



The internal exposure of phthalate metabolites and bisphenols in waste incineration plant workers and the associated health risks

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ABSTRACT

Many hazardous substances can be released during incineration of municipal solid waste (MSW), which pose a potential threat to human health. As additives, phthalates (PAEs) and bisphenols (BPs), which are widely used in daily goods, are likely to be present in the released hazardous substances. In the present study, we investigated the urinary levels of phthalate metabolites (mPAEs) and BPs in workers in an MSW incineration plant (the exposed group) and in residents 8 km away (the control group) in Shenzhen, China. The results showed that the median total urinary concentration of mPAEs in workers was significantly higher than that in residents (1.02×10^3 vs. 375 ng/mL). However, there was no significant difference between workers and residents for BPs. Among the mPAEs measured, the most abundant compound was mono-*n*-butyl phthalate in both exposed and control groups. Monoethyl phthalate and monomethyl phthalate might be potential markers for MSW incineration because of significantly high levels in the exposed group. The workers engaged in different types of workshops showed no significant differences in the urinary levels of mPAEs, also for BPs. It was worth noting that 70.8% of workers were at risk of the non-carcinogenic effects caused by PAEs with diethylhexyl phthalate having the highest risk. Actions should be taken to reduce the risks caused by these hazardous chemicals.

1. Introduction

Municipal solid waste (MSW) originates from daily life and various industries. With a large volume and different types, the treatment of MSW and the effects on the environment have attracted great attention. Incineration is a common way of handling MSW, which not only reduces the stock of MSW quickly, but also recovers energy via power generation. By 2015, 1179 MSW incineration plants with power generation capabilities existed around the world, and more than 20% of them are in China (Lu et al., 2017). In China, the production of MSW in large and medium cities in 2018 was about 1.8 billion tons (China MEE, 2019). However, studies showed that toxicants, such as polychlorinated dibenzofuran and dibenzo-*p*-dioxin compounds, were detected in flue gas and fly ash (Chang et al., 2011; Chen et al., 2020; Chi and Chang, 2005), and the emission of some additives in the bottom ash during the MSW incineration (Lin et al., 2010). These toxicants can be transported and transformed in the environment, and ultimately pose potential

threats to the environment and human health (Herrero et al., 2020).

As a type of plasticizer, phthalates (PAEs), i.e., diesters of phthalic acids, are mainly used in personal care products, food packaging, children toys, and even medical devices (Lv et al., 2018). According to the substituent groups, PAEs are classified into low molecular weight (LMW) ones with methyl, ethyl, *n*-butyl, benzyl, and cyclohexyl, and high molecular weight (HMW) ones with 2-ethylhexyl, *n*-octyl, *iso*-decyl, and *iso*-nonyl (Kasper-Sonnenberg et al., 2012). Due to non-covalently binding to materials, PAEs have a tendency to escape from PAE-containing products into environmental matrices (Chen et al., 2018b). More than 8 million tons of PAEs are used every year in the world. PAEs are detected in all kinds of environmental matrices, including water and sediment, soil, air, organisms, and even human bodies as a result of their widespread use (Chen et al., 2019; Kong et al., 2012; Zeng et al., 2009; Zhang et al., 2019). Currently, PAEs and their metabolites (mPAEs) can be detected in various human samples, such as breast milk, serum, and urine (Hines et al., 2009; Hogberg et al., 2008).

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Humans exposed to PAEs are associated with obesity and reproductive diseases, especially endocrine disruption because of its anti-androgenic effect (Lee et al., 2019; Luisa et al., 2018; Sathyanarayana et al., 2016). Currently, the utilization of PAEs is gradually regulated in the world. In China, there also exist some regulations on the usage of several PAEs, such as dimethyl phthalate (DMP) and di-n-butyl phthalate (DBP), in plastic products and even on the concentration limits in drinking water with di (2-ethylhexyl) phthalate (DEHP) less than 0.008 mg/L (GB 5749–2006, 2006; GB 9685–2008, 2008).

Bisphenol analogues (BPs) are a class of compounds in which two phenols are connected at the *para*-position of each hydroxyl group via linkers with different structures. Bisphenol A (BPA) is the most common chemical among BPs. The global usage of BPA reached 7.7×10^6 tons in 2015, and was estimated to increase to 1.06×10^7 tons by 2022 (Lehmler et al., 2018). BPA is often incorporated in various resins and paper products, which are used to manufacture daily necessities, such as water bottles, internal lining of cans, and thermal paper (Peng et al., 2016). Due to similar toxicity concerns as PAEs, products containing BPA are regulated in North America, the European Union, and other countries. As a result, a series of BPA substitutes, such as bisphenol AF (BPAF), bisphenol S (BPS), and bisphenol F (BPF), are produced and used widely (Chen et al., 2016). However, the BPA substitutes also pose adverse health risks. It has been reported that BPAF and BPS concentrations in urine are positively correlated with Type II diabetes, and BPS exposure is associated with increased risk of hypertension and neurodevelopment disorders in children (Duan et al., 2018; Jiang et al., 2020a; 2020b). Even worse, some studies have shown that BPs have estrogen activities similar to or higher than BPA (Moreman et al., 2017; Mu et al., 2018).

Because MSW has a wide range of sources and complex composition, various pollutants are released during incineration. Although studies have shown that PAEs are present in the incinerator bottom ash and leachates of treatment processes in MSW incineration plants (Lin et al., 2010; Liu et al., 2016), it has been unclear whether or not PAEs affect the health of workers and the residents living at surrounding areas. Also, the release of BPs during MSW incineration has not been reported so far. Thus, in the present study, we hypothesized that MSW incineration released PAEs and BPs, and the chemicals posed potential health risks for workers engaged in incineration compared with general populations. Urine is a very useful matrix that can reflect human exposure to PAEs and BPs, because PAEs, which can be converted to mPAEs, i.e., phthalic acid monoesters, and these metabolites and BPs can be excreted rapidly via urine (Chen et al., 2012). Therefore, to provide evidence for this hypothesis, we collected urine samples of workers in an MSW incineration plant, measured their urinary concentrations of mPAEs and BPs, and assessed the related health risks. Meanwhile, urinary concentrations of mPAEs and BPs in residents living 8 km away from the plant were also analyzed. These results provide evidence of the release of PAEs during MSW incineration and high health risks for workers, although this was not the case for BPs.

2. Materials and methods

2.1. Reagents and materials

The standards of BPs, including BPA, BPF, BPS, BPAF, bisphenol AP (BPAP), bisphenol P (BPP), and bisphenol Z (BPZ), and the isotope-labeled internal standards of $^{13}\text{C}_{12}$ -BPA were purchased from Cambridge Isotope Laboratories (Andover, MA, USA). Standards of mPAEs and isotope-labeled internal standards used in the present study are list in Table 1. Methanol, acetonitrile, glacial acetic acid, and formic acid were obtained from Fisher Scientific (Houston, TX, USA). β -Glucuronidase/arylsulfatase (85000 β -glucuronidase units/mL, 7500 sulfatase units/mL) was purchased from Sigma (St. Louis, MO, USA). Other reagents were of analytical grade. Oasis MAX (60 mg/3 mL) and Bond Elut C18 (500 mg/6 mL) solid phase extraction (SPE) cartridges for

mPAEs and BPs were obtained from Waters Corp. (Milford, MS, USA) and ANPEL laboratory Technologies Inc. (Shanghai, China), respectively.

2.2. Sampling

During September 2016 to June 2017, a total of 104 urine samples of workers were collected from an MSW incineration plant in Shenzhen as the exposed group. According to the ages of the exposed group, at a ratio of approximately 1:2, 205 residents were randomly selected from a residential area living 8 km away from the incineration plant, whose urine samples were used as the control group. Since most workers are male in the MSW incineration plant, we only collect male urine samples in the present study. Usually, approximately 50 mL first morning urine was collected and sent to the laboratory within 2 h. The samples were stored at $-20\text{ }^\circ\text{C}$ until use. Each participant were requested to fill in a questionnaire to provide age, gender, height, weight, total working time, workshops, and other information, and sign an informed consent form. In the present study, 89 urine samples of workers and 183 control samples were used due to incomplete data on demographic characteristics of some subjects. The general information are listed in Table 2. The present study was approved by the ethics committee of the School of Public Health (Shenzhen), Sun Yat-sen University.

2.3. Sample treatment and chemical analysis

For measurements of mPAEs and BPs, the sample treatment protocols were similar to our previous studies (Chen et al., 2018a, 2018b, 2019; Yu et al., 2021). They are described in detail in the Supporting Information. The target mPAEs were detected by LC-ESI-MS/MS as described previously (Chen et al., 2019). A Waters XTerra Phenyl column (100 mm \times 2.1 mm, 3.5 μm) was used with the column temperature being set at $40\text{ }^\circ\text{C}$. The injection volume was 10 μL . Acetonitrile and water, both of which contained 0.1% acetic acid, were used as the mobile phases. BPs were measured similarly as reported in the literature (Chen et al., 2018a). A Waters Atlantis C₁₈ column (150 mm \times 2.1 mm, 5 μm) was used with the column temperature at $40\text{ }^\circ\text{C}$. The mobile phases were acetonitrile-methanol (v/v = 1:1) and 5 mM ammonium acetate. A linear gradient program started at acetonitrile-methanol, which was held for 25.6 min, increased from 20% to 100%, dropped to 20% within 0.1 min, and then held for 1.6 min.

2.4. Quality assurance and quality control

All glassware was baked at $450\text{ }^\circ\text{C}$ for 4 h to remove contamination. Each batch of samples included two quality control samples (low and high concentrations) and one reagent blank. For mPAEs, the limits of detection (LOD) were 0.02–0.42 ng/mL and the limits of quantification (LOQ) were 0.06–1.30 ng/mL. The linear range was 0.01–100 ng/mL with the correlation coefficient (R^2) being above 0.999. The recoveries ranged from 85.8% to 119%. For BPs, the LODs and LOQs were 0.002–0.339 and 0.04–5.6 ng/mL, respectively. The linear range was 0.1–200 ng/mL with $R^2 > 0.999$. The recoveries were between 84% and 109%.

2.5. Health risk assessments and statistical analysis

The non-carcinogenic risks from exposure to PAEs and BPs were calculated based on the hazard quotients (HQ, dimensionless) for individual compounds and hazard indices (HI, dimensionless) for accumulative risks on the basis of the additive method. They were calculated based on the following formulae (Chen et al., 2018a, 2019):

$$HQ = \frac{EDU}{RfD} \quad (1)$$

Table 1
Standards of mPAEs and their corresponding isotope-labeled mPAEs used in this study.

Parent compounds	Metabolite standards	Isotope-labeled mPAEs
Low molecular weight		
Dimethyl phthalate	Monomethyl phthalate (mMP)	¹³ C ₂ -mMP
Diethyl phthalate (DEP)	Monoethyl phthalate (mEP)	¹³ C ₂ -mEP
Di- <i>n</i> -butyl phthalate	Mono- <i>n</i> -butyl phthalate (mBP)	¹³ C ₂ -mBP
Butylbenzyl phthalate (BzBP)	Monobenzyl phthalate (mBzP)	¹³ C ₂ -mBzP
Dicyclohexyl phthalate (DCHP)	Monocyclohexyl phthalate (mCHP)	¹³ C ₂ -mCHP
High molecular weight		
Di (2-ethylhexyl) phthalate	Mono (2-ethylhexyl) phthalate (mEHP)	¹³ C ₂ -mEHP
	Mono (2-ethyl-5-hydroxyhexyl) phthalate (mEHHP)	¹³ C ₄ -mEHHP
	Mono (2-ethyl-5-oxohexyl) phthalate (mEOHP)	¹³ C ₄ -mEOHP
Di- <i>n</i> -octyl phthalate (DOP)	Mono- <i>n</i> -octyl phthalate (mOP)	¹³ C ₂ -mOP
Di-3-methyl-7-methyloctyl phthalate (<i>iso</i> -decyl, DDP)	Mono-3-methyl-7-methyloctyl phthalate (<i>iso</i> -decyl, mDP)	¹³ C ₂ -mDP
Di-3-methyl-5-dimethylhexyl phthalate (<i>iso</i> -nonyl, DNP)	Mono-3-methyl-5-dimethylhexyl phthalate (<i>iso</i> -nonyl, mNP)	¹³ C ₂ -mNP

All mPAE standards and corresponding isotope-labeled mPAEs were purchased from Cambridge Isotope Laboratories (Andover, MA, USA).

Table 2
Demographic characteristics of subjects in the exposed and control groups.

Demographic characteristics	Numbers (%)
Exposed group	
Age (years)	89 (100)
≤ 25	29 (32.6)
26–30	36 (40.4)
≥ 31	24 (27.0)
Body mass index (kg/m ²)	
Underweight (< 18.5)	4 (4.5)
Normal Weight (18.5–25)	66 (74.2)
Overweight (> 25)	19 (21.3)
Total working time (years)	
≤ 5	49 (55.1)
6–10	26 (29.2)
≥ 11	14 (15.7)
Type of work ^a	
Boiler workshop	71 (79.8)
Steam workshop	67 (75.3)
Flue gas treatment workshop	72 (80.9)
Water treatment workshop	8 (9.0)
Control group	
Age (years)	183 (100)
≤ 25	68 (37.2)
26–30	74 (40.4)
≥ 31	41 (22.4)
Body mass index (kg/m ²)	
Underweight (< 18.5)	32 (17.5)
Normal Weight (18.5–25)	123 (67.2)
Overweight (> 25)	28 (15.3)

^a Some workers were engaged in more than one type of work.

$$HI = \Sigma HQ \quad (2)$$

$$EDU_{PAEs} = \frac{C_u \times V_u \times MW_p}{F_{ue} \times BW \times MW_m} \quad (3)$$

$$EDU_{BPs} = \frac{C_u \times V_u}{BW} \quad (4)$$

where EDU is the estimated daily uptake (μg/kg-bw/day) of an individual compound; RfD is the reference dose (μg/kg-bw/day); C_u is the concentrations of the individual compound in urine (μg/L); V_u is the daily excretion volume of urine for an adult (L/day); BW is the body weight of each subject obtained through the questionnaire (kg); MW_p is the molecular weight of the parent PAE compound and MW_m is that of its metabolite (g/mol); F_{ue} (dimensionless) is the ratio of the excreted metabolite to the uptake parent PAE compound. The parameters used are given in Table S1.

Statistical analysis was conducted using SPSS 13 (IBM, USA). The urinary concentrations of the chemicals were discussed with median value due to non-normal distribution of data. The significant differences

between the exposed and control groups were analyzed using Mann-Whitney *U* test, while the correlations among the concentrations of the target substances were analyzed with Spearman rank correlation. The statistically significant level was set at *p* < 0.05.

3. Results and discussions

3.1. Detection frequencies of mPAEs and BPs

With the exception of mMP, mPAEs with LMW (mMP, mEP, mBP, and mBzP) had a wide distribution in both exposed and control groups. The two congeners of mEP and mBP were detected in over 99% urine samples (Table 3). The detection frequencies of mBzP were 38.2% and 69.4% in the exposed and control group, respectively. On the contrary, mMP was detected with a high frequency (98.9%) in the exposed group, whereas the detection frequency was extremely low (1.1%) in the control group. mEHP, mEHHP, and mEOHP (the monoester metabolites and the oxidation products of DEHP) were detected in almost all samples in both exposed and control groups. However, mPAEs with HMW, such as mCHP, mOP, mDP, and mNP, had very low detection frequencies in both exposed and control groups.

Among BPs, BPA had the highest detection frequency with 100% detection in the exposed group and 98.4% in the control group, followed by BPF, which was detected in almost 70% samples. BPS was detected in 25.8% and 9.3% urine samples in the exposed and control groups, respectively. Other BPs, including BPP, BPZ, BPAF, and BPAP, showed low detection frequencies, which were generally lower than 15% with the exception of BPAF in the exposed group (19.1%).

3.2. Urinary concentrations of mPAEs and BPs

The total concentrations of the target mPAEs (ΣmPAEs) ranged from 217 to 3.48 × 10³ ng/mL (median: 1.02 × 10³ ng/mL) in the exposed group and from 34.2 to 1.85 × 10³ ng/mL (median: 375 ng/mL) in the control group (Table 3). The median concentrations of mBP, the most abundant mPAE compound, were 477 and 280 ng/mL, respectively, which were higher than the mBP concentration in primiparas (139 ng/mL) in the same city (Chen et al., 2019). Other studies from different regions in China all showed that mBP had the highest concentrations, such as school children in Yangtze River Delta (47.1 ng/mL), people of various occupations in Qiqihaer, Shanghai, and Guangzhou (61.2 ng/mL), and young adults from whole China (71.1 ng/mL) (Gao et al., 2016; Guo et al., 2011b; Wang et al., 2014). In general, our results were higher than those reported in other studies in China and other countries (Guo et al., 2011a; Koch et al., 2017; Langer et al., 2014; Zota et al., 2014). Therefore, the workers could be considered to be a population with an occupational exposure, which was caused by the emission from MSW incineration.

Table 3
Concentrations (ng/mL) of urinary mPAEs and BPs in the exposed and control groups.

Parents	Metabolites	Exposed group						Control group					
		25th percentile	Median	Mean	75th percentile	Range	DF	25th percentile	Median	Mean	75th percentile	Range	DF
Phthalate metabolites													
DMP	mMP	80.2	97.2	103	119	n.d.-212	98.9%	n.d.	n.d.	0.22	n.d.	n.d.-34.7	1.1%
DEP	mEP	50.4	89.2	222	189	n.d.-1.77 × 10 ³	98.9%	4.47	8.81	19.8	18.1	1.01-322	100%
DBP	mBP	281	477	592	824	n.d.-1.99 × 10 ³	98.9%	152	280	355	458	n.d.-1.72 × 10 ³	99.5%
BzBP	mBzP	n.d.	n.d.	2.61	0.96	n.d.-58.2	38.2%	n.d.	0.80	0.89	0.95	n.d.-17.2	69.4%
DEHP	mEHP	21.2	31.4	46.5	49.8	4.41-410	100%	7.60	11.7	14.4	18.6	n.d.-117	99.5%
	mEHHP	54.1	82.4	112	126	6.33-762	100%	15.7	27.3	34.6	40.6	3.32-627	100%
	mEOHP	29.3	47.4	58.7	71.6	n.d.-377	98.9%	8.60	14.5	18.1	21.0	1.76-307	100%
	ΣDEHP metabolites	111	178	217	248	17.8-1.39 × 10 ³	100%	33.2	54.4	67.0	79.5	9.53-1.05 × 10 ³	100%
DCHP	mCHP	n.d.	n.d.	n.d.	n.d.	-	-	n.d.	n.d.	0.09	n.d.	n.d.-1.37	7.1%
DOP	mOP	n.d.	n.d.	n.d.	n.d.	-	-	n.d.	n.d.	2.12	n.d.	n.d.-35.8	10.9%
DDP	mDP	n.d.	n.d.	0.08	n.d.	n.d.-7.56	1.1%	n.d.	n.d.	1.90 × 10 ⁻³	n.d.	n.d.-0.35	0.5%
DNP	mNP	n.d.	n.d.	0.02	n.d.	n.d.-1.67	1.1%	n.d.	n.d.	0.01	n.d.	n.d.-1.91	0.5%
	ΣmPAEs	645	1.02 × 10 ³	1.14 × 10 ³	1.47 × 10 ³	217-3.48 × 10 ³	100%	221	375	445	571	34.2-1.85 × 10 ³	100%
Bisphenols													
BPA		2.32	4.36	7.10	7.66	0.30-69.8	100%	2.15	4.32	6.14	7.21	n.d.-35.2	98.4%
BPS		n.d.	n.d.	0.10	0.10	0-1.58	25.8%	n.d.	n.d.	0.02	n.d.	n.d.-0.74	9.3%
BPF		n.d.	2.18	3.23	4.20	0-20.6	70.8%	n.d.	1.46	2.06	2.96	n.d.-12.5	68.9%
BPP		n.d.	n.d.	n.d.	n.d.	-	-	n.d.	n.d.	0.04 × 10 ⁻³	n.d.	n.d.-0.48	1.1%
BPZ		n.d.	n.d.	n.d.	n.d.	-	-	n.d.	n.d.	0.04	n.d.	n.d.-1.35	12.6%
BPAF		n.d.	n.d.	0.08	n.d.	0-0.97	19.1%	n.d.	n.d.	0.04	n.d.	n.d.-2.14	12.6%
BPAP		n.d.	n.d.	n.d.	n.d.	-	-	n.d.	n.d.	n.d.	n.d.	-	-
ΣBPs		4.89	7.53	10.5	12.5	0.86-75.7	100%	3.19	6.36	8.29	10.3	n.d.-45.3	98.9%

DF: detection frequency; n.d.: not detected; BPA: bisphenol A; BPAP: bisphenol AP; BPAF: bisphenol AF; BPF: bisphenol F; BPS: bisphenol S; BPP: bisphenol P; BPZ: bisphenol Z; mNP: mono-iso-nonyl phthalate; mBzP: monobenzyl phthalate; mMP: monomethyl phthalate; mBP: mono-*n*-butyl phthalate; mDP: mono-*iso*-decyl phthalate; mEHP: mono (2-ethylhexyl) phthalate; mCHP: monocyclohexyl phthalate; mOP: mono-*n*-octyl phthalate; mEOHP: mono (2-ethyl-5-oxohexyl) phthalate; mEP: monoethyl phthalate; mEHHP: mono (2-ethyl-5-hydroxyhexyl) phthalate; DMP: dimethyl phthalate; DEP: diethyl phthalate; DBP: di-*n*-butyl phthalate; BzBP: butylbenzyl phthalate; DEHP: di (2-ethylhexyl) phthalate; DCHP: dicyclohexyl phthalate; DOP: di-*n*-octyl phthalate; DDP: di-*iso*-decyl phthalate; DNP: di-*iso*-nonyl phthalate.

Unexpectedly, urinary mMP was generally at low levels within one or two dozens ng/mL (Hogberg et al., 2008), whereas the concentrations of mMP in the exposed group (median: 97.2 ng/mL) were far higher than those in the control group (median: n.d.) in our study. The extremely high levels of mMP seemed to be related to MSW incineration. Similar results were observed with mEP, whose concentrations were 89.2 and 8.81 ng/mL in the exposed and control groups, respectively. For the three monoester and oxidation metabolites of DEHP, similar differences were also observed (Table 3). However, the differences observed with these compounds were not as large as those observed with the two mPAEs above. Based on the present results, mMP and mEP might be candidates to indicate PAE emissions by MSW incineration. However, more works are needed to support this speculation.

The total urinary concentrations of BPs (Σ BPs) were 0.86–75.7 and n.d.–45.3 ng/mL with the medians being 7.53 and 6.36 ng/mL in the exposed and control groups, respectively. Among the BPs detected, BPA had the highest concentrations, followed by BPF (Table 3). This was consistent with the observations in most studies (Chen et al., 2018a; Ye et al., 2015), although some studies showed that BPS was the compound with the second highest abundance (Zhang et al., 2020a). The median concentrations of BPA in the exposed and control groups were 4.36 and 4.32 ng/mL, respectively, which were much higher than those in workers in a hazardous waste incinerator in Spain (0.86 ng/mL) (Gonzalez et al., 2019) and in pregnant women living in an electronic waste area (0.9 ng/mL) (Zhang et al., 2020a). The urinary BPA levels were also slightly higher than those in people living in an electronic waste area in South China (3.00 ng/mL) (Zhang et al., 2016b) and in college students in Guangzhou (3.57 ng/mL) (Zhang et al., 2020b). The data were significantly higher than those obtained from other regions in China (0.25–1.6 ng/mL), although people in different regions, and with different ages and occupations seemed to have different degrees of exposure to BPA (Chen et al., 2018a; Liu et al., 2019; Yang et al., 2014).

Significantly higher concentrations of Σ mPAEs in the exposed group were observed in comparison with the control group ($p < 0.05$). As reported in the literature, a large number of PAEs in the leachates of treatment processes in MSW incineration plants were observed (Liu et al., 2016). In terms of Σ BPs, there was no significant difference between the two groups ($p = 0.074$), and also no significant differences were observed for individual compound, such as BPF ($p = 0.063$) and BPA ($p = 0.740$). However, a previous biomonitoring study implied that electronic waste dismantling activities could result in human exposure to the two compounds (Zhang et al., 2016b). This may be attributed to the fact that electronic waste is mostly composed of polymer resin materials containing BPA, which can be released during dismantling. Therefore, MSW incineration indeed emits PAEs and causes elevated exposure of workers engaged in incineration of these chemicals. However, MSW incineration might not be the major source of the workers exposed to BPs.

3.3. Composition profiles and source implications

To understand the possible sources of the chemicals, the composition profiles of mPAEs and BPs were examined on the basis of the means. In the present study, the compounds with the mean concentrations lower than their LODs were excluded (Fig. 1). In the exposed group, mBP accounted for 51.1% of the total mPAEs, followed by mEP (16.2%). However, in the control group, a different situation was observed, although mBP was still the predominant contributor, which accounted for 77.1% of the total mPAEs. Differently from mPAEs, bisphenols were predominantly composed of BPA and BPF, which accounted for 63.6% and 34.1% in the exposed group, and 72.3% and 25.8% in the control group, respectively.

Many studies showed the predominance of mBP among urinary mPAEs in several cities in China, such as Shenzhen (Chen et al., 2019), Shanghai (Shen et al., 2015), Nanjing (Zhang et al., 2016a), Beijing

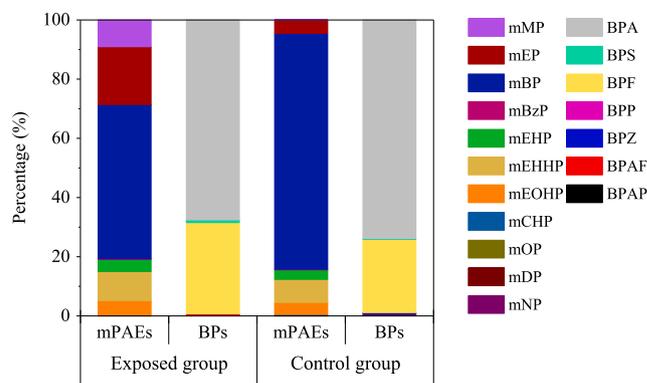


Fig. 1. Composition profiles of mPAEs and BPs in the urine of the exposed group and the control group.

(Gong et al., 2015; Zhang et al., 2020c), and Jilin (Ding et al., 2019). This can be attributed to the wide usage of dibutyl phthalate (DBP), the parent compound of mBP, in many products. The annual production of DBP in 2004 was 6×10^4 tons in China (Guo et al., 2011b). The composition of MSW is complex and it is likely to contain products carrying DBP. As a result, DBP is released during MSW incineration and causes human exposure by various pathways.

Compared to its negligible contribution in the control group, mMP accounted for 11.8% of Σ mPAEs in the exposed group. Specially, in the urine of employees in an electronic waste recycling area in Tianjin, the proportion of mMP is as high as 32.3% of totals (Li et al., 2019). In contrast, the urinary mMP proportion in general population was very small (Chen et al., 2019). Similarly, a much higher proportion of mEP in the exposed group (16.2%) was observed than that in the control group (4.5%), with the latter being similar to the low contribution in general populations, including school children and primiparas (Chen et al., 2019; Wang et al., 2014; Zhang et al., 2020c). The two PAE metabolites, mMP and mEP, had very different composition contributions in the exposed group compared with the control group, suggesting that the special sources in MSW incineration may be present.

To further understand the sources of the chemicals, Spearman correlation was used for the analysis (Fig. 2 and Table S2). The results showed that in the exposed group, mMP was significantly positively correlated with mBP ($r_s = 0.288$) and mEP ($r_s = 0.481$) (Fig. 2A and B). However, no significant correlations were found in the control group. The results indicated that mMP, mBP, and mEP had the same sources, i.e., the emission from the MSW incineration process, whereas the sources were different for the control group. As the metabolites of DEHP, the total mEHP, mEHHP, and mEOHP accounted for 17.8% in the exposed group and 9.8% in the control group. The highly positive and significant correlations among them were expected because they are metabolites from the same parent compound. Additionally, they were moderately positively related to mPAEs with LMW (Fig. 2A), which meant that DEHP and mPAEs with LMW had similar sources, such as the emission of MSW incineration. Meanwhile, there were studies showing that general populations were exposed to DEHP mainly via diets (Dong et al., 2017; Koch et al., 2013; Trasande et al., 2013). Considering the significantly higher urinary concentrations of mEHP, mEHHP, and mEOHP in the exposed group than those in the control group ($p < 0.05$), both diets and MSW incineration emission should be the two important sources of DEHP for the exposed group.

BPA dominated urinary Σ BPs in the present study. Currently, almost all environmental matrices, including human fluids such as urine, serum, breast milk, semen, and follicular fluid, are contaminated by BPA (Vandenberg et al., 2007). As aforementioned, there was no significant difference of the BPA concentrations between the exposed and the control groups, which suggested that urinary BPA in the exposed group might not be affected by MSW incineration. In addition, in the

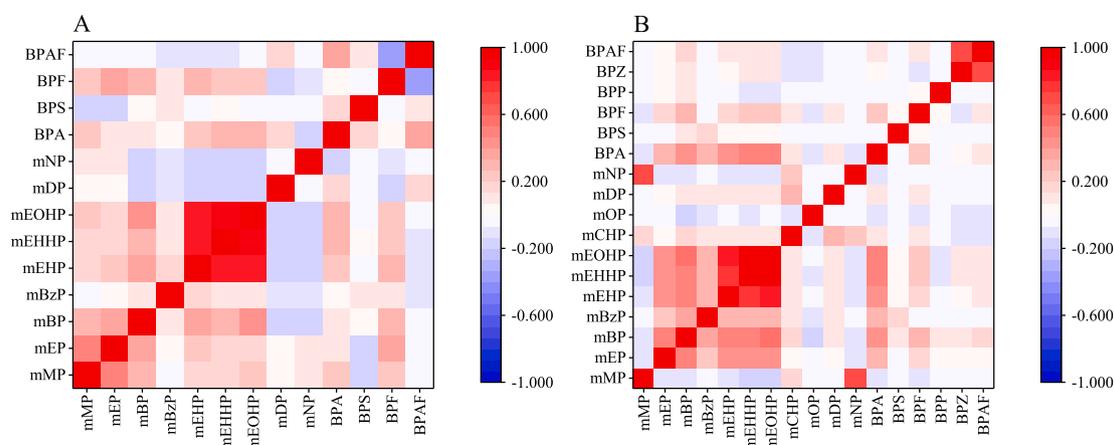


Fig. 2. Spearman correlation heat maps of urinary mPAEs and BPs in the exposed group (A) and the control group (B).

control group, BPA showed moderately positive and significant correlations with mEP ($r_s = 0.281$), mBP ($r_s = 0.454$), mBzP ($r_s = 0.290$), mEHP ($r_s = 0.451$), mEHHP ($r_s = 0.501$), and mEOHP ($r_s = 0.505$) with $p < 0.01$ (Table S2B). However, this phenomenon was almost not observed in the exposed group (Table S2A). This further illustrated that MSW incineration was not the main factor that led to an increase in the BPA levels in the exposed group, because mPAEs in the exposed group were mainly from MSW incineration. Meanwhile, correlations also indicated that BPA and these PAEs may have other common sources in control group. There are studies showing that both food and in- and out-door air can increase the exposure to PAEs and BPs (Geens et al., 2012; Lin et al., 2016). Of course, these exposure sources also play a role in the exposed group, but their contribution ratio is small compared with the source of MSW incineration.

3.4. Correlations between urinary levels and factors of working types and years

To understand the possible influence of the type of work and working years of the workers on the exposure burden of mPAEs and BPs, their relationships were analyzed (Table 4). More information about each mPAE and BP compound are listed in Table S3. There were no significant differences of total mPAE or BPs among the workers who worked in boiler, steam, flue gas treatment, and chemical treatment workshops ($p > 0.05$). Similar results were also observed with working years. We assumed that this might be because PAE emissions

Table 4
Effects of the workshops and total working time on the urinary concentrations (ng/mL) of mPAEs and BPs in the exposed group.

	Numbers (%)	ΣmPAEs			ΣBPs		
		Median	IQR	p	Median	IQR	p
Boiler workshop							
Yes	71 (79.8)	1.01×10^3	840	0.713	7.10	8.26	0.327
No	18 (20.2)	1.02×10^3	697		8.95	5.79	
Steam workshop							
Yes	67 (75.3)	1.04×10^3	873	0.697	6.65	9.20	0.050
No	22 (24.7)	937	692		9.52	5.22	
Flue gas treatment workshop							
Yes	72 (80.9)	894	847	0.446	7.63	9.55	0.699
No	17 (19.1)	1.20×10^3	686		7.53	3.89	
Water treatment workshop							
Yes	8 (9.0)	1.12×10^3	445	0.576	9.66	11.3	0.156
No	81 (91.0)	947	829		7.14	8.04	
Total working time							
≤ 5	49 (55.1)	1.02×10^3	861	0.346	8.26	7.81	0.943
6–10	26 (29.2)	1.14×10^3	796		7.40	7.48	
≥ 11	14 (15.7)	809	516		8.15	7.52	

IQR: interquartile range; mPAEs: phthalate metabolites; BPs: bisphenols.

from MSW incineration do not have typical point sources from different workshops and the chemicals are mainly emitted from the exhaust gas, which causes human exposure by exhaust gas diffusion. Thus, there were no significant differences among different workshops. In addition, PAEs can be metabolized quickly in the human body and as a result, the concentration of PAEs in urine reflects only the short-term exposure level of the human body. However, it is likely to increase the long-term exposure risk because of the high burdens of PAEs, although the working years did not cause the differences in their concentrations.

Additionally, we also analyzed the effects of different age and body mass index (BMI) groups on the urinary concentration of mPAEs and BPs (Tables S3C and 3D). In general, no significant differences caused by ΣmPAEs and ΣBPs were observed ($p > 0.05$). However, there was a significant difference in the urinary concentration of mEP of workers with different ages ($p < 0.05$), and the same phenomenon also observed in the effect of BMI on mBP and mBzP in the urine of surrounding residents ($p < 0.05$). This indicated that workers at different ages and surrounding residents with different BMIs have different exposure to mEP, mBP, and mBzP. For BPs, only BPS showed significant difference in ages excluding control group and BMIs in both exposed and control groups ($p < 0.05$). Nevertheless, considering low detection frequency and low concentration in urine, the effect of BPS on the human health can be neglected.

3.5. Estimated daily uptake and human health risks

To evaluate the human health risks caused by PAEs and BPs, the EDU of the chemicals were calculated on the basis of the concentrations of mPAEs and BPs in urine. Among the parent compounds of the target mPAEs, DBP was the most abundant PAE compound in both exposed and control groups. The mean EDU of DBP was 32.0 and 21.2 $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$ with the 95th being 74.8 and 52.3 $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$, respectively (Table S4). According to the RfD (100 $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$) of DBP supplied by the United States Environmental Protection Agency (USEPA), the present EDU based on the 95th DBP in both exposed and control groups exceeded half of the reference value. What is worse, the EDUs of DBP were several times higher than the tolerable daily intake (TDI) of DBP provided by the European Food Safety Authority. Even the mean EDU values were two or three times higher than the TDI value.

Next to DBP, DEHP showed the mean EDU values of 15.5–33.0 and 5.26–11.3 $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$ with the 95th being 36.9–75.1 and 11.9–24.7 $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$ calculated on the basis of the metabolites of DEHP for the exposed and control groups, respectively. According to the principle of USEPA to protect human health to the greatest extent, we used the maximum EDU values calculated for mEHP for the later discussion. The mean EDU of DEHP from mEHP for the exposed group was higher than the RfD value and that in the control group also

exceeded half of the reference value. All the results indicated that the workers suffered non-carcinogenic risks caused by DBP and DEHP.

For bisphenols, the mean EDU values of the most abundant chemical, BPA, were 0.21 and 0.20 $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$ with the 95th being 0.69 and 0.63 $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$ for the exposed and control groups, respectively. They were approximately 1–2 orders of magnitude lower than those of PAEs. They were also far lower than the RfD or TDI (Table S4). Nevertheless, higher exposure in the present subjects may pose adverse effects on human health, although BPA can be quickly eliminated after ingestion with a half-life of approximately 6 h (Thayer et al., 2015). Excessive exposure to BPA is likely to cause Type II diabetes (Ranciere et al., 2019), hypertension (Jiang et al., 2020a), asthma (Mendy et al., 2020), and so on. Next to BPA, the 95th EDU values of BPF were 0.38 and 0.23 $\mu\text{g}/\text{kg}\text{-bw}/\text{day}$ for the exposed and control groups, respectively. Currently, no reference data for BPF are available. Nevertheless, the risk of BPF should be low as an alternative to BPA because the concentrations of BPF were lower than those of BPA.

To further understand the non-carcinogenic risks caused by exposure to these chemicals, the HQs of individual compounds and the HIs obtained using the additive method were calculated on the basis of the RfD and the EDU of PAEs and BPs (Fig. 3A). The HQ values of individual compounds exhibited large variations with those of DEHP being the largest. The HQ values in the exposed group varied from 0.15 to 16.2, which were much higher than those (0–4.28) in the control group. The results suggested that the workers engaged in incineration were at higher risk of non-carcinogenic effects of these compounds than the residents in the nearby areas. Except for DEHP, the non-carcinogenic risk caused by these chemicals did not exceed the risk level of a unit. The result showed that special attention should be paid to the non-carcinogenic risk of DEHP. As shown in Fig. 3A, 51.7% workers and 9.3% residents exceeded the risk level based on the HQ values. Furthermore, 70.8% and 25.1% of them exceeded the risk level considering the accumulative risks of the chemicals using the additive method, and the risks of DEHP accounted for 79.9% and 72.4% of the total HI values, respectively. In addition, PAEs contributed more than 99% of the HI values, rendering the risks of BPs to be negligible (Fig. 3B). In other studies, DEHP was also very important. In school children from three regions of Yangtze River Delta in China, 4.1% of them were suffered higher risk of DEHP, while none for other mPAEs (Wang et al., 2014). In general population in Beijing, 5.7% participants exceeded the RfD value for DEHP, however, when based on TDI, DBP and DEHP all have more participants exceeded the threshold (Zhang et al., 2020c).

Additionally, DBP showed highest risk with 87.6% of exposed group and 71.6% of control group exceeding a unit, while only 16.9% of

exposed group had the ratios of EDU to TDI higher than a unit because of DEHP (Fig. S1). Such a large difference was caused by the values of RfD and TDI. However, it need to note that only one sample was collected for a person in the present study. For those subjects with high risks, continuous sampling for biomonitoring is necessary.

With the development of epidemiological investigation and toxicology research, many adverse health risks related to PAEs have been found. Countries around the world regulate PAEs with relatively high toxicity, such as DBP, DEHP, and so on. However, PAEs have not been completely banned and are still widely used all over the world. Their potential health risks will be a long-term concern. The epidemiological studies of the adverse health effects of these compounds are urgently needed.

4. Conclusions

The urinary concentrations of mPAEs and BPs in MSW incineration workers and control subjects were investigated, and the sources and health risks were evaluated. The concentrations of mPAEs in the workers were much higher than those in the control group, while there was no significant difference for BPs. The elevated concentrations of mPAEs in the urine of workers were related to MSW incineration. mBP was the most abundant mPAE in both exposed and control groups because of the huge usage of DBP, the parent compound of mBP. Two PAE metabolites, mMP and mEP, which were the sub-dominant mPAEs, might be markers for MSW incineration emissions. No significant differences in the urinary concentration of mPAEs or BPs among workers engaged in different types of work were found. Our data showed that 70.8% of workers and 25.1% of residents were at risk of the non-carcinogenic effects of PAEs with DEHP being the most important contributor. Non-carcinogenic health effects caused by occupational exposure to these compounds via MSW incineration deserve great concern.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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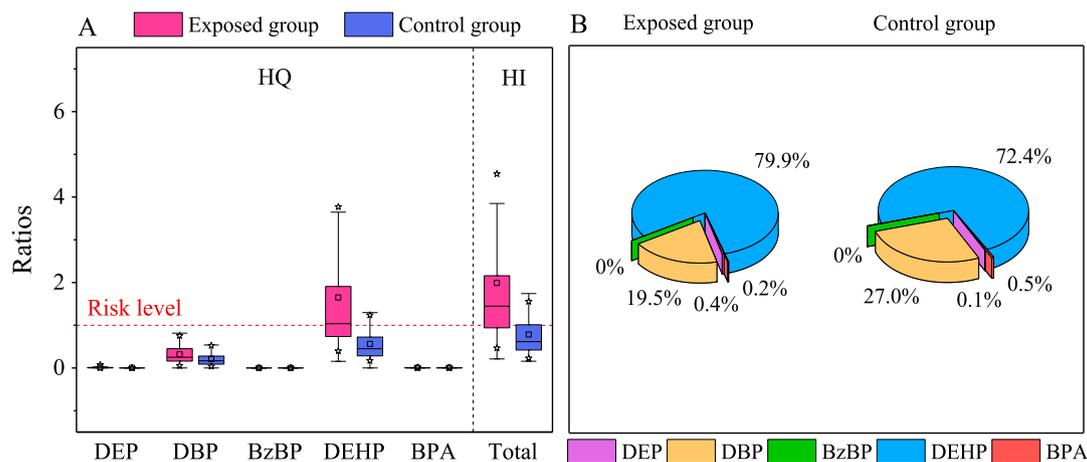


Fig. 3. Non-carcinogenic risks (A) and the relative contributions (B) of the target substances (the horizontal lines within the boxes represent the 50th values; the upper and lower limits of the boxes represent the 75th and 25th values; the length of whisker indicates 1.5 times interquartile range, and the asterisks indicate the 5th and 95th values; relative contributions caused by PAEs and BPA were based on the median HQ values; DEHP: diethylhexyl phthalate; DEP: diethyl phthalate; DBP: di-*n*-butyl phthalate; BzBP: butylbenzyl phthalate; BPA: bisphenol A).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2020.106101>.

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