Science of the Total Environment 640–641 (2018) 1214–1220

Contents lists available at ScienceDirect

Science of the Total Environment

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

Benzophenone-UV filters in personal care products and urine of schoolchildren from Shenzhen, China: Exposure assessment and possible source

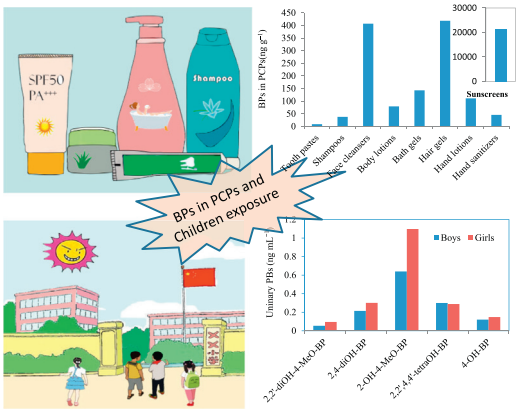
Shaoyou Lu [a,e], Fei Long [b], Ping Lu [b], Bingli Lei [d], Zi'an Jiang [d], Guihua Liu [a], Jianqing Zhang [a], Shengtao Ma [c], Yingxin Yu [c,d,*]

[a] Shenzhen Center for Disease Control and Prevention, Shenzhen 518055, PR China
[b] School of Chemistry and Environment, South China Normal University, Guangzhou 510006, PR China
[c] Guangzhou Key Laboratory of Environmental Catalysis and Pollution Control, School of Environmental Science and Engineering, Institute of Environmental Health and Pollution Control, Guangdong University of Technology, Guangzhou 510006, Guangdong, PR China
[d] Institute of Environmental Pollution and Health, School of Environmental and Chemical Engineering, Shanghai University, Shanghai 200444, PR China
[e] Guangzhou Key Laboratory of Environmental Exposure and Health, School of Environment, Jinan University, Guangzhou 510632, PR China

HIGHLIGHTS

- BPs in PCPs and urine of schoolchildren from Shenzhen China were measured.
- Sunscreens contained the highest BP concentrations among all PCP goods.
- Girls exhibited higher urinary BPs concentrations than boys.
- Body mass index has positive influence on urinary BPs.
- PCPs might play an important role for children exposure to BPs.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 3 February 2018
Received in revised form 2 June 2018
Accepted 2 June 2018
Available online 7 June 2018

Editor: Adrian Covaci

Keywords:
Benzophenone-type UV filter

ABSTRACT

The use of benzophenone (BP)-type UV filters in personal care products (PCPs) has rapidly increased in China over the past decade, leading to growing concerns on the potential adverse effects associated with the usage. Urine analysis is an ideal non-invasive approach for human biomonitoring of xenobiotics that are excreted mainly through urinary system. To investigate human exposure of PCPs to children from South China, we determined BP-type UV filters in a total of 156 commercial PCP goods covering 11 categories, as well as 280 urine samples collected from elementary school students in Shenzhen, China. Five BP analogues (i.e., BP1, BP2, BP3, BP8, and 4HB) were frequently detected in both PCPs and urine, among which BP3 was the dominant analogue, accounting for 96.3% of the total BPs in PCPs and 53.2% in urine, respectively. Sunscreens contained the highest BP concentrations (mean: 2.15×10^4 ng g^{-1}) among all PCP goods. Girls exhibited higher urinary BP

Abbreviations: BMI, body mass index; BP, benzophenone; BW, body weight; EDI, estimated dermal intake; EDU, estimated dermal uptake; LODs, limits of detection; LOQs, limits of quantification; TEDED, total estimated daily excretion dose; UV, ultraviolet.

* Corresponding author at: Guangzhou Key Laboratory of Environmental Catalysis and Pollution Control, School of Environmental Science and Engineering, Institute of Environmental Health and Pollution Control, Guangdong University of Technology, Guangzhou 510006, Guangdong, PR China.
E-mail address: yuyingxin@gdut.edu.cn (Y. Yu).

https://doi.org/10.1016/j.scitotenv.2018.06.015

Dermal intake
Dermal uptake
Personal care products
Urine

concentrations than boys, and body mass index positively influenced BP concentrations. However, no regional difference in urinary BP concentration was observed. The estimated dermal uptake of BPs from PCPs after considering the percutaneous absorption rates was much lower than the estimated dermal intake. The total daily excretion doses estimated from urinary BPs were 74.4 and 47.4 ng·kg$^{-1}_{bw}$ day^{-1} for girls and boys, respectively. The higher usage of body lotions, hand lotions, and sunscreens by girls than boys (1.49 vs. 1.03 times week^{-1}) might play an important role.

1. Introduction

The harmful effects from ultraviolet (UV) radiation have been well demonstrated. UV-filters are a group of compounds designed to protect skin and hair from UVA and UVB radiation, but they are also included in plastics, furniture, and many other goods to minimize light damage (Ramos et al., 2015). Most organic UV-filters can absorb UV radiation and attenuate the negative effects on human skin and hair (Kunisue et al., 2010). The family of benzophenone (BP)-type UV filters includes approximately 29 structurally related compounds, including benzophenone-1 (BP1) to benzophenone-12 (BP12) and other less documented analogues, such as 4-hydroxybenzophenone (4HB) and 2-hydroxybenzophenone (2-OH-BP).

These chemicals are broadly used in personal care products (PCPs), a large family of consumer products used for personal hygiene or beautification, including sunscreen products, cosmetics, beauty creams, skin lotions, lipsticks, hair dyes, shampoos, and others (Asimakopoulos et al., 2014; Balmer et al., 2005; Frederiksen et al., 2013a; Jiménez-Díaz et al., 2016; Zhang et al., 2013). These products are generally intended for external use and considered harmless or relatively safe (Han et al., 2016). In the European Union, 26 different organic chemicals, including BPs, are permitted for the usage as UV-filters. The maximum allowable contents of these additives in PCPs range from 0.1% to 10% by weight (Vela-Soria et al., 2014). In China, the use of BP3 in cosmetics has rapidly increased over the past decade (Gao et al., 2011; Zhang et al., 2013), leading to growing concerns on the potential adverse effects of BP substances on human health (Han et al., 2016).

Previous studies suggested that BP-type UV filters could interfere with endocrine systems (Schlumpf et al., 2001; Watanabe et al., 2015). Estrogen receptor-mediated reporter gene and uterotropic assays indicated that BP3 is a potential endocrine-disrupting chemical, possessing weak estrogenic activities (Schlumpf et al., 2001). In vivo and in vitro tests suggested BP3 can be biotransformed into its hydroxylated forms, some of which (e.g., BP8 and 2,3,4-trihydroxy benzophenone) may exhibit greater estrogenic activities than BP3 (Jeon et al., 2008; Kim and Choi, 2014). Other endocrine disrupting activities, such as the stimulation of the proliferation of the breast cancer cell line MCF-7, have also been reported for BPs such as *p*-hydroxybenzophenone (Nakagawa and Suzuki, 2002).

Because of their large use in PCPs and the subsequent discharges via domestic sewage or release from BPs-containing products, BPs have become ubiquitous in the environment (Balmer et al., 2005; Han et al., 2016; Kim and Choi, 2014). Although some reports have assumed that PCPs, particularly sunscreen products, were likely the main BP source to humans, other studies did frequently detect BPs in people who did not use sunscreens (Frederiksen et al., 2017). In fact, knowledge still remains limited in the types and concentrations of BPs in a wide range of PCPs. Exposure of children to BPs was subjected to much less investigations than the studies on adults or general populations. To date only a few studies have investigated BPs in PCPs or the associated exposure in Chinese children (Gao et al., 2011; Liao and Kannan, 2014a; Wang and Kannan, 2013; Zhang et al., 2013). It remains unclear whether PCPs are the main BP source to children.

Urine is an ideal non-invasive matrix for human biomonitoring of many xenobiotics with short half-lives (e.g., BPs) that are excreted mainly as free and conjugated forms (Asimakopoulos et al., 2014; Chen et al., 2018a, 2018b). The objectives of our study were to determine the estimated dermal intake (percutaneous absorption rates of chemicals are not considered) and uptake (percutaneous absorption rates are factored into the calculation) of BPs via PCP usage and the internal exposure estimated from urinary BPs. In the present study, we investigated urinary BPs in schoolchildren from Shenzhen of Guangdong province, South China. A variety of PCP products were also sampled and analyzed for BP compositions and concentrations.

2. Material and methods

2.1. Reagents and materials

Reference standards of five target BPs, including BP3 (purity >98%), 4HB (purity >98%), BP1 (purity >99%), BP2 (purity >97%), and BP8 (purity >98%), were purchased from Sigma-Aldrich, USA. Internal standards BP3-$^{13}C_6$ (purity >99%) and BP1-d_5 (purity >98.8%) were obtained from the Cambridge Isotope Laboratories, Inc (USA) and the CDN Isotopes (Quebec, Canada), respectively. The β-glucuronidase/arylsulfatase (85,000 β-glucuronidase units mL^{-1}) was obtained from Sigma-Aldrich, USA. High performance liquid chromatography grade methanol and acetonitrile were purchased from Merck (Darmstadt, Germany). The other reagents were analytical grade, and water was obtained by using a Millipore water purification system (Millipore Co., Ltd., Billerica, MA, USA). The NaAC-HAC buffer solution (pH = 5) was prepared by dissolving 30.2 g anhydrous sodium acetate into 500 mL of water containing 34 mL acetic acid (6 mol L^{-1})

2.2. Sample collection

A total of 156 PCP samples grouped into 11 categories were purchased from supermarkets and retail stores in Shenzhen in 2015. These products were mainly produced in China. The 11 categories were tooth paste (n = 28), shampoo (n = 15), face cleanser (n = 18), sunscreen (n = 12), body lotion (n = 8), bath gel (n = 21), hair gel (n = 7), hand lotion (n = 17), mask (n = 11), hand sanitizer (n = 17), and lipstick (n = 2). The PCP samples were kept at −4 °C until treatment.

A total of 280 urine samples were collected from children recruited from six elementary schools located in six administrative districts (Longhua, Bao'an, Futian, Luohu, Nanshan, and Yantian) of Shenzhen city during July–August of 2015. The recruited volunteers aged from 8 to 12 years old, including 145 boys and 135 girls. Before urine sample collection, the participants were asked to complete questionnaires under the direction of their parents or teachers. The questionnaire included demographic information such as age, sex, weight, height, and daily use habits of PCPs. The detailed demographic characteristics are summarized in Table S1. Approximately 50 mL of first-voided morning urine was sampled in a glass jar pre-cleaned with 0.1 mol L^{-1} hydrochloric acid. After collection, the urine samples were stored with dry ice and immediately sent to the analytical laboratory where they were kept at −20 °C until use.

2.3. Sample treatment protocols

The PCP samples were processed using a previously described method with some modifications (Liao and Kannan, 2014a). Briefly, approximately 0.1 g of each sample was weighted and added into 4 mL methanol. After 200 μL internal standards (BP3-$^{13}C_6$ and BP1-d_5; 1 μg mL^{-1} each) were spiked, the sample was ultrasonically extracted for 30 min. After the supernatant was collected, ultrasonic extraction was repeated twice with 3 and 2 mL methanol, respectively. Extracts were combined and reconstituted in 10 mL methanol, filtered through a 0.22 μm filter membrane, and then kept at −20 °C until instrumental analysis.

Extraction of BPs from urine was conducted through liquid-liquid extraction (Liao and Kannan, 2014a). Briefly, a 2 mL aliquot of thawed urine sample was transferred to a 10 mL glass tube with a lid. After 200 μL internal standards (BP3-$^{13}C_6$ and BP1-d_5; 1 μg mL^{-1} each) were spiked, 1.5 mL of NaAC-HAC buffer solution and 10 μL of β-glucuronidase/arylsulfatase were successively added to the sample and incubated by shaking at 37 °C for 8 h. After that, 3 mL ethyl acetate was added and the resulting solution was shaken for 1 min with hand and then centrifugated at 6000 ×*g* for 3 min. The supernatant was collected and the extraction was repeated twice. The combined extract was concentrated to near dryness under nitrogen gas, reconstituted in 1 mL methanol, filtered through a 0.22 μm filter membrane and stored at −20 °C until instrumental analysis.

2.4. Instrumental analysis

The determination of BPs was performed on a 20A HPLC system (Shimadzu, Japan), coupled with an AB Sciex Q-Trap 5500 mass spectrometer (MS/MS; Applied Biosystems, Foster City, CA, USA) with electrospray ionization (ESI) in the negative ion mode. An Atlantis C_{18} column (2.1 mm × 150 mm, 5 μm, Waters, Ireland) was used for chromatographic separation. The column temperature was set at 40 °C. The mobile phases were methanol (containing 5% acetonitrile) and water with a flow rate of 0.3 mL min^{-1}. The linear gradient program started with 15% of methanol, increased to 80% of methanol in 5 min and held for 1 min, increased to 100% of methanol in 1 min and held for 4.5 min, then dropped to 15% of methanol within 2 min and held for 4 min. The injection volume was 10 μL. The ion source was set at 550 °C, and the ion spray voltage was set at −4500 V. The multiple reaction monitoring mode was performed for mass spectroscopic analysis. The MS parameters, including precursor ion, product ion, declustering potential, entrance potential, collision energy, and collision cell exit potential, are listed in Table S2.

2.5. Quality assurance and quality control

A procedural blank was processed along with every batch of 20 samples. No target compounds were detected in procedural blanks. Internal standards were spiked to check for the signal variations during instrumental analysis and use for the quantification of the target substances. The mean recoveries of target BPs at three spiking levels (1, 10, and 50 ng mL^{-1}) ranged from 61.9% to 116% for PCP analysis and 73.7%–107% for urine analysis. The enzymatic hydrolysis extent of the conjugated BPs was investigated using 4-methylumbelliferyl glucuronide and 4-methylumbelliferyl sulfate. The deconjugation efficiencies were both higher than 85%. The regression coefficients (R^2) of calibration curves developed from standard solutions with concentrations ranging from 0.1 to 50 ng mL^{-1} were 0.991–0.999. The limits of quantification (LOQs) and limits of detection (LODs) of BP8, BP1, BP3, BP2, and 4HB, defined as ten or three times the signal-to-noise ratio (S/N), were 0.002, 0.044, 0.002, 0.197, 0.014, and 0.047 ng mL^{-1} and 0.001, 0.014, 0.001, 0.059, 0.005, and 0.014 ng mL^{-1}, respectively.

2.6. Data analysis

To determine external BP exposure from the usage of PCPs, two estimation methods were used in the present study, including the estimated dermal intake (EDI ng·kg^{-1}_{bw} day^{-1}) of a target substance, i.e., the daily dose applied to skin, and the estimated dermal uptake (EDU, ng·kg^{-1}_{bw} day^{-1}), i.e., the daily dose absorbed into skin. They were calculated according to the following equations (Zhang et al., 2017):

$$\mathrm{EDI}_{\mathrm{PCPs}} = \frac{C_{\mathrm{P}} \times M \times \mathrm{f}}{BW} \quad (1)$$

$$\mathrm{EDU}_{\mathrm{PCPs}} = \frac{C_{\mathrm{P}} \times M \times \mathrm{f} \times R}{BW} \quad (2)$$

where C_P (ng g^{-1}) is the mean concentration of an individual BP in PCPs; M (g day^{-1}) is the application amount of PCPs per day; f (dimensionless) is the retention factor of a BP on human skin; R (%) is the percutaneous absorption rate; and BW (kg) is the body weight of a subject. The parameters employed in the estimation are summarized in Table 1.

The internal BP exposure was estimated as the total estimated daily excretion dose (TEDED, ng·kg^{-1}_{bw} day^{-1}) according to the following equation.

$$\mathrm{TEDED} = \frac{C_{\mathrm{u}} \times V_{\mathrm{u}}}{BW} \quad (3)$$

where C_u (ng mL^{-1}) is the urinary concentration of an individual BP analogue; BW (kg) is the body weight; and V_u (L day^{-1}) is the daily urine excretion volume. In the present study, a volume of 1.28 L was used as the 24 h urine volume for children, given that the urine volume is nearly equal to the total water intake including direct and indirect intake which is estimated to be 1.28 L/day (Exposure Factors Handbook of Chinese Population, 2016).

Table 1
Parameters for the determination of dermal exposure to benzophenone -containing PCPs.

PCP types	Application quantities (g day^{-1})	Retention factor	References
Tooth pastes	2.75	0.05	SCCS, 2012
Shampoos	12.8	0.01	Liao and Kannan, 2014b
Face cleansers	4.06	0.001	Liao and Kannan, 2014b
Sunscreens	0.41[a]	1[b]	SCCS, 2012
Body lotions	8.69	1	Liao and Kannan, 2014b
Bath gels	14.5	0.001	Liao and Kannan, 2014b
Hair gels	13.8	0.01	Liao and Kannan, 2014b
Hand lotions	2.05	1	Liao and Kannan, 2014b
Hand sanitizers	4.8[c]	0.01	Bickers et al., 2003

[a] There were assumptions: (1) the schoolchildren used sunscreens one time per week; (2) sunscreens used only on face and hand with 2 mg per cm^2 (Klimová et al., 2015); (3) the surface area of 1/2 area head and area hands were used (SCCS, 2012), and they are 650 and 700 cm^2 for 9–12 years, respectively (Exposure Factors Handbook of Chinese Population, 2016).
[b] It is used for leave-on products as body lotions.
[c] We used the data of toilet soap from the report by Bickers et al. (2003) in the present study because we could not obtain the data for hand sanitizers from literature.

The BP concentrations were expressed as ng g^{-1} in PCPs or ng mL^{-1} in urine. The sum concentrations of the five BP analogues were denoted as Σ_5BPs. For a measurement below the LOD, it was considered non-detectable and a zero was assigned. For a measurement higher than LOD but lower than LOQ, half of the LOQ value was assigned for statistical analysis when the detection frequency of the target was higher than 50%; otherwise a quarter of the LOQ value was assigned (GB 17378.2-2007, 2007). Statistical analysis was carried out using SPSS 19 (SPSS Inc., Chicago, IL, USA). The relationships among concentrations of target substances or between concentrations and other factors were analyzed using nonparametric correlation (Spearman) unless otherwise specified. The statistical significance level was set as the *p*-value lower than 0.05.

3. Results and discussion

3.1. Concentrations of BPs in PCPs

The BP analogues were detected in 87.3% of the analyzed PCP samples, indicating their ubiquitous occurrence in PCPs (Table 2). Among the target BP analogues, BP2 and BP1 had the highest and lowest detection rate, i.e., 74.0% and 34.0%, respectively. The mean and the highest concentrations of Σ_5BPs (sum concentrations of five BP analogues) were 1.84×10^3 and 4.67×10^4 ng g^{-1}, respectively (Table 2). The BP analogues constitute the main chemicals within the group of UV filters, and are extensively used as sunscreen agents to protect skin and hair from UV damage. Therefore, it was expected that sunscreen products could contain high BP concentrations. Indeed, the highest mean concentration of Σ_5BPs (2.15×10^4 ng g^{-1}) was observed in sunscreens with concentrations up to 4.67×10^4 ng g^{-1}. These levels are much lower than the allowed maximum levels of BP3 in sunscreens, i.e., 10%, 6%, and 5% (*w*/w) in Europe, USA, and Japan, respectively (Ko et al., 2016). Data of BPs (except BP3) in PCP products remain overall limited. Compared with the study by Liao and Kannan (2014a), the concentrations of BPs in PCPs collected from Shenzhen were comparable with those collected from other regions in China but much lower than those from the United States.

The compositional profiles of BP analogues revealed a dominance of BP3 in most PCP products, particularly in sunscreen, hair gel, hand lotion and mask products (Fig. 1). Although the detection rate of BP3 was not the highest, it appeared to be the most abundant (mean: 1.77×10^3 ng g^{-1}) among the five BPs in all PCPs, accounting for 96.3% of the Σ_5BPs and approximately 2–3 orders of magnitude higher than the other analogues. Among the BP analogues, BP3 is the most commonly used UV-filter because of its excellent ability to absorb and dissipate UV light. Consequently, sunscreen products contained the highest BP3 concentrations (mean: 2.12×10^4 ng g^{-1}) compared with other PCP products. A few BP3 metabolites, such as BP1 and BP8, are also used in different cosmetic products as sunscreen agents (Ma et al., 2015). However, the concentrations of BP1 and 4HB contributed <0.01% of Σ_5BPs, reflecting their limited use compared to BP3.

3.2. Urinary BPs

Human exposure to BPs occurs through direct absorption via dermal contact, ingestion via food and dust, or air inhalation (Gao et al., 2015; Han et al., 2016; Kim and Choi, 2014; Wan et al., 2015; Wang et al., 2013). These chemicals are also rapidly excreted following uptake, mainly through urine (Ko et al., 2016). The detection frequency of BPs was 99.3% in urine from schoolchildren in Shenzhen, indicating their ubiquitous occurrence in human bodies (Table 3). The highest detection frequency was 99.3% for BP1, followed by 4HB (85.4%). This was distinctly different from the results in PCPs, where BP1 exhibited the lowest detection frequency.

Urinary BP concentrations varied greatly in the present study, from not detected to 57.1 ng mL^{-1} with an average of 1.62 ng mL^{-1} (Table 3). BP3 exhibited the highest concentration (mean: 0.86 ng mL^{-1}) among the BP analogues, although its detection frequency was not the highest. Concentrations of BP1 in urine were comparable with those of BP2, although the latter had concentrations approximately 15 times higher than the former in PCPs. Urinary concentrations of BPs from Shenzhen schoolchildren are moderate when compared with BP3 data from other regions (median: <0.22 to 62 ng mL^{-1}) as reviewed by Kim and Choi (2014).

To illustrate the occurrences and sources of BPs, the composition pattern of BPs was analyzed and shown in Fig. 2. Because of the relatively high concentrations of BP3 in PCPs and in environmental matrices

Table 2
Concentrations (ng g^{-1}) of benzophenone-type UV filters in personal care products.

		BP8	BP1	BP3	BP2	4HB	$\sum_5$BPs
Tooth pastes	Mean	2.28	<LOD	6.33	0.22	<LOD	8.84
(n = 28)	Median	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	Min.	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	Max.	39.6	<LOD	135	6.26	<LOD	135
	DF (%)	21.4	0	14.3	3.57	0	32.1
Shampoos	Mean	1.24	<LOD	0.52	36.1	<LOD	37.9
(n = 15)	Median	<LOD	<LOD	<LOD	35.6	<LOD	36.7
	Min.	<LOD	<LOD	<LOD	11.1	<LOD	11.1
	Max.	18.6	<LOD	7.78	67.3	<LOD	67.3
	DF (%)	6.67	0	6.67	100	0	100
Face cleansers	Mean	101	0.15	234	66.7	5.54	407
(n = 18)	Median	70.7	<LOD	86.3	53.7	2.34	255
	Min.	19.5	<LOD	<LOD	<LOD	<LOD	45.6
	Max.	452	1.80	1.28×10^3	199	32.4	1.84×10^3
	DF (%)	100	11.1	88.9	88.9	88.9	100
Sunscreens	Mean	305	6.24	2.12×10^4	28.2	<LOD	2.15×10^4
(n = 12)	Median	<LOD	<LOD	2.33×10^4	<LOD	<LOD	2.33×10^4
	Min.	<LOD	<LOD	1.67×10^3	<LOD	<LOD	1667
	Max.	2.66×10^3	74.9	4.40×10^4	150	<LOD	4.67×10^4
	DF (%)	41.7	8.33	100	25.0	0	100
Body lotions	Mean	28.4	<LOD	18.4	30.5	2.13	79.4
(n = 8)	Median	27.5	<LOD	8.80	29.5	2.10	73.2
	Min.	15.6	<LOD	7.81	23.8	1.86	53.1
	Max.	44.5	<LOD	46.3	39.2	2.60	111
	DF (%)	100	0	100	100	100	100
Bath gels	Mean	21.2	<LOD	96.1	25.7	<LOD	143
(n = 21)	Median	<LOD	<LOD	82.5	22.6	<LOD	104
	Min.	<LOD	<LOD	8.51	<LOD	<LOD	32.9
	Max.	182	<LOD	288	107	<LOD	464
	DF (%)	42.9	0	100	95.2	0	100
Hair gels	Mean	2.77	1.78	410	2.13	2.15	419
(n = 7)	Median	2.00	1.74	364	2.19	2.13	378
	Min.	1.93	1.70	<LOD	1.70	2.07	8.10
	Max.	7.41	2.04	754	2.46	2.23	762
	DF (%)	100	100	85.7	100	100	100
Hand lotions	Mean	2.72	1.78	102	2.31	2.21	111
(n = 17)	Median	2.13	1.81	96.3	2.25	2.27	103
	Min.	<LOD	1.18	<LOD	1.76	1.79	7.68
	Max.	8.37	2.53	196	3.19	2.55	208
	DF (%)	88.2	100	94.1	100	100	100
Masks	Mean	1.83	1.60	29.6	1.81	1.95	36.8
(n = 11)	Median	1.82	1.60	31.9	1.84	1.94	38.4
	Min.	1.52	0.89	7.31	1.54	1.63	13.6
	Max.	2.24	2.02	44.3	2.12	2.40	53.0
	DF (%)	100	100	100	100	100	100
Hand	Mean	22.6	5.17	0.82	13.1	4.03	45.7
sanitizers	Median	15.9	3.82	<LOD	12.0	2.28	37.4
(n = 11)	Min.	8.65	1.06	<LOD	3.81	1.94	17.1
	Max.	61.6	17.8	9.01	35.0	12.1	118
	DF (%)	100	100	9.09	100	100	100
Lipsticks	Mean	7.91	1.70	<LOD	2.66	1.88	14.2
(n = 2)	Median	7.91	1.70	<LOD	2.66	1.88	14.2
	Min.	7.22	1.63	<LOD	2.60	1.73	13.6
	Max.	8.60	1.77	<LOD	2.71	2.03	14.7
	DF (%)	100	100	<LOD	100	100	100
All PCPs	Mean	43.9	1.32	1.77×10^3	20.6	1.59	1.84×10^3
(n = 156)	Median	2.00	<LOD	25.0	2.87	<LOD	64.3
	Min.	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	Max.	2.66×10^3	74.9	4.40×10^4	199	32.4	4.67×10^4
	DF (%)	62.0	34.0	64.0	74.0	48.0	87.3

DF: detection frequency; LOD: limit of detection.

(Kim and Choi, 2014), BP3 remained to be the dominant analogue in urine, but its composition in urine (53.2%) was much less than that in PCPs (96.3%), likely due to biological transformation in human bodies. In the present study, BP1 accounted for 15.8% of the Σ_5BPs in urine, but only 0.07% in PCPs. A significant positive correlation was observed between the urinary concentrations of BP1 and BP3 (Pearson correlation coefficient $r = 0.921$, $p < 0.001$) and between BP2 and 4HB ($r = 0.264$, $p < 0.001$). No correlations were observed among the other analogues. Animal study revealed that BP3 is metabolized mainly to BP1 (Jeon et al., 2008), which may explain the correlation between these two substances. The BP2 and 4HB might share similar sources, but the information on their exact sources is limited. Overall, the composition profiles of BP analogues in urine suggested that demethylation is a major route of BP3 metabolism (Jeon et al., 2008).

In the present study, we observed that the detection frequency of 4HB (85.4%) and its contribution (8.3%) to Σ_5BPs in urine were significantly elevated when compared with those in PCPs (48% and 0.09%, respectively). The result was consistent with the findings by Zhang et al. (2013) who reported a high detection frequency of 4HB in urine (61%) and suggested its extensive application in China. PCPs may be a likely, but not the most important source of 4HB, given the low concentrations of 4HB in PCP products. The BP3 may be another possible source of 4HB. Although there was no direct evidence showing that BPs can be metabolized to 4HB in humans, it has been reported that benzophenone can be metabolized to 4HB following oral administration in rats (Jeon et al., 2008). Considering there was no significant correlation between urinary concentrations of BP3 and 4HB, we believed that BP3 was not a main source of the latter chemical, although the possibility of metabolic formation cannot be completely excluded. By contrast, non-PCP sources (e.g., dusts) may be an important source for 4HB because of high 4HB concentrations found in dust (Wang et al., 2013). Additionally, 4HB exhibited a slower clearance rate than other BP analogues such as BP3 in human bodies (Zhang et al., 2013), despite that 4HB is even more hydrophilic (log $K_{OW} = 3.07$) than BP3 (log $K_{OW} = 3.52$). This may also result in relatively elevated compositions of 4HB in human urine compared with that in PCPs.

3.3. Gender, body mass index (BMI), and regional differences in urinary BP concentrations

Previous studies suggested that the presence of some chemicals in human bodies appears to correlate with personal habits rather than environmental exposure (Fent et al., 2010; Ko et al., 2016). For example, Ko et al. (2016) suggested that the differences in urinary BP concentrations between Korean and other populations could be explained by differences in ethnic groups, lifestyle, genetic factors, and PCP use patterns.

Table 3
Concentrations (ng mL^{-1}) of benzophenone-type UV filters in urine of schoolchildren from Shenzhen, Guangdong province of China.

		BP8	BP1	BP3	BP2	4HB	$\sum_5$BPs
Longhua (n = 50)	Mean	0.12	0.13	0.33	0.86	0.15	1.59
	Median	0.04	0.08	0.20	0.26	0.12	0.91
	Min.	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	Max.	2.58	0.75	3.43	10.5	0.63	11.3
	DF (%)	56.0	98.0	58.0	80.0	82.0	98.0
Bao'an (n = 46)	Mean	0.08	0.13	0.40	0.43	0.18	1.23
	Median	0.04	0.08	0.20	0.32	0.14	1.07
	Min.	<LOD	<LOD	<LOD	<LOD	<LOD	0.06
	Max.	0.58	1.21	4.27	1.41	0.67	5.99
	DF (%)	78.3	100	60.9	84.8	95.7	100
Futian (n = 44)	Mean	0.05	0.17	0.21	0.26	0.15	0.84
	Median	0.04	0.08	<LOD	0.04	0.10	0.58
	Min.	<LOD	0.03	<LOD	<LOD	<LOD	0.06
	Max.	0.22	2.38	2.55	2.09	0.55	4.85
	DF (%)	63.6	100	40.9	75.0	88.6	100
Luohu (n = 49)	Mean	0.03	0.28	1.23	0.05	0.06	1.64
	Median	<LOD	0.04	<LOD	<LOD	0.05	0.17
	Min.	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	Max.	0.43	7.53	44.2	0.51	0.35	52.0
	DF (%)	20.4	98.0	34.7	42.9	61.2	98.0
Nanshan (n = 49)	Mean	0.08	0.57	2.47	0.10	0.17	3.38
	Median	0.04	0.13	0.44	0.01	0.05	0.91
	Min.	<LOD	0.01	<LOD	<LOD	<LOD	0.01
	Max.	0.36	8.88	47.8	1.32	1.42	57.1
	DF (%)	63.3	100	87.8	59.2	95.9	100
Yantian (n = 42)	Mean	0.08	0.25	0.37	0.03	0.09	0.81
	Median	0.04	0.08	0.20	<LOD	0.05	0.48
	Min.	<LOD	0.01	<LOD	<LOD	<LOD	0.01
	Max.	0.83	5.86	6.62	0.24	0.28	12.9
	DF (%)	52.4	100	69.1	42.9	90.5	100
Shenzhen (n = 280)	Mean	0.07	0.26	0.86	0.29	0.13	1.62
	Median	0.04	0.08	0.20	0.02	0.05	0.59
	Min.	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
	Max.	2.58	8.88	47.8	10.5	1.42	57.1
	DF (%)	55.4	99.3	58.6	64.3	85.4	99.3

DF: detection frequency; LOD: limit of detection.

These factors could lead to great inter-individual variation of human exposure to UV filters (Schlumpf et al., 2010).

To investigate the influence of gender, BMI, and regional differences on urinary BP concentrations, the characteristics of the study subjects were surveyed and summarized in Table S1. Urinary BP concentrations were positively associated with BMI ($p = 0.048$) which had a mean value of 17.5 in the studied population. We did not observe significant differences in urinary BPs among participants from the six districts (one-way analysis of variance, $p = 0.145$). Statistically significant difference in urinary BP concentrations ($p = 0.048$) was found between girls (1.93 ng mL^{-1}) and boys (1.33 ng mL^{-1}) (Table S3). This was likely

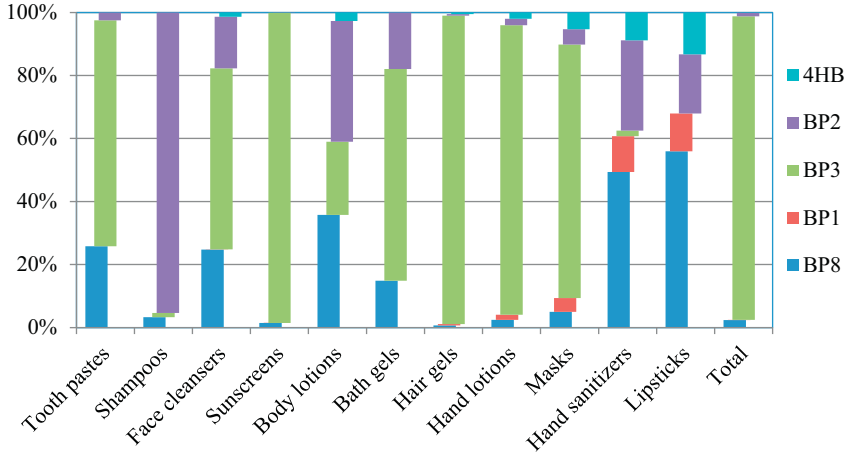


Fig. 1. Composition profiles of benzophenone-type UV filters in personal care products.

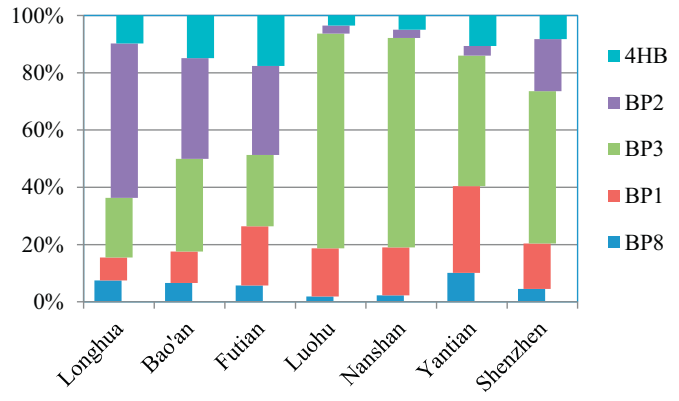


Fig. 2. Composition profiles of benzophenone-type UV filters in urine of schoolchildren from Shenzhen.

attributed to the higher usage frequency and amount of sunscreen and other cosmetic products containing UV filters used by girls than boys, especially for body and hand lotion (1.49 vs. 1.03 times week^{-1}) (Table S1).

Previous studies generally revealed greater urinary BP concentrations in females than those in males (Kim and Choi, 2014; Sun et al., 2016). Sun et al. (2016) reported greater BP3 concentrations in females than in males and attributed the results to more use of cosmetics by females, while suggesting that PCPs were a group of important BP sources to humans, especially for BP3. Kunisue et al. (2010) analyzed BPs in urine collected from a male sunscreen user and two non-sunscreen users, and found notably higher concentrations of BP3 and BP1 in urine from the sunscreen user. A similar pattern was also reported for other PCP-related chemicals. For example, a Swedish study reported a positive correlation between urinary methyl/propyl paraben concentrations and an increased PCP use (Larsson et al., 2014). They also found that the participants who used sunscreen products had significantly higher urinary ethyl paraben concentrations than those who did not use sunscreens.

3.4. Estimation of human external and internal exposure to BPs

Dermal absorption is one of the main pathways of human exposure to chemicals (e.g., synthetic musks and BPs) added to PCPs, despite that skin could provide a protective barrier (Kunisue et al., 2012; Nakata et al., 2015). However, knowledge on children exposure to BPs via dermal absorption of PCPs is very limited. The EDI of BPs and the EDU incorporating the percutaneous absorption rates were calculated and shown in Table 4. It was reported that approximately 10% of the applied dermal dose of BP3 can be absorbed and reach the systemic circulation (Jiang et al., 1999). A similar dermal absorption rate (i.e., approximately 10%) was also reported for bisphenol A, triclosan, and synthetic musks, and used to assess the human dermal uptake (von Goetz et al., 2017; Demierre et al., 2012; Zhang et al., 2017). The BP chemicals have octanol-water partition coefficients similar to those chemicals. Therefore, in the present study, the absorption rate of 10% was used for BP3. Given a lack of published percutaneous absorption rates for the four BP analogues other than BP3, an absorption rate of 10% was assigned to them to estimate the EDU through dermal contact with PCPs. In addition, mask and lipstick products were not included in the EDI estimation because the schoolchildren hardly use these products.

Table 4
Human external and internal exposure to benzophenone-type UV filters.

	External exposure (ng·kg$^{-1}_{bw}$ day^{-1})		Internal exposure (TEDED, ng·kg$^{-1}_{bw}$ day^{-1})		
	EDI	EDU	Girls	Boys	All children
BP8	11.0	1.10	3.66	1.91	2.71
BP1	0.19	0.02	11.6	7.66	9.45
BP3	262	26.3	42.3	22.9	31.7
BP2	8.27	0.83	11.1	10.7	10.9
4HB	0.68	0.07	5.72	4.29	4.93
$\sum_5$BPs	283	28.3	74.4	47.4	59.7

EDI: estimated dermal intake; EDU: estimated dermal uptake; TEDED: total estimated daily excretion dose.

The mean total EDI value for Σ_5BPs was estimated to be 283 ng·kg$^{-1}_{bw}$ day^{-1} (Table 4). BP3 was the main contributor, accounting for 92.9% of the total EDI. Sunscreen products contributed 89.9% of the total EDIs among all PCPs (Table S4). This was mainly attributed to the much higher BP concentrations in sunscreen products. These findings were consistent with the data from other studies (Kim and Choi, 2014; Ko et al., 2016). However, the amount of a chemical in PCPs does not necessarily reflect the absorbed fraction because a portion still remains on the skin and can be washed. Only those absorbed through skin can reach the systemic circulation and exert adverse effects on humans. Thus, the percutaneous absorption rate is very important to the estimation of the dermal uptake of a chemical (von Goetz et al., 2017; Yu et al., 2012; Zhang et al., 2017). Therefore, a total EDU of 28.3 ng·kg$^{-1}_{bw}$ day^{-1} was estimated for schoolchildren by considering the percutaneous absorption rate.

Urinary concentrations of certain xenobiotics can be used in the assessment of daily exposure doses (Asimakopoulos et al., 2014). In addition, urinary BP3 has been used as a biomarker of BP exposure (Wang and Kannan, 2013). In the present study, the TEDED from urinary BPs was determined from urinary BPs and summarized in Table 4. The TEDED was 59.7 ng·kg$^{-1}_{bw}$ day^{-1} for all schoolchildren. By gender, the TEDED was 74.4 ng·kg$^{-1}_{bw}$ day^{-1} for girls, 1.57 times that for boys (47.4 ng·kg$^{-1}_{bw}$ day^{-1}), which might reflect the elevated usage of body lotion, hand lotion, and sunscreen products by girls as aforementioned (1.49 and 1.03 times week^{-1} for girls and boys, respectively, in Table S1). BP3 was the main contributor, accounting for 56.8% and 48.2% of the total TEDED for girls and boys, respectively (Fig. S1). The elevated BP1 levels in urine may also be resulting from BP3 exposure. The mean exposure doses of BP1 and BP3 in girls were generally higher than those in boys, although there were no statistical differences (Table 4). We also found that the exposure doses of BP2 and 4HB were comparable between girls and boys. It is very likely that BP2 and 4HB were originated from sources other than sunscreen products or the PCPs in general (Frederiksen et al., 2013b; Han et al., 2016; Kim and Choi, 2014; Wang et al., 2013). To more understand the sources of BPs in children, many studies are needed.

4. Conclusions

The present study determined BP-type UV filters in a total of 156 commercial PCP goods covering 11 categories and 280 urine samples collected from elementary school children in Shenzhen, China. Five BP analogues were frequently detected in both PCPs and urine, among which BP3 was the dominant analogue. Sunscreens contained the highest BPs among all PCP products. Girls exhibited higher urinary BPs and the total daily excretion doses than boys because of a more use frequency of body lotions, hand lotions, and sunscreens by girls. The PCPs appear to an important source for BP exposure in children. To better understand the sources of BPs in children, many investigations should be done.

Acknowledgements

This study was funded by the Natural Science Foundation of Guangdong Province, China (No. 2015A030313869), the Shenzhen Municipal Government Research Projects (No. JCYJ20160428143348745, JCYJ20170306160146913), and the Guangzhou Key Laboratory of Environmental Exposure and Health (No. GZKLEEH201610).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2018.06.015.

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.

Balmer, M., Buser, H.R., Müller, M., Poiger, T., 2005. Occurrence of some organic UV filters in wastewater, in surface waters, and in fish from Swiss Lakes. Environ. Sci. Technol. 39, 953–962.

Bickers, D.R., Calow, P., Greim, H.A., Hanifin, J.M., Rogers, A.E., Saurat, J.H., Sipes, G., Robert, L., Smith, R.L., Tagami, H., 2003. The safety assessment of fragrance materials. Regul. Toxicol. Pharmacol. 37, 218–273.

Chen, Y., Fang, J.Z., Ren, L., Fan, R.F., Zhang, J.Q., Liu, G.H., Zhou, L., Chen, D.Y., Yu, Y.X., Lu, S.Y., 2018a. Urinary metabolites of organophosphate esters in children in South China: concentrations, profiles and estimated daily intake. Environ. Pollut. 235, 358–364.

Chen, Y., Fang, J.Z., Ren, L., Fan, R.F., Zhang, J.Q., Liu, G.H., Zhou, L., Chen, D.Y., Yu, Y.X., Lu, S.Y., 2018b. Urinary bisphenol analogues and triclosan in children from South China and implications for human exposure. Environ. Pollut. 238, 299–305.

Demierre, A.L., Peter, R., Oberli, A., Bourqui-Pittet, M., 2012. Dermal penetration of bisphenol A in human skin contributes marginally to total exposure. Toxicol. Lett. 213, 305–308.

Exposure Factors Handbook of Chinese Population (6–17 years), 2016. The Chinese Environmental Protection Agency. China Environmental Science Press.

Fent, K., Zenker, A., Rapp, M., 2010. Widespread occurrence of estrogenic UV-filters in aquatic ecosystems in Switzerland. Environ. Pollut. 158, 1817–1824.

Frederiksen, H., Aksglaede, L., Sorensen, K., Nielsen, O., Main, K.M., Skakkebaek, N.E., Juul, A., Andersson, A.M., 2013a. Bisphenol A and other phenols in urine from Danish children and adolescents analyzed by isotope diluted TurboFlow-LC-MS. Int. J. Hyg. Environ. Health 216, 710–720.

Frederiksen, H., Nielsen, J.K., Morck, T.A., Hansen, P.W., Jensen, J.F., Nielsen, O., Andersson, A.M., Knudsen, L.E., 2013b. Urinary excretion of phthalate metabolites, phenols and parabens in rural and urban Danish mother–child pairs. Int. J. Hyg. Environ. Health 216, 772–783.

Frederiksen, H., Nielsen, O., Skakkebaek, N.E., Juul, A., Andersson, A.M., 2017. UV filters analyzed by isotope diluted TurboFlow-LC-MS/MS in urine from Danish children and adolescents. Int. J. Hyg. Environ. Health 220, 244–253.

Gao, L.X., Zhang, W.Q., Yu, X.Y., 2011. Analysis of frequency on the use of sunscreen agents in cosmetic products. Mod. Prev. Med. 38, 1324–1326.

Gao, C.J., Liu, L.Y., Ma, W.L., Zhu, N.Z., Jiang, L., Li, Y.F., Kannan, K., 2015. Benzonphenone-type UV filters in urine of Chinese young adults: concentration, source and exposure. Environ. Pollut. 203, 1–6.

GB 17378.2-2007, 2007. State standard of the People's Republic of China. The specification for marine monitoring. Part 2: Data Processing and Quality Control of Analysis.

von Goetz, N., Pirow, R., Hart, A., Bradley, E., Poças, F., Arcella, D., Lillegard, I.T.L., Simoneau, C., van Engelen, J., Husoy, T., Theobald, A., Leclercq, C., 2017. Including non-dietary sources into an exposure assessment of the European food safety authority: the challenge of multi-sector chemicals such as bisphenol A. Regul. Toxicol. Pharmacol. 85, 70–78.

Han, C., Xia, B.Q., Chen, X.Z., Shen, J.C., Miao, Q., Shen, Y., 2016. Determination of four paraben-type preservatives and three benzophenone-type ultraviolet light filters in seafoods by LC-QqLIT-MS/MS. Food Chem. 194, 1199–1207.

Jeon, H.K., Sarma, S.N., Kim, Y.J., Ryu, J.C., 2008. Toxicokinetics and metabolisms of benzophenone type UV filters in rats. Toxicology 248, 89–95.

Jiang, R., Roberts, M.S., Collins, D.M., Benson, H.A., 1999. Absorption of sunscreens across human skin: an evaluation of commercial products for children and adults. Br. J. Clin. Pharmacol. 48, 635–637.

Jiménez-Díaz, I., Iribarne-Durán, L.M., Ocón, O., Salamanca, E., Fernández, M.F., Olea, N., Barranco, E., 2016. Determination of personal care products–benzophenones and parabens–in human menstrual blood. J. Chromatogr. B 1035, 57–66.

Kim, S., Choi, K., 2014. Occurrences, toxicities, and ecological risks of benzophenone-3, a common component of organic sunscreen products: a mini-review. Environ. Int. 70, 143–157.

Klimová, Z., Hojerová, J., Beránková, M., 2015. Skin absorption and human exposure estimation of three widely discussed UV filters in sunscreens e in vitro study mimicking real-life consumer habits. Food Chem. Toxicol. 83, 237–250.

Ko, A., Kang, H.S., Park, J.H., Kwon, J.E., Moon, G.I., Hwang, M.S., Hwang, I.G., 2016. The association between urinary benzophenone concentrations and personal care product use in Korean adults. Arch. Environ. Contam. Toxicol. 70, 640–646.

Kunisue, T., Wu, Q., Tanabe, S., Aldous, K.M., Kannan, K., 2010. Analysis of five benzophenone-type UV filters in human urine by liquid chromatography-tandem mass spectrometry. Anal. Methods 2, 707–713.

Kunisue, T., Chen, Z., Louis, G.M.B., Sundaram, R., Hediger, M.L., Sun, L.P., Kannan, K., 2012. Urinary concentrations of benzophenone-type UV filters in U.S. women and their association with endometriosis. Environ. Sci. Technol. 46, 4624–4632.

Larsson, K., Ljung Björklund, K., Palm, B., Wennberg, M., Kaj, L., Lindh, C.H., Jonsson, B.A.G., Berglund, M., 2014. Exposure determinants of phthalates, parabens, bisphenol A and triclosan in Swedish mothers and their children. Environ. Int. 73, 323–333.

Liao, C.Y., Kannan, K., 2014a. Widespread occurrence of benzophenone-type UV light filters in personal care products from China and the United States: an assessment of human exposure. Environ. Sci. Technol. 48, 4103−4109.

Liao, C.Y., Kannan, K., 2014b. A survey of alkylphenols, bisphenols, and triclosan in personal care products from China and the United States. Arch. Environ. Contam. Toxicol. 67, 50–59.

Ma, T., Li, Z., Niu, Q., Li, Y.Y., Zhou, W.H., 2015. Double dispersant-assisted ionic liquid dispersive liquid-liquid microextraction coupled with capillary electrophoresis for the determination of benzophenone-type ultraviolet filters in sunscreen cosmetic product. Electrophoresis 36, 2530–2537.

Nakagawa, Y., Suzuki, T., 2002. Metabolism of 2-hydroxy-4-methoxybenzophenone in isolated rat hepatocytes and xenoestrogenic effects of its metabolites on MCF-7 human breast cancer cells. Chem. Biol. Interact. 139, 115–128.

Nakata, H., Hinosaka, M., Yanagimoto, H., 2015. Macrocyclic-, polycyclic-, and nitro musks in cosmetics, household commodities and indoor dusts collected from Japan: implications for their human exposure. Ecotoxicol. Environ. Saf. 111, 248–255.

Ramos, S., Homem, V., Alves, A., Santos, L., 2015. Advances in analytical methods and occurrence of organic UV-filters in the environment-a review. Sci. Total Environ. 526, 278–311.

SCCS (Scientific Committee on Consumer Safety), 2012. SCCS/1501/12. The SCCS's notes of Guidance for the Testing of Cosmetic Substances and Their Safety Evaluation, 8th Revision. The SCCS Adopted This Opinion at its 17th Plenary Meeting of 11 December 2012.

Schlumpf, M., Cotton, B., Conscience, M., Haller, V., Steinmann, B., Lichtensteiger, W., 2001. In vitro and in vivo estrogenicity of UV screens. Environ. Health Perspect. 109, 239–244.

Schlumpf, M., Kypke, K., Wittassek, M., Angerer, J., Mascher, H., Mascher, D., VöKt, C., Birchler, M., Lichtensteiger, W., 2010. Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: correlation of UV filters with use of cosmetics. Chemosphere 81, 1171–1183.

Sun, H.Q., Du, Y., Zhang, Z.Y., Jiang, W.J., Guo, Y.M., Lu, X.W., Zhang, Y.M., Sun, L.W., 2016. Acute toxicity and ecological risk assessment of benzophenone and N,N-diethyl-3 methylbenzamide in personal care products. Int. J. Environ. Res. Public Health 13, 925.

Vela-Soria, F., Ballesteros, O., Zafra-Gómez, A., Ballesteros, L., Navalón, A., 2014. A new method for the determination of benzophenone-UV filters in human serum samples by dispersive liquid–liquid micro extraction with liquid chromatography–tandem mass spectrometry. Talanta 121, 97–104.

Wan, Y.J., Xue, J.C., Kannan, K., 2015. Occurrence of benzophenone-3 in indoor air from Albany, New York, USA, and its implications for inhalation exposure. Sci. Total Environ. 537, 304–308.

Wang, L., Kannan, K., 2013. Characteristic profiles of benzonphenone-3 and its derivatives in urine of children and adults from the United States and China. Environ. Sci. Technol. 47, 12532–12538.

Wang, L., Asimakopoulos, A.G., Moon, H.B., Nakata, H., Kannan, K., 2013. Benzotriazole, benzothiazole, and benzophenone compounds in indoor dust from the United States and east Asian countries. Environ. Sci. Technol. 47, 4752–4759.

Watanabe, Y., Kojima, H., Takeuchi, S., Uramaru, N., Sanoh, S., Sugihara, K., Kitamura, S., Ohta, S., 2015. Metabolism of UV-filter benzophenone-3 by rat and human liver microsomes and its effect on endocrine-disrupting activity. Toxicol. Appl. Pharmacol. 282, 119–128.

Yu, Y.X., Li, C.L., Zhang, X.L., Zhang, X.Y., Pang, Y.P., Zhang, S.H., Fu, J.M., 2012. Route-specific daily uptake of organochlorine pesticides in food, dust, and air by Shanghai residents, China. Environ. Int. 50, 31–37.

Zhang, T., Sun, H.W., Qin, X.L., Wu, Q., Zhang, Y.F., Ma, J., Kannan, K., 2013. Benzophenone-type UV filters in urine and blood from children, adults, and pregnant women in China: partitioning between blood and urine as well as maternal and fetal cord blood. Sci. Total Environ. 461/462, 49–55.

Zhang, X.L., Yu, Y.L., Gu, Y., Li, X.J., Zhang, X.Y., Yu, Y.X., 2017. In vitro determination of transdermal permeation of synthetic musks and estimated dermal uptake through usage of personal care products. Chemosphere 173, 417–424.