrations (Fig. S2). The highest concentration of EtP was found in a soy sauce sample (1140 ng/g), a bean paste sample (372 ng/g), and a vinegar sample (133 ng/g) in the condiment category. Notable concentrations of PrP were found in a soy sauce sample (547 ng/g) and in two dried pepper samples (323 and 61 ng/g, respectively) in the vegetable category (Table S5). Overall, the mean concentrations of EtP and PrP were significantly lower than those of MeP ($p < 0.05$).

The major source of parabens in foods remains unclear, and the use of parabens as antimicrobial preservatives in certain foods or ingredients used in prepared/processed foods is considered a potential source (Soni et al., 2005). In addition, packaging materials can be a source of parabens in foods. The food samples analyzed in our study were sorted into four categories according to the packaging materials, as cans, glass, paper, or plastic, and the concentrations of parabens among the four categories were compared. Although the mean concentration of Σ Parabens varied by over an order of magnitude, the concentrations and profiles were not significantly different among foodstuffs sold in different packaging materials ($p > 0.05$; Fig. 3). It is known that epoxy resins used as liners for metal cans release bisphenol A (BPA) into canned foods. Elevated concentrations of BPA have been reported in canned foods (Cao et al., 2010; Noonan et al., 2011; Schecter et al., 2010). Our results suggest that there is no association between the concentration of parabens in foods and

Fig. 1. Composition profiles of several parabens in foodstuffs collected from nine cities in China. The numbers within parentheses on y-axis represent the number of samples analyzed.

packaging materials and that the concentrations of parabens in canned foods were low (Fig. 3).

3.3. Human dietary exposure to parabens

Diet can be an important source of human exposure to parabens (Soni et al., 2005). The estimated daily intake (EDI; ng/kg bw/day) of parabens for the general Chinese population is based on Eq. (1) (USEPA, 2011), as shown below:

$$EDI = \frac{\sum_{i=1}^n C_i \times DC_i}{BW} \quad (1)$$

where C is the concentration of parabens in food samples (ng/g), DC is the daily consumption rate of food (g/day), and BW is the body weight (kg). For C , the mean and 95th percentile concentrations of parabens were used for average and high exposure scenarios, respectively. For DC , reported values for adult men and adult women by several nationwide or regional surveys in China were used (Ma et al., 2007; Zhai, 2008; Zhang et al., 2011; Zhong et al., 2006). For BW , 62.7 kg and 54.8 kg were used for adult men and adult women, respectively, which were calculated from a previous study on weight and height of the Chinese people (Yang et al., 2005). Details on the consumption

Table 2
Pearson correlations among concentrations of parabens in foodstuffs from China.

	BzP	BuP	EtP	MeP	PrP	ΣParabens
BzP	1					
BuP	0.023	1				
EtP	−0.006	0.100	1			
MeP	0.113	0.248**	0.018	1		
PrP	0.004	0.156**	0.806**	0.492**	1	
ΣParabens	0.083	0.264**	0.570**	0.829**	0.874**	1

The entire sample set: $n = 282$.

** Correlations are significant at 0.01 levels (2-tailed).

Fig. 2. Comparison of total concentrations of parabens in various categories of foods. The box plot shows 5th (lower whisker), 25th (bottom edge of the box), 75th (top edge of the box), and 95th (upper whisker) percentiles. The low and upper stars represent 1st and 99th percentiles. The dots are outliers and the open square and the line within the box represent the mean and median concentrations. The number within parentheses on x-axis is the sample number for each group. Cereals, fruits and vegetables include processed products.

pattern of foods for EDI calculation are shown in Table S6 (Supporting Information).

The daily intakes of individual and total parabens for the general population in China through consumption of different food categories are summarized in Table 3 and Table S7 (Supporting Information). The mean and 95th percentile EDI values of total parabens for men were 1010 and 3040 ng/kg bw/day, respectively, which were comparable to those estimated for women (1060 and 3170 ng/kg bw/day) (Table 3). Among several food categories, vegetable products were the predominant contributors to dietary exposure in men, accounting for 64% of the total paraben intake (calculated from the mean EDIs); this is followed, in decreasing order, by cereal products (19%), fruits (7.4%), and condiments (3.2%) (Table S7). The highest exposure dose for individual parabens was contributed by MeP, and the mean daily dietary intakes were 696 and 730 ng/kg bw/day for men and women, respectively. Dietary exposure doses of EtP and PrP were comparable to the mean daily intake values of 166 and 124 ng/kg bw/day for men and 174 and 132 ng/kg bw/day for women, respectively (Table S7). The contributions of MeP,

Fig. 3. Individual and total concentrations of parabens in food samples sold in different packaging materials. The box plot shows 5th (lower whisker), 25th (bottom edge of the box), 75th (top edge of the box), and 95th (upper whisker) percentiles. The low and upper stars represent 1st and 99th percentiles. The open square and the line within the box represent the mean and median concentrations.

Table 3
Estimated daily dietary intakes (EDI, ng/kg bw/day) of parabens by Chinese.

	Male		Female	
	Mean	95th percentile	Mean	95th percentile
BzP	1.57	4.86	1.66	5.12
BuP	22.8	87.3	23.3	89.5
EtP	166	885	174	922
HepP	0.242	0.239	0.248	0.244
MeP	696	1490	730	1560
PrP	124	426	132	447
ΣParabens	1010	3040	1060	3170

EtP, and PrP to the total paraben intakes were 69%, 16%, and 12%, respectively (Fig. S3; Supporting Information).

4. Conclusions

In summary, the occurrence and concentration of MeP, EtP, PrP, BuP, BzP, and HepP in foodstuffs from nine cities in China were investigated. Parabens were found in almost all (99%) food samples, and the concentrations varied by four to five orders of magnitude, from below LOQ to 2530 ng/g. Among paraben analogs, MeP, EtP, and PrP were predominant in foodstuffs, accounting for 59%, 24%, and 10%, respectively, of the total paraben concentrations. The estimated daily dietary intake of parabens (calculated from the mean concentration) was 1010 ng/kg bw/day for men and 1060 ng/kg bw/day for women in China. Further studies are needed to investigate the sources, pathways, and fate of parabens in the environment.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.envint.2013.04.001>

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