Chemosphere 294 (2022) 133701

Contents lists available at ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere

Bisphenol A and its analogues in paired urine and house dust from South China and implications for children's exposure

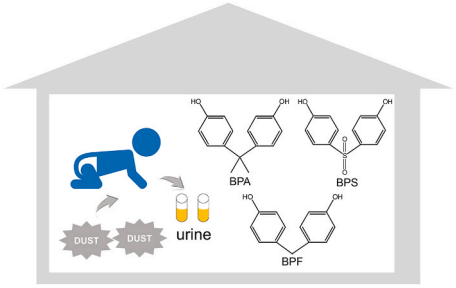
Yan Yang [a,b,c], Yumeng Shi [d], Da Chen [d], Haojia Chen [a,b], Xiaotu Liu [d,*]

[a] School of Environmental Science and Engineering, Institute of Environmental Health and Pollution Control, Guangdong University of Technology, Guangzhou, 510006, Guangdong, China
[b] Synergy Innovation Institute of GDUT, Shantou, 515041, Guangdong, China
[c] Chemistry and Chemical Engineering Guangdong Laboratory, Shantou, 515041, Guangdong, China
[d] School of Environment, Jinan University, Guangzhou, 511443, Guangdong, China

HIGHLIGHTS

- Thirteen bisphenol analogues were determined in paired house dust and child urine.
- BPA was the dominant analogue both in dust and urine samples.
- No association was found between urinary and house dust BPs.
- Dust intake contributed a small proportion to the overall exposure of children.

GRAPHICAL ABSTRACT



ARTICLE INFO

Handling Editor: Jian-Ying Hu

Keywords:
Bisphenol analogues
House dust
Urinary concentrations
Daily intake
Exposure assessment

ABSTRACT

Following the restriction of bisphenol A (BPA) in certain products, a number of bisphenol analogues (BPs) have been used as BPA replacements in different applications, raising environmental and health concerns. The present study determined a total of 13 bisphenol analogues in house dust and children urine from South China families (n = 46). Among all BPs, BPA, bisphenol S (BPS) and bisphenol F (BPF) were frequently detected in house dust, with concentrations ranging from 0.54 to 26.2 μg/g (median: 2.60 μg/g), 0.07–11.5 μg/g (median: 0.32 μg/g) and 0.02–2.4 μg/g (median: 0.29 μg/g), respectively. BPA (median: 2.43 ng/mL) was also the dominant BP in children urine samples, accounting for 75.2 ± 27.4% of the total concentrations of urinary BPs, followed by BPS (0.23 ng/mL), whereas BPF was only detected in less than 30% of urine samples. Children's daily intake of bisphenols through dust ingestion and total daily intakes were estimated based on the dust and urine concentrations, respectively. The estimated intake of BPA, BPS and BPF via house dust ingestion accounted for 9%, 12% and 38% of the total intakes predicted based on urinary concentrations, respectively, and exhibited very low exposure risks.

* Corresponding author.
E-mail address: liuxiaotu@jnu.edu.cn (X. Liu).

https://doi.org/10.1016/j.chemosphere.2022.133701
Received 31 August 2021; Received in revised form 5 January 2022; Accepted 18 January 2022
Available online 19 January 2022
0045-6535/© 2022 Elsevier Ltd. All rights reserved.

1. Introduction

BPA (bisphenol A, 2,2-bis(4-hydroxyphenyl) propane) is one of the most popular industrial chemicals with high production volumes worldwide. It has been used as an additive in the production of polycarbonate plastic and epoxy resin, as well as in many consumer products, such as toys, electronics, paper products and plastic food containers (Vandenberg et al., 2007; Chen et al., 2016). Long-term and large-scale applications have resulted in ubiquitous occurrence of BPA in global environment (Chen et al., 2016; Liu et al., 2021b). *In vitro* and *in vivo* studies have demonstrated a variety of toxic effects of BPA, mainly including endocrine disruption, neural networks, genotoxicity, reproductive toxicity, and neurotoxicity (Bonefeld-Jørgensen et al., 2007; Rochester, 2013). Especially, childhood exposure to BPA were reported to be associated with increased adiposity and higher levels of anxiety (Ejaredar et al., 2017). Consequently, BPA has been restricted from use in polycarbonate baby bottles and sippy cups from North American and European Union (Usman and Ahmad, 2016). However, the restriction has stimulated the manufacturing and applications of many alternative chemicals as BPA replacements (Chen et al., 2016; Qiu et al., 2019).

A number of chemicals with two hydroxyphenyl functionalities, which are structurally similar to BPA and referred to as bisphenol analogues (BPs), have been widely used as BPA replacements. Typical ones include BPB (bisphenol B, 2,2-bis(4-hydroxyphenyl)butane), BPC (bisphenol C, 2,2-Bis(4-hydroxy-3-methylphenyl) propane), BPE (bisphenol E, 4,4′-ethylidenebisphenol), BPF (bisphenol F, 4,4 –methylenediphenol), and BPS (bisphenol S, 4-hydroxyphenyl sulfone) (Chen et al., 2016). However, some of the BPs were reported to exhibit toxic potentials comparable to or even greater than those of BPA (Lee et al., 2019; Lei et al., 2019; Rochester and Bolden, 2015). BPF and BPS were reviewed to have hormonal potencies of the same magnitude as BPA both *in vitro and in vivo* (Rochester and Bolden, 2015). BPF was found to induce thyroid hormone disruption at a concentration (2.0 mg/L) lower than that of BPA in *Danio rerio* (Lee et al., 2019). This raised concerns on the environmental and health safety of the variety of bisphenol analogues as BPA replacements.

Residential environment has been suggested as an important source of environmental chemicals to human exposure. House dust has been broadly employed to investigate the occurrences of environmental chemicals in indoor environment (Dong et al., 2019). Additive chemicals may migrate from host consumer products and attach to dust particles. A variety of chemicals, including BPA, has been demonstrated with ubiquitous presence in house dust (Tan et al., 2018; Liao et al., 2012b). Humans may be exposed to dust-associated chemicals via dust ingestion, inhalation, and dermal contact (Geens et al., 2012; Wang et al., 2015). Previous studies have reported significant correlations between house dust-associated and urinary BPA (Liu et al., 2019a), suggesting a link between indoor pollution and human exposure. However, information remains limited on indoor contamination by BPA analogues and potential influence on human exposure.

Although several studies had reported human exposure of BPs (Chen et al., 2018; Liu et al., 2019c), data on children exposure to BPs other than BPA remained limited in China. Therefore, in the present study, we investigated BPA and 15 bisphenol analogues in paired house dust and children urine samples from the city of Guangzhou, South China. Primary aims were to: (1) determine the exposure profiles of bisphenol analogues in house dust and urine samples and their potential relationships; and (2) estimate children's daily intake of bisphenol analogues via dust ingestion and its contribution to overall exposure to BPs.

2. Method and materials

2.1. Chemical and reagents

Reference standards of 13 BPs were purchased from AccuStandard (New Haven, CT), including BPA, BPAP (bisphenol AP, 4,4′-(1-phenylethylidene)- bisphenol), BPB, BPBP (bisphenol BP, bis(4-hydroxyphenyl)-diphenylmethane), BPC, BPE, BPF, BPG (bisphenol G, 2,2- bis(4- hydroxy-3-isopropylphenyl) propane), BPM (bisphenol M, 4,4'-(1,3-phenylenediisopropylidene)bisphenol), BPP (bisphenol P, 4,4′-(1,4-phenylenediisopropylidene)bisphenol), BPPH (bisphenol PH, 2,2-bis(2-hydroxy-5-biphenylyl)propane), BPS and BPZ (bisphenol Z, 4,4′-cyclohexylidenebisphenol). Two surrogate standards, BPA-d_6 and BPS-$^{13}C_{12}$, as well as an internal standard BPA-d_{16}, were also purchased from AccuStandard (New Haven, CT). High performance liquid chromatography grade solvents included methanol, acetonitrile, isopropanol hexane, methyl *tert*-butyl ether and ethyl acetate were purchased from Fisher Scientific (Hanover Park, IL). Optima grade water was also purchased from Fisher Scientific (Hanover Park, IL).

2.2. Sample collection

A total of 46 families residing in the city of Guangzhou, South China, were recruited for the study. House dust was collected from each family's dwelling between October 2017 and May 2018 (n = 46). First-voided morning urine was also collected from one child of each of the families (n = 46). The children who participated were aged from 0.75 to 6 years; 37 were boys and 9 girls. Informed consent was obtained from the children's parent prior to sample collection. A questionnaire was also filled by the parent regarding demographic characteristics and basic information on the dwelling environment (Table S1). The study was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (2017-S225).

Dust was collected using a commercial vacuum cleaner (Electrolux, ZMO1511, 1400 W) attached with a customized and pre-cleaned nylon bag (with a pore size = of approximately 25 μm) following our previous method (Tan et al., 2018). A field blank was prepared for every ten homes by vacuuming pre-cleaned sodium sulfate. After collection, dust samples were wrapped in pre-clean aluminum foil and transported to the analytical lab. Then dust was sieved through a 125-μm stainless cloth sieve (Hogentogler & Co., Inc., Columbia, MD). First-voided morning urine was collected from the children by their parents and stored at pre-cleaned glass jars. Dust and urine samples were kept at −80 °C until analysis (Guo et al., 2013).

2.3. Chemical analysis

Dust and urine were analyzed using the methods described previously (Liu et al., 2019b). Briefly, 50 mg dust samples were spiked with surrogate standards and then extracted by a mixture of 3 mL methanol and water (6:4, v/v), 3 mL acetonitrile (ACN) and water (8:2, v/v), 3 mL of ACN and isopropanol (1:1, v/v), and 3 mL of hexane and isopropanol (1:1, v/v) under shaking in water bath. The combined extract was further purified by solid phase extraction with a HLB cartridge (3 cc, 60 mg sorbent, Waters Corporation). The final extract was spiked with the internal standard. An aliquot of 1 mL urine was spiked with surrogate standards, 200 μl of 1 M ammonium acetate (pH 6.5) and 20 μl β-glucuronidase (*Helix pomatia*), incubated at 37 °C overnight. The mixture was extracted by a mixture of methyl *tert*-butyl ether and ethyl acetate (5:1, v/v) under an ultrasound bath. The extraction repeated twice and the combine extract was concentrated and spiked with the internal standard. The specific gravity (SG) of each urine sample was measured by a handheld refractometer (Atago, Japan).

Determination of BPs was conducted on a Shimadzu UPLC coupled to an AB Sciex 5500 Q Trap triple quadrupole mass spectrometry (MS/MS, Toronto, Canada). Chromatographic separation was achieved with a Luna® 2.5 μm C18 (2) 100 Å column (100 mm × 2.1 mm, 2.5 μm particle size; Phenomenex, Torrance, CA, U.S.). The mobile phase consisted of water (A) and methanol (B), both spiked with 0.02 mM ammonium acetate. A flow rate of 200 μL/min was used. The gradient was programmed as: 0–2 min, 5% B; 2–3 min, 5% ramped to 60% B (linear); followed by a linear increase to 100% B in 20 min (held for 5 min) and

then a change to 5% B in 1 min (held for 5 min).

2.4. Quality assurance and quality control

In order to evaluate potential background contamination, a procedural blank was processed along with every batch of ten samples (n = 10 in total). Only BPA was detected in the procedural blanks (3.0–15.6 ng) for dust analysis, whereas none was detected in the procedural blanks for urine analysis. To evaluate the recovery efficiencies of analytical procedures, pre-cleaned sodium sulfate was spiked with 5 ng each of the target BPs along with surrogate standards and processed in five replicates along with two matrix blanks. An aliquot of 1 mL of a urine composite pooled from selected participants was also spiked with 5 ng each of the target BPs along with surrogate standards and processed in five replicates along with two matrix blanks. The recoveries of target BPs, after subtracting the original levels in matrix blanks, ranged from 86 ± 13% to 103 ± 18% and from 64 ± 25% to 115 ± 16% during the analysis of sodium sulfate and urine composite, respectively. The recoveries of surrogate standards (BPA-d_6 and BPS-$^{13}C_{12}$) from the analysis of authentic dust samples were 91 ± 21% and 89 ± 23%, respectively, and 89 ± 31% and 80 ± 22% in the analysis of authentic urine samples, respectively. The concentrations of BPs in dust (μg/g) and urine (ng/mL) were adjusted with blank data and the recoveries of surrogate standards, and urine concentrations were additionally adjusted with SG. The limit of detection (LOD) of an BP was defined as its response three times the standard deviation of the noise. The limit of quantification (LOQ) was defined as a response ten times the standard deviation of the noise level; whereas the LOQ for BPA in dust was estimated as the average blank contamination + 3 × standard deviation of blank contamination. The determined LOQs and LODs of dust and urine samples was provided in Table S2.

2.5. Exposure assessment

The daily intake of BPs via house dust ingestion (DI_d, ng/kg BW/day) was estimated based on the following equation:

$$DI_d = \frac{DIR \times C_d \times IEF}{BW} \quad (1)$$

where DIR is the dust ingestion rate (g/day), C_d is the concentration of BPs in house dust (ng/g), IEF represents the hours spent over a day in homes, and BW is body weight (kg).

The total daily intakes of BPs (DI_t, ng/kg BW/day) based on urinary BPs were estimated via the below equation

$$DI_t = C_u \times UV \quad (2)$$

where C_u is the concentration of BPs in urine (ng/mL) and UV is the urinary volume excreted per day by a child (mL/kg BW day).

Considering that every parameter varies because of interference by external confounding factors without control, the uncertainty of DI_d and DI_t was analyzed by means of a Monte-Carlo simulation. Each modeling parameter was expressed as a probability distribution function. Detailed information of the probabilistic parameters is provided in supporting information (Table S3). The Monte Carlo simulation was implemented using SPSS Software (Version 22). For each parameter, 100,000 runs were conducted. Sensitivity analysis was assessed by conducting correlation between each input and output during Monte Carlo simulations. Correlation coefficient (r_s) was used to determine the most influential parameters.

2.6. Data analysis

Statistical analysis was conducted with the SPSS statistics software package V20.0 (PASW Statistics 18.0, IBM Inc.) and the level of significance was set at α = 0.05. For analytes more than 30% of samples had concentrations below the LOD were therefore excluded from statistical analysis. Therefore, only BPA, BPS and BPF were included. Any measurement below LOD or LOQ was assigned with a value of LOD/$\sqrt{2}$ or LOQ/$\sqrt{2}$, respectively. Spearman correlation coefficients (r_s) were used to examine the correlations between different groups of data. Linear regression models were employed to determine the associations between concentrations of BPA and BPS in children urine and several predictors, including dust concentrations, gender, age (≤2, 2–3, 3–6 years), and drinking water container type (plastic or non-plastic). All categorical variables were dichotomized for analysis.

3. Results and discussion

3.1. Bisphenol analogues in indoor dust

The concentrations and detection rates of the BPs in dust are presented in Table 1. Out of 13 target BPs, BPA, BPS and BPF were detected in all dust samples with detection frequencies of 100%, whereas the others were generally below LOD. The total concentrations of detectable BPs ranged from 0.72 to 27 μg/g (median: 3.6 μg/g). BPA was the dominant analogue in dust, reaching a geometric mean and median of 2.7 μg/g and 2.6 μg/g, respectively, which accounted for 74.7 ± 15.2% of total concentration of BPs. BPS and BPF exhibited dust concentrations generally one order of magnitude lower than BPA, with a median concentration of 0.32 μg/g and 0.29 μg/g, respectively.

A number of studies have investigated the occurrence of BPs, other than BPA in house dust from different regions. In comparison with other studies (Fig. 1), concentrations of BPA in this study were a little higher than the concentrations in house dust from Japan (1.7 μg/g), South Korea (0.72 μg/g), Greece (1.5 μg/g) and U.S. (1.5 μg/g), but comparable to the level in house dust from Canada (Wang et al., 2015; Fan et al., 2021). The BPS and BPF concentration in house dust varied in orders of magnitude across different studies. The median concentration of BPF in this study was 50-fold higher than those in dust from six geographical regions across China (Zhu et al., 2020a). The concentration ratio of BPS to BPA has been used as a reflection of the degree of substitution of BPA, which was determined to be 0.13 in our study and lower than those determined in house dust from Singapore (0.20), Japan (0.28) and U.S. (0.36) (Liu et al., 2019a; Liao et al., 2012b). The predominance of BPA in dust samples suggested that BPA is still the most widely used bisphenol in China, and the frequently detection of BPS and BPF was compelling evidence that they are the important substitution of BPA. The prevalence of BPA followed with BPS and BPF was also observed in other environmental matrix in China, such as surface water and sediment (Jin and Zhu, 2016).

The spearman correlation analysis indicated a significant correlation between BPA and BPF ($r_s = 0.51$, $p < 0.01$). However, no correlations were observed between BPS and BPA or BPF (Table S4). The results may suggest that BPA and BPF could share similar applications in household consumer products. Available data indicate that BPF is commonly used in epoxy resin products, such as water pipes, plastics, or food packaging (Ye et al., 2015). Jurek and Leitner (2017) measured BPs in paper and paperboard samples, and found only BPA and BPF were detected in all samples. By contrast, BPS may have some unique usage. For instance, BPS was found with high concentrations in thermal receipt paper, where only low or nondetectable concentrations of BPA were detected (Liao et al., 2012c).

Overall, our data demonstrated that BPF and BPS occurred as the main bisphenol analogues other than BPA in house environment, indicating that they were the major substituents with applications in consumer products. Although BPA remained as the most dominant bisphenol analogue in house dust, increasing use of BPA replacements may result in higher concentrations in natural and human living environments as well as human exposure risks.

Table 1
Concentrations and detection frequencies (DF) of bisphenol analogues in house dust (μg/g) and children urine (ng/mL) from South China.

	Dust (n = 46, μg/g)				Children urine (n = 46, ng/mL)			
	DF[a] (%)	GM[b]	Median	Range	DF (%)	GM	Median	Range
BPA	100	2.68	2.59	0.54–26.2	100	3.05	2.43	0.24–38.8
BPS	100	0.36	0.32	0.07–11.5	98	0.25	0.23	n.d.-5.90
BPF	100	0.31	0.29	0.02–2.37	28	0.09	<LOQ[d]	n.d.-7.25
BPE	0	n.d.[c]	n.d.	n.d.	26	2.75	<LOQ	n.d.-1.20
BPB	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.
BPC	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.
BPG	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.
BPP	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.
BPM	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.
BPAP	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.
BPBP	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.
BPPH	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.
BPZ	0	n.d.	n.d.	n.d.	0	n.d.	n.d.	n.d.

[a] DF: detection frequency.
[b] GM: geometric mean.
[c] n.d.: not detected; values less than the limit of detection (LOD).
[d] < LOQ: the limit of quantification; values less than LOQ but higher than LOD.

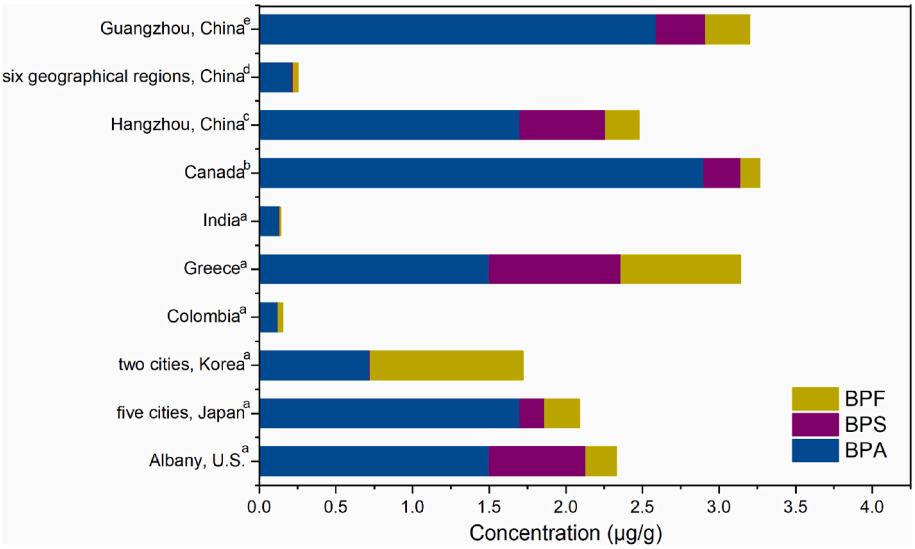


Fig. 1. Comparison of median concentration (ng/mL) of BPA, BPS and BPF in house dust from different regions. Data are from Wang et al. (2015)[a], Fan et al. (2021)[b], Liu et al. (2021a)[c], Zhu et al. (2020a)[d], and this study[e].

3.2. Urinary concentrations of bisphenol analogues

The total urinary concentrations of BPs ranged from 0.38 to 24.45 ng/mL with a median of 2.08 ng/mL. In addition to BPA and BPS which were detected in more than 98% of urine samples, BPF and BPE were also detected at a rate of 28% and 26%, respectively (Table 1). Other BPs were below LOD. BPA was the most abundant bisphenol analogue, with a median concentration of 2.43 ng/mL, accounting for 75 ± 27% of the total BP concentrations. By contrast, BPS concentrations ranged from <LOQ to 5.90 ng/mL with a median concentration of 0.23 ng/mL.

To date, only a few studies have investigated urinary concentrations of bisphenol analogues not only BPA in children or adults (Fig. 2). In comparison with other studies, urinary concentrations of BPA and BPS of South China children were within the range of those measured in children urine from Japan, Norway, Brazil, U.S. and Sweden (Gys et al., 2020; Sakhi et al., 2018; Rocha et al., 2018; Lehmler et al., 2018; Hoffman et al., 2018; Chen et al., 2018; Larsson et al., 2017). In most cases, BPA remained as the most abundant bisphenol analogue in human urine. However, a few exceptions occurred. For instance, BPS had higher concentrations than BPA and BPF determined in a population from Jeddah, Saudi Arabia (Asimakopoulos et al., 2014).

There was no significant difference in both urinary BPA and BPS concentrations between gender and age groups (≤2, 2–3, 3–6 years) of children. These were consistent with most previous adult or child studies (Zhang et al., 2011; Liao et al., 2012a; Stacy et al., 2016; Chen et al., 2018). However, we could not rule out the possibility that the null results were caused by a small sample size and narrow age range of our participants. Overall, our study provides more data to understand the exposure of BPs other than BPA for Chinese children, which have much less been investigated in biomonitoring studies before.

3.3. Associations between paired urine and dust samples

Dust intake has been suggested as one of the routes for human exposure to indoor chemicals. However, no significant correlation was observed between paired dust and urine samples in the present study (Table S3). We further categorized the urine BP concentrations into two groups according to the distribution of paired dust concentrations, namely the high (dust concentration higher than median value) and low (dust concentrations lower than median value) exposure group. Although the median concentration of urinary BPA in the high exposure group (2.71 ng/mL) was higher than that in the low exposure group

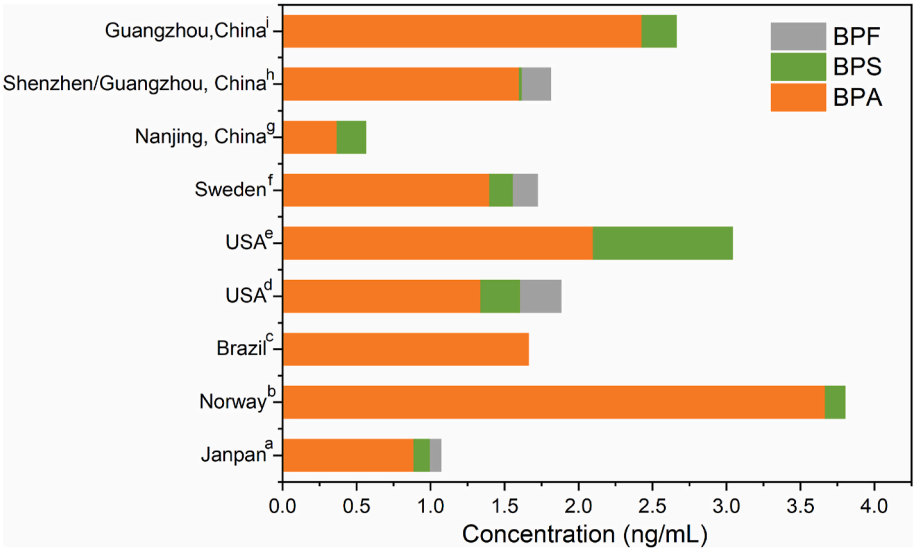


Fig. 2. Comparison of median concentration (ng/mL) of BPA, BPS and BPF in child urine from different regions. Data are from Gys et al. (2020)[a], Sakhi et al. (2018)[b], Rocha et al. (2018)[c], Lehmler et al. (2018)[d], Hoffman et al. (2018)[e], Larsson et al. (2017)[f], Liu et al., (2019c)[g], Chen et al. (2018)[h], and this study[i].

(2.20 ng/mL), the differences were not statistically significant. By contrast, the median concentration of urinary BPS in the high exposure group was even lower than that in the low exposure group (i.e., 0.18 vs. 0.25 ng/mL), although no significant difference was observed. To better interpret the data, linear regression models were further employed. BPA and BPF concentrations in child urine were not associated with dust concentration with adjustment for age, gender and water container type. All these results indicated the influence of house dust on urinary BP concentration of child was insignificant.

The lack of associations between dust and urinary levels suggested that other exposure pathways than dust intake may contribute to human exposure. Dietary intake has been suggested to be one of the most important exposure pathways for human exposure to BPA (Chen et al., 2016). Dietary intake of BPA could be orders of magnitude higher than that from nondietary sources (Geens et al., 2012). An observational study collected and analyzed environmental matrix samples (dust, air etc.) as well as food and urine samples of preschool children from the U. S., found that the daily exposure to BPA via dietary ingestion accounted for 99% to the aggregate exposure, while the in total contributions from inhalation and ingestion of dust and soil were less than 1% (Wilson et al., 2007). BPF and other non-BPA analogues were also detected in food-stuffs (Cao et al., 2019; Liao and Kannan, 2013, 2014). A U.S. survey reported that BPF occurred as the second most abundant bisphenol analogue in a variety of food items (Liao and Kannan, 2013). In addition, given a few analogues are employed in some specialized applications, other exposure pathways may exist. For example, BPS has been reported as a major bisphenol broadly used in receipts and other thermal papers (Liao et al., 2012c). Humans may be exposed via thermal contact and hand-to-mouth contact. The use of hand sanitizers may facilitate the intake via these exposure routes (Hormann et al., 2014).

Therefore, while dust intake could constitute a ubiquitous exposure pathway for human exposure to bisphenol analogues, other pathways also exist and could contribute to human exposure in a chemical-specific pattern. The exposure pattern may also differ between genders and age groups due to different lifestyles and behaviors. These aspects should be taken into consideration in future investigation of human exposure to bisphenols.

3.4. *Predicted intake from dust ingestion and total intake of BPs by children*

Based on dust concentrations, we estimated the daily intake of BPA, BPS, BPF and ΣBPs via house dust ingestion (DI_d) by children, while the total daily intake of the three BPs (DI_t) was estimated based on urinary data (Table 2). The results of point assessment were in consistent with those of probabilistic assessment from Monte Carlo simulation (Table 2), indicating that the exposure dose can be estimated from the monitoring results. The sensitivity analysis indicated that the most influential parameters for estimating DI_d were BP concentrations in dust (r_s: 0.68–0.72) and the dust ingestion rate (r_s: 0.37–0.53), and the most influential parameter for estimating DI_t were BP concentrations (r_s: 0.99–1.0) in urine (Fig. S1).

The median DI_d of BPA, BPS, BPF and ΣBPs were estimated to be 5.5, 0.8, 0.6 and 7.5 ng/kg bw day, respectively. The median DI_t of BPA, BPS, BPF and ΣBPs were determined to be 65.6, 4.9, 2.0 and 175 ng/kg bw day, respectively. Dust ingestion contributed approximately 9%, 12% and 38% of the total intake of BPA, BPS, and BPF, respectively. These data are consistent with the findings from previous studies which suggested that the estimated contribution from preschool dust ingestion to the total BPA intake was 6% for Swedish preschool students (Larsson et al., 2017; Wilson et al., 2007) and 9.23% for children in Guangzhou (Lv et al., 2016). This further demonstrates the complexity of exposure sources and pathways. It should be noted that the influence of dust intake on total BPS or BPF exposure seems to be greater than that for BPA. As pointed out earlier, dietary intake has been suggested as the predominant exposure pathway for BPA (Geens et al., 2012), whereas for other bisphenols non-dietary sources might be more important compared with that for BPA. Indeed, a recent dietary intervention study found dietary sources constituted an important contributor of children exposure to BPA but not BPS (Kim et al., 2020). This once again raises the need of elucidating analogue-dependent exposure sources and pathways.

Both the DI_d and DI_t of BPA or other analogues were far lower than the temporary tolerable reference dose of 4000 ng/kg bw/day recommended for BPA by the European Food Safety Authority (EFSA, 2015). This indicates low exposure risks via dust intake or a combination of pathways. However, the risk should not be overlooked. Exposure to multiple BPs could produce mixture effects different from what can be predicted from exposure to individual chemicals. For example, a mixture of eight estrogenic chemicals, including BPA, at concentrations below its effect threshold, exhibited significant mixture effects (Silva et al., 2002). In an *in vitro* cytotoxicity study, additive and synergism effects were observed after exposure to the binary bisphenol mixture (Zhu et al., 2020b). In addition, a lack of relevant refence dose or other toxic

Table 2
Estimated daily intake via dust ingestion (DI_d) and the total daily intake (DI_t) of bisphenol analogues.

	DI_d (ng/kg BW day)			DI_t (ng/kg BW day)		
	25th percentile	median	75th percentile	25th percentile	median	75th percentile
Point Estimation calculated with measured concentration						
BPA	3.7	5.0	7.4	33.2	53.8	114
BPS	0.4	0.6	1.1	1.8	5.1	17.2
BPF	0.4	0.5	1.0	0.7	1.4	5.5
ΣBPs	5.1	7.0	10.2	105	157	304
Probabilistic Estimation from the Monte Carlo simulation						
BPA	3.1	5.5	9.6	31.0	65.6	139
BPS	0.4	0.8	1.7	1.6	4.9	15.9
BPF	0.3	0.6	1.3	0.7	2.0	5.2
ΣBPs	4.4	7.5	12.9	96.8	175	311

thresholds for bisphenols other than BPA also limits an accurate determination of exposure risks. Although many bisphenol analogues exhibit similar modes of action as BPA, some could induce toxic potencies similar to or even greater than that of BPA (Chen et al., 2016). For instance, although BPS was generally less estrogenic and antiandrogenic than BPA, the former exhibited greater efficacy on 17α-hydroxyprogesterone (Rosenmai et al., 2014). Therefore, cautions should be taken when interpreting exposure data and predicting exposure risks.

Overall, the small contribution of indoor dust ingestion to the total exposure suggested dust alone may not provide comprehensive and accurate information for children exposure to BPs. The study presents several limitations. First, our sample size was relatively small. Second, most parameters in exposure assessments were cited from other studies. Third, only house dust ingestion route was considered in the exposure assessment, but additional exposure route such as dermal absorption may exist.

4. Conclusions

In the present study we characterized the exposure profiles of bisphenol analogues in house dust and paired children urine samples from South China. BPA was the dominant analogue in both house dust and urine; however, the data also demonstrated the wide use of BPS and BPF in household and related humane exposure. No significant correlations were observed between paired house dust and children urine, indicating a complexity of exposure pathways beyond dust intake. Indeed, the estimated daily intake via dust ingestion only accounted for a small proportion of the total daily intake of major bisphenol analogues. Although the current exposure unlikely induces any considerable health risk, potential mix effects from co-existing chemicals, as well as the influencing factors, merit further studies.

Author statement

Yan Yang: Writing – original draft, Investigation, Funding acquisition, **Yumeng Shi:** Writing – original draft, Data curation, **Da Chen:** Supervision, Writing-Reviewing and Editing, **Haojia Chen:** Investigation, Visualization, **Xiaotu Liu:** Supervision, Methodology, Writing-Reviewing and Editing.

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.

Acknowledgements

The authors thank Dr. Xiongfei Pan from Tongji Medical College, Huazhong University of Science and Technology for intellectual support and all families participating in the present study. The present study was financially supported by National Key R&D Program of China (No. 2018YFC1801102), Chemistry and Chemical Engineering Guangdong Laboratory (No. 2032008), and Science and Technology Planning Project of Guangdong Province (Nos. 190325224778589, 190807115560881, 200119095942659).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2022.133701.

References

Asimakopoulos, A.G., Thomaidis, N.S., Kannan, K., 2014. Widespread occurrence of bisphenol A diglycidyl ethers, p-hydroxybenzoic acid esters (parabens), benzophenone type-UV filters, triclosan, and triclocarban in human urine from Athens, Greece. Sci. Total Environ. 470–471, 1243–1249.
Bonefeld-Jørgensen, E.C., Long, M., Hofmeister, M.V., Vinggaard, A.M., 2007. Endocrine-disrupting potential of bisphenol A, bisphenol A dimethacrylate, 4-n-nonylphenol, and 4-n-octylphenol in vitro: new data and a brief review. Environ. Health Perspect. 115 (Suppl. 1), 69–76.
Cao, X.L., Kosarac, I., Popovic, S., Zhou, S., Smith, D., Dabeka, R., 2019. LC-MS/MS analysis of bisphenol S and five other bisphenols in total diet food samples. Food Addit. Contam. 1–8.
Chen, D., Kannan, K., Tan, H., Zheng, Z., Feng, Y., Wu, Y., Widelka, M., 2016. Bisphenol analogues other than BPA: environmental occurrence, human exposure, and toxicity—a review. Environ. Sci. Technol. 50, 5438–5453.
Chen, Y., Fang, J., Ren, L., Fan, R., Zhang, J., Liu, G., Zhou, L., Chen, D., Yu, Y., Lu, S., 2018. Urinary bisphenol analogues and triclosan in children from south China and implications for human exposure. Environ. Pollut. 238, 299–305.
Dong, T., Zhang, Y., Jia, S., Shang, H., Fang, W., Chen, D., Fang, M., 2019. Human indoor exposome of chemicals in dust and risk prioritization using EPA's ToxCast database. Environ. Sci. Technol. 53, 7045–7054.
EFSA, 2015. Scientific opinion on the risks to public health related to the presence of Bisphenol A (BPA) in foodstuffs: executive summary. EFSA J. 13 (1), 3978.
Ejaredar, M., Lee, Y., Roberts, D.J., Sauve, R., Dewey, D., 2017. Bisphenol A exposure and children's behavior: a systematic review. J. Expo. Sci. Environ. Epidemiol. 27, 175–183.
Fan, X., Katuri, G.P., Caza, A.A., Rasmussen, P.E., Kubwabo, C., 2021. Simultaneous measurement of 16 bisphenol A analogues in house dust and evaluation of two sampling techniques. Emerg. Contamin. 7, 1–9.
Geens, T., Aerts, D., Berthot, C., Bourguignon, J.P., Goeyens, L., Lecomte, P., Maghuin-Rogister, G., Pironnet, A.M., Pussemier, L., Scippo, M.L., Loco, J.V., Covaci, A., 2012. A review of dietary and non-dietary exposure to bisphenol-A. Food Chem. Toxicol. 50, 3725–3740.
Guo, Y., Wang, L., Kannan, K., 2013. Effect of storage time and temperature on levels of phthalate metabolites and bisphenol A in urine. Adv. Environ. Res. 2, 9–17.
Gys, C., Ait Bamai, Y., Araki, A., Bastiaensen, M., Caballero-Casero, N., Kishi, R., Covaci, A., 2020. Biomonitoring and temporal trends of bisphenols exposure in Japanese school children. Environ. Res. 191, 110172.
Hoffman, K., Hammel, S.C., Phillips, A.L., Lorenzo, A.M., Chen, A., Calafat, A.M., Ye, X., Webster, T.F., Stapleton, H.M., 2018. Biomarkers of exposure to SVOCs in children and their demographic associations: the TESIE Study. Environ. Int. 119, 26–36.
Hormann, A.M., Vom Saal, F.S., Nagel, S.C., Stahlhut, R.W., Moyer, C.L., Ellersieck, M.R., Welshons, W.V., Toutain, P.L., Taylor, J.A., 2014. Holding thermal receipt paper and eating food after using hand sanitizer results in high serum bioactive and urine total levels of bisphenol A (BPA). PLoS One 9, e110509.
Jin, H., Zhu, L., 2016. Occurrence and partitioning of bisphenol analogues in water and sediment from Liaohe river basin and Taihu lake, China. Water Res. 103, 343–351.
Jurek, A., Leitner, E., 2017. Analytical determination of bisphenol A (BPA) and bisphenol analogues in paper products by GC-MS/MS. Food Addit. Contam. 34, 1225–1238.

Kim, S., Lee, I., Lim, J.E., Lee, A., Moon, H.B., Park, J., Choi, K., 2020. Dietary contribution to body burden of bisphenol A and bisphenol S among mother-children pairs. Sci. Total Environ. 744.
Larsson, K., Lindh, C.H., Jonsson, B.A., Giovanoulis, G., Bibi, M., Bottai, M., Bergstrom, A., Berglund, M., 2017. Phthalates, non-phthalate plasticizers and bisphenols in Swedish preschool dust in relation to children's exposure. Environ. Int. 102, 114–124.
Lee, S., Kim, C., Shin, H., Kho, Y., Choi, K., 2019. Comparison of thyroid hormone disruption potentials by bisphenols A, S, F and Z in embryo-larval zebrafish. Chemosphere 221, 115–123.
Lehmler, H.-J., Liu, B., Gadogbe, M., Bao, W., 2018. Exposure to bisphenol A, bisphenol F, and bisphenol S in US adults and children: the national health and nutrition examination survey 2013–2014. ACS Omega 3, 6523–6532.
Lei, B., Sun, S., Zhang, X., Feng, C., Xu, J., Wen, Y., Huang, Y., Wu, M., Yu, Y., 2019. Bisphenol AF exerts estrogenic activity in MCF-7 cells through activation of Erk and PI3K/Akt signals via GPER signaling pathway. Chemosphere 220, 362–370.
Liao, C., Kannan, K., 2013. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. J. Agric. Food Chem. 61 (19), 4655–4662.
Liao, C., Kannan, K., 2014. A survey of bisphenol A and other bisphenol analogues in foodstuffs from nine cities in China. Food Addit. Contam. 31 (2), 319–329.
Liao, C., Liu, F., Alomirah, H., Loi, V.D., Mohd, M.A., Moon, H.-B., Nakata, H., Kannan, K., 2012a. Bisphenol S in urine from the United States and seven Asian countries: occurrence and human exposures. Environ. Sci. Technol. 46, 6860–6866.
Liao, C., Liu, F., Guo, Y., Moon, H.B., Nakata, H., Wu, Q., Kannan, K., 2012b. Occurrence of eight bisphenol analogues in indoor dust from the United States and several Asian countries: implications for human exposure. Environ. Sci. Technol. 46 (16), 9138–9145.
Liao, C., Liu, F., Kannan, K., 2012c. Bisphenol S, a new bisphenol analogue, in paper products and currency bills and its association with bisphenol A residues. Environ. Sci. Technol. 46, 6515–6522.
Liu, D., Wu, P., Zhao, N., Nie, S., Cui, J., Zhao, M., Jin, H., 2021a. Differences of bisphenol analogue concentrations in indoor dust between rural and urban areas. Chemosphere 276, 130016.
Liu, J., Zhang, L., Lu, G., Jiang, R., Yan, Z., Li, Y., 2021b. Occurrence, toxicity and ecological risk of bisphenol A analogues in aquatic environment – a review. Ecotoxicol. Environ. Saf. 208, 111481.
Liu, M., Jia, S., Dong, T., Han, Y., Xue, J., Wanjaya, E.R., Fang, M., 2019a. The occurrence of bisphenol plasticizers in paired dust and urine samples and its association with oxidative stress. Chemosphere 216, 472–478.
Liu, X., Peng, C., Shi, Y., Tan, H., Tang, S., Chen, D., 2019b. Beyond phthalate diesters: existence of phthalate monoesters in South China house dust and implications for human exposure. Environ. Sci. Technol. 53, 11675–11683.
Liu, Y.H., Yan, Z.Y., Zhang, Q., Song, N.H., Cheng, J., Torres, O.L., Chen, J.Q., Zhang, S. H., Guo, R.X., 2019c. Urinary levels, composition profile and cumulative risk of bisphenols in preschool-aged children from Nanjing suburb, China. Ecotoxicol. Environ. Saf. 172, 444–450.
Lv, Y., Rui, C., Dai, Y., Pang, Q., Li, Y., Fan, R., Lu, S., 2016. Exposure of children to BPA through dust and the association of urinary BPA and triclosan with oxidative stress in Guangzhou, China. Environ. Sci.: Proc. Impact. 18, 1492–1499.
Qiu, W., Zhan, H., Hu, J., Zhang, T., Xu, H., Wong, M., Xu, B., Zheng, C., 2019. The occurrence, potential toxicity, and toxicity mechanism of bisphenol S, a substitute of bisphenol A: a critical review of recent progress. Ecotoxicol. Environ. Saf. 173, 192–202.
Rocha, B.A., Asimakopoulos, A.G., Honda, M., da Costa, N.L., Barbosa, R.M., Barbosa Jr., F., Kannan, K., 2018. Advanced data mining approaches in the assessment of urinary concentrations of bisphenols, chlorophenols, parabens and benzophenones in Brazilian children and their association to DNA damage. Environ. Int. 116, 269–277.
Rochester, J.R., Bolden, A.L., 2015. Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol A substitutes. Environ. Health Perspect. 123, 643–650.
Rochester, J.R., 2013. Bisphenol A and human health: a review of the literature. Reprod. Toxicol. 42, 132–155.
Rosenmai, A.K., Dybdahl, M., Pedersen, M., Alice van Vugt-Lussenburg, B.M., Wedebye, E.B., Taxvig, C., Vinggaard, A.M., 2014. Are structural analogues to bisphenol a safe alternatives? Toxicol. Sci. 139, 35–47.
Sakhi, A.K., Sabaredzovic, A., Papadopoulou, E., Cequier, E., Thomsen, C., 2018. Levels, variability, and determinants of environmental phenols in pairs of Norwegian mothers and children. Environ. Int. 114, 242–251.
Silva, E., Rajapakse, N., Kortenkamp, A., 2002. Something from "nothing" - eight weak estrogenic chemicals combined at concentrations below NOECs produce significant mixture effects. Environ. Sci. Technol. 36 (8), 1751–1756.
Stacy, S.L., Eliot, M., Calafat, A.M., Chen, A., Lanphear, B.P., Hauser, R., Papandonatos, G.D., Sathyanarayana, S., Ye, X., Yolton, K., Braun, J.M., 2016. Patterns, variability, and predictors of urinary bisphenol A concentrations during childhood. Environ. Sci. Technol. 50 (11), 5981–5990.
Tan, H., Chen, D., Peng, C., Liu, X., Wu, Y., Li, X., Wu, Y., Li, X., Du, R., Wang, B., Guo, Y., Zeng, E.Y., 2018. Novel and traditional organophosphate esters in house dust from South China: association with hand wipes and exposure estimation. Environ. Sci. Technol. 52 (19), 11017–11026.
Usman, A., Ahmad, M., 2016. From BPA to its analogues: is it a safe journey? Chemosphere 158, 131–142.
Vandenberg, L.N., Hauser, R., Marcus, M., Olea, N., Welshons, W.V., 2007. Human exposure to bisphenol A (BPA). Reprod. Toxicol. 24 (2), 139–177.
Wang, W., Abualnaja, K.O., Asimakopoulos, A.G., Covaci, A., Gevao, B., Johnson-Restrepo, B., Kumosani, T.A., Malarvannan, G., Minh, T.B., Moon, H.B., Nakata, H., Sinha, R.K., Kannan, K., 2015. A comparative assessment of human exposure to tetrabromobisphenol A and eight bisphenols including bisphenol A via indoor dust ingestion in twelve countries. Environ. Int. 83, 183–191.
Wilson, N.K., Chuang, J.C., Morgan, M.K., Lordo, R.A., Sheldon, L.S., 2007. An observational study of the potential exposures of preschool children to pentachlorophenol, bisphenol-A, and nonylphenol at home and daycare. Environ. Res. 103 (1), 9–20.
Ye, X., Wong, L.Y., Kramer, J., Zhou, X., Jia, T., Calafat, A.M., 2015. Urinary concentrations of bisphenol A and three other bisphenols in convenience samples of US adults during 2000–2014. Environ. Sci. Technol. 49, 11834–11839.
Zhang, Z., Alomirah, H., Cho, H.S., Li, Y.F., Liao, C., Minh, T.B., Mohd, M.A., Nakata, H., Ren, N., Kannan, K., 2011. Urinary bisphenol A concentrations and their implications for human exposure in several Asian countries. Environ. Sci. Technol. 45, 7044–7050.
Zhu, Q., Wang, M., Jia, J., Hu, Y., Wang, X., Liao, C., Jiang, G., 2020a. Occurrence, distribution, and human exposure of several endocrine-disrupting chemicals in indoor dust: a nationwide study. Environ. Sci. Technol. 54, 11333–11343.
Zhu, X.L., Wu, G.L., Xing, Y., Wang, C.Z., Yuan, X., Li, B.K., 2020b. Evaluation of single and combined toxicity of bisphenol A and its analogues using a highly-sensitive micro-biosensor. J. Hazard Mater. 381.