Zhu et al. J Environ Expo Assess 2023;2:7 DOI: 10.20517/jeea.2022.34

Journal of Environmental Exposure Assessment

Research Article



Occurrence and distribution of several endocrinedisrupting chemicals in a chemical park: exploring the health risks of multiple pollutants

Qingqing Zhu¹, Minrui Fang^{1,2}, Xin Wang^{1,4}, Chunyang Liao^{1,2,3,4}, Guibin Jiang^{1,2,3,4}

¹State Key Laboratory of Environmental Chemistry and Ecotoxicology, Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing 100085, China.

²Institute of Environment and Health, Hangzhou Institute for Advanced Study, UCAS, Hangzhou 310024, Zhejiang, China. ³Hubei Key Laboratory of Environmental and Health Effects of Persistent Toxic Substances, School of Environment and Health, Jianghan University, Wuhan 430056, Hubei, China.

⁴College of Resources and Environment, University of Chinese Academy of Sciences, Beijing 100049, China.

Correspondence to: Dr. Chunyang Liao, State Key Laboratory of Environmental Chemistry and Ecotoxicology, Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing 100085, China. E-mail: cyliao@rcees.ac.cn

How to cite this article: Zhu Q, Fang M, Wang X, Liao C, Jiang G. Occurrence and distribution of several endocrine-disrupting chemicals in a chemical park: exploring the health risks of multiple pollutants. *J Environ Expo Assess* 2023;2:7. https://dx.doi.org/10.20517/jeea.2022.34

Received: 15 Sep 2022 First Decision: 13 Dec 2022 Revised: 7 Feb 2023 Accepted: 20 Feb 2023 Published: 24 Feb 2023

Academic Editor: Stuart Harrad Copy Editor: Ying Han Production Editor: Ying Han

Abstract

Triclosan (TCS), triclocarban (TCC), parabens, bisphenols (BPAs), tetrabromobisphenol A and its alternatives (TBBPAs), and phthalate esters (PAEs) are typical endocrine-disrupting chemicals (EDCs), which have received increasing attention due to their potential adverse effects on ecological and human health. Human exposure to these EDCs is widespread. However, data regarding the distribution and related health risks of multiple EDCs in chemical parks are relatively scarce. In this study, 28 EDCs were determined in surface soil, sediment, and sludge samples collected from the Yangkou Chemical Industrial Park (Jiangsu, China). With the exception of TBBPAs, the distributions of Σ (TCS + TCC), Σ_6 parabens, Σ_8 BPAs, and Σ_9 PAEs in environmental media were as follows: sludge > sediment ≥ soil. No obvious differences were found regarding the concentrations of Σ_9 PAEs within the soil samples. Higher levels of Σ (TCS + TCC) (186 µg kg⁻¹ dw) and Σ_3 TBBPAs (154 µg kg⁻¹ dw) were found in the soil near a chemical manufacturer and the main sewage outlet of a wastewater treatment plant, respectively. The non-carcinogenic risks of EDCs from soil were estimated, and the risk levels were found to be a few orders of magnitude lower than the reported reference dose (*RfD*) values. The hazard indexes for all the samples were smaller than one, suggesting that the chemical industrial park posed a low risk to the workers. Additionally, the mass inventories of Σ



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, sharing, adaptation, distribution and reproduction in any medium or format, for any purpose, even commercially, as

long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.





(TCS + TCC), Σ_6 parabens, Σ_8 BPAs, Σ_3 TBBPAs, and Σ_9 PAEs were estimated to be 507, 90.6, 133, 20.7, and 1090 kg, respectively. These findings help to establish baseline concentrations for EDCs in soil, sediment, and sludge in a chemical industrial park.

Keywords: Chemical park, endocrine-disrupting chemicals, pollution status, distribution, risk assessment

INTRODUCTION

Synthesized chemicals, triclosan (TCS; antimicrobial) and (TCC; antimicrobial), *p*-hydroxybenzoic acid esters (parabens; preservatives), bisphenols (BPAs; plastics), tetrabromobisphenol A and its alternatives (TBBPAs; flame retardants), and phthalate esters (PAEs; plasticizers) are widely used in industrial and consumer products^[1-5]. There is increasing concern regarding exposure to these endocrine-disrupting chemicals (EDCs) due to their potential adverse impact on wildlife and human health.

TCS and TCC are used as antimicrobials in personal care products (PCPs), including toothpaste, soaps, shampoos, and cosmetic products^[6]. The estrogenic activities of TCS and TCC have been reported in *in vitro* and *in vivo* experiments^[7,8]. The results of previous studies have suggested that TCS has potential endocrine-disrupting effects on aquatic species (e.g., algae, invertebrates, and fish), which manifest as an influence on their thyroid hormone homeostasis and the reproductive axis^[9]. Due to its potential adverse effects, in 2010, TCS was banned from being applied in plastic food-contact materials by the European Union (EU)^[9]. In 2016, TCC and TCS were removed from the United States Food and Drug Administration (FDA) approved list of over-the-counter consumer antiseptic wash products^[10].

Products of parabens are widely used as preservatives in pharmaceuticals, cosmetics, food packagingcommodities, and industrial products^[11,12]. Parabens have been reported to elicit adverse effects on different organs and systems in the body, such as the reproductive system, breast tissue, adipose tissue, pancreas, *etc*. ^[11]. For example, the results of experimental studies suggest that *n*-butylparaben could alter the processes of steroidogenesis and spermatogenesis by changing E_2 levels in male rats^[13]. Denmark banned the use of parabens in cosmetic products for children under three years old in 2011^[14]. The European Union, the US FDA, and Health Canada have also proposed a limit of 0.4% for single compounds and 0.8% for mixtures in cosmetics^[15,16].

Bisphenol A (BPA) is used in a variety of polycarbonate plastics and epoxy resins, as well as in consumer products including food containers, dental sealants, thermal receipt papers, children's toys, and medical equipment^[17]. BPA is one of the most commonly produced chemicals worldwide. In 2020, the global production volume for BPA was approximately 6.35 million tons, and the annual growth rate from 2020 to 2025 was 5.0%^[18]. Recent monitoring studies have shown that BPA is ubiquitous in the environment, and can be found in sediment, water, soil, sludge, and indoor dust^[3]. The findings of a few studies that focused on the toxicity of BPA indicated that it has adverse effects on the reproductive systems, and can be a cause of metabolic syndrome and breast cancer^[11]. Hence, BPA was added to the list of chemicals prohibited for use in infant bottles by the governmental units of Canada and the EU^[19,20]. Due to strict regulations on the application of BPA, structural alternatives have been developed, including bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF). Similarly, BPA analogues have attracted considerable attention due to their exposure to humans exposure and their estrogen-like effects. BPF and BPS can exhibit estrogenic and antiandrogenic activities, which are similar to those of BPA^[21]. The findings of epidemiological studies have shown associations between human exposure to BPA analogues and adverse health outcomes (e.g., endocrine disrupting effects, cytotoxicity, genotoxicity, reproductive toxicity, and neurotoxicity)^[3].

TBBPA is the most commonly used brominated flame retardant (BFR), representing about 60% of the total BFR market^[22]. TBBPA alternatives, such as tetrabromobisphenol S (TBBPS) and tetrachlorobisphenol A (TCBPA), are also widely applied in various consumer products. They have been found in air, dust, soil, water, sediment, and sewage sludge^[23]. The findings of several studies have shown that the main toxic effect of TBBPA is disruption to thyroid balance^[24]. The results of one study indicated that TBBPA, TBBPS, and TCBPA could also disrupt hepatic differentiation, and TCBPA exhibited stronger potential developmental hepatic toxicity than TBBPA and TBBPS^[25]. Currently, the production and use of TBBPA, TBBPS, and TCBPA are still permitted worldwide, despite their potential toxicity.

PAEs, the esters of 1,2-benzenedicarboxylic acid, are extensively used as plasticizers in the plastic industry^[5]. They are also used in cosmetics, pharmaceuticals, and printing inks^[26]. Human exposure to PAEs has been linked to adverse health outcomes, as di-2-ethylhexyl phthalate (DEHP) causes reproductive and developmental toxicities, especially in men^[27]. This has prompted the establishment of regulations for PAEs by the United States Environmental Protection Agency (EPA)^[28].

The Yangkou Chemical Industrial Park is located in Jiangsu Province, specifically in the northeast Yangtze River Delta. The chemical park contains more than 100 industries in which various chemical products are mainly produced, such as pharmaceuticals, materials, daily necessities, and plastic products. This activity creates emissions of a large number of organic pollutants (e.g., EDCs) around the Yangkou Chemical Industrial Park, leading to ubiquitous environmental contamination and human exposure. To date, regulations regarding the discharge of chemical waste in wastewater or waste gas by the government of China mainly focus on heavy metals (e.g., lead, cadmium, mercury, arsenic, etc.), nitrobenzene, aniline, N,N-dimethylformamide, volatile organic compounds, and among others. However, relatively few regulations exist regarding endocrine-disrupting chemicals. In the national standard of "Emission standard of pollutants for synthetic resin industry" (GB 31572-2015), the discharge threshold of BPA in wastewater for epoxy resin, polycarbonate resin, and polysulfone resin industries is 0.1 mg/L. Two phthalates, di-nbutyl phthalate (DBP) and di-n-octyl phthalate (DNOP), have been identified as common organic pollutants in waste gas in the synthetic leather industry (GB 21902-2008). The findings of a previous study showed high levels of BPA (5450 μ g kg⁻¹ dw) and TBBPA (1350 μ g kg⁻¹ dw) in sediment in Shouguang, Shandong, China, where various BFR factories are located^[29]. High BPA concentrations have also been found in soil surrounding electronic waste recycling areas in Longtang, Guangdong, South China, with a maximum value of 325 µg kg⁻¹ dw^[30]. Additionally, people living or working in chemical parks may encounter higher health risks due to long-term exposure to high concentrations of chemicals. The human exposure routes to EDCs are multiple. Although the primary route of human exposure to EDCs has been shown to be the dietary pathway, non-dietary sources, such as soil, need to be more thoroughly identified. Therefore, human health concerns should be raised regarding these chemicals in chemical parks.

In this study, we focused on the Yangkou Chemical Industrial Park, and surface soil, sediment, and sludge samples from this area were analyzed to detect the levels of TCS, TCC, parabens, BPAs, TBBPAs, and PAEs. The composition profiles and distributions were discussed in order to better understand their source and fate in the environment. The non-carcinogenic risks of these chemicals were also evaluated. Mass inventories for EDCs were further estimated. This may provide new insight into the environmental behaviors and health risks related to EDCs in chemical parks.

EXPERIMENTAL SECTION

Sample collection

A total of 20 soil samples (S1-S20) were collected in the Yangkou Chemical Industrial Park. In order to compare the concentrations of pollutants outside and inside the park, three soil samples outside the chemical park were also collected. The sampling sites outside the chemical park were determined based on the distance (~5 km) and prevailing wind direction (southeast wind). The sampling sites of S1 and S8 selected are approximately 5 km away from the chemical park, and S6 is approximately 2.5 km away due to the site near the sea. These three sampling sites are residential areas with no chemical plants nearby. S6 and S8 are located in downwind and upwind directions, respectively. Surface soil samples (0-20 cm deep) were collected with a stainless steel auger. At each site, a diagonal 5-point sampling method was used to collect the surface soil samples, and then the 5 sub-samples were mixed to obtain a single sample. Each sample was wrapped in aluminum foil and transferred to the laboratory. They were freeze-dried, ground, sieved using a stainless steel sieve with a mesh size of 250 μ m, and then stored at -20 $^\circ$ C until further analysis. Each soil sample from the sampling location and surrounding area was classified as soil from a wastewater treatment plant (WWTP Soil), soil along a canal (Canal Soil), or soil from a roadside (Road Soil)^[31]. Three sediment samples (S21-S23) from the surrounding area and a sludge sample from the wastewater treatment plant (WWTP) were collected in the chemical park. The sampling of sediment sites in the chemical park was mainly according to the prevailing wind direction. S21 and S22 are located in downwind and upwind directions, respectively. Referring to the national standard of China (GB 18918-2002), we collected one sludge sample every two hours, and, finally, five sludge samples were collected. The five sludge samples were mixed to obtain a sludge sample with a weight of more than 1 kg. Further details and a map showing the sampling locations are provided in Supplementary Table 1 and Supplementary Figure 1.

Standards and chemicals

In this study, 28 target chemicals were analyzed. Six standards of parabens, including methyl paraben (MeP), ethyl paraben (EtP), propyl paraben (PrP), butyl paraben (BuP), heptyl paraben (HepP), and benzyl paraben (BzP) were purchased from AccuStandard Inc. (New Heaven, CT, USA). Seven BPA standards and three TBBPA standards, including BPA, BPS, BPF, BPAF, 4,4'-(1-phenylethylidene)bisphenol (BPAP), 4,4'-(1,4-phenylenediisopropylidene)bisphenol (BPP), 4,4'-cyclohexylidenebisphenol (BPZ), TCBPA, TBBPA, and TBBPS, were purchased from Sigma-Aldrich (St. Louis, MO, USA). Nine PAE standards, including dimethyl phthalate (DMP), diethyl phthalate (DEP), DBP, di-iso-butyl phthalate (DIBP), benzyl butyl phthalate (BzBP), DEHP, di-*n*-hexyl phthalate (DNHP), dicyclohexyl phthalate (DCHP), and DNOP, as well as TCC and 2,2-bis(4-hydroxyphenyl)butane (BPB), were purchased from TCI America (Portland, OR, USA). TCS was obtained from Alfa Aesar (Lancashire, UK). Isotope-labeled MeP-d₄, PrP-d₄, HepP-d₄, BzP-d₄, TCS-d₃, TCC-d₄, BPA-d₁₆, BPAF-d₄, DMP-d₄, DBP-d₄, BzBP-d₄, and DEHP-d₄ were purchased from CDN Isotopes (Pointe-Claire, Quebec, Canada). TBBPA-d₁₀ was obtained from Dr. Ehrenstorfer Gmbh (Augsburg, Germany). Details of the target chemicals are listed in Supplementary Table 2. Hexane and dichloromethane were purchased from JT Baker (Phillipsburg, NJ, USA). Methanol (MeOH) and acetonitrile (ACN) were purchased from Fisher Scientific (Fair Lawn, NJ, USA). Analytical grade formic acid and ammonium acetate were supplied by Sigma-Aldrich. The purity of all of the standards was > 95%. Ultrapure water was prepared using the Milli-Q ultrapure system (Millipore, Bedford, MA, USA).

Sample preparation

The extraction and purification of the target compounds in the soil, sediment, or sludge samples were performed using similar methods to those used in our previous studies^[32,33]. For TCS, TCC, parabens, BPAs, and TBBPAs, each sample (~0.1 g, dry weight) was extracted in a 15 mL glass tube. Prior to extraction, mass-labeled standards (MeP-d₄, PrP-d₄, HepP-d₄, BzP-d₄, TCS-d₃, TCC-d₄, BPA-d₁₆, BPAF-d₄, and TBBPA-d₁₀, 50 ng each) were added to each sample. A total of 5 mL of a mixed solution of MeOH and ACN (v:v,

1:1) was added to the sample. The mixture was shaken using an orbital shaker (250 r/min; IKA HS 501 digital horizontal shaker, Janke & Kunkel & Co IKA Labortechnik, Staufen, Germany) for 60 min, and centrifuged at 1811 g for 10 min. The supernatant was transferred to another clean glass tube. This extraction process was repeated two more times. The combined extracts were concentrated to approximately 1 mL under nitrogen and reconstituted to 10 mL with the solution containing ultrapure water (99.8%) and formic acid (0.2%). The extract was passed through a solid phase extraction cartridge (Oasis MCX, 60 mg/3 cc, Waters, Milford, MA, USA), which was preconditioned with 6 mL of MeOH and 6 mL of ultrapure water (which contained 0.2% formic acid). The residual water in the cartridge was removed under vacuum for 10 min. The target compounds were eluted with 6 mL of MeOH. The elute was concentrated to 1 mL and kept at -20 $^{\circ}$ prior to UPLC-MS/MS analysis.

For PAEs, each sample (~0.1 g, dry weight) was spiked with 50 ng of surrogate standard (DMP-d₄, DBP-d₄, and DEHP-d₄), and then extracted twice with a 7 mL solution [a mixture of hexane and dichloromethane (v/v, 1:1)] via oscillation extraction (300 r/min) for 60 min, followed by centrifugation at 1811 g for 10 min. The extracted solution was allowed to evaporate under nitrogen to approximately 1 mL and filtered by a 0.22 μ m polytetrafluoroethylene (PTFE) membrane filter. Finally, 20 ng of BzBP-d₄ was added to the sample prior to GC-MS/MS analysis.

Chemical analysis

For the analysis of TCC, TCS, parabens, BPAs, and TBBPAs, we used a method similar to that used in our previous study^[34]. An Exion LC AD Series UPLC system with an API 5500 triple-quadrupole MS/MS system (AB Sciex, Framingham, MA, USA) was used for the quantification of these EDCs. Target analytes were detected using multiple reaction monitoring (MRM). Electrospray ionization (ESI) was operated in the negative mode. Chromatographic separation was carried out using an analytical column (BEH C18, 100 mm × 2.1 mm, 1.7 μ m; Waters) connected to a BEH C18 guard column (5 mm × 2.1 mm, 1.7 μ m; Waters).

For PAE analysis, we used a method similar to that used in our previous study^[35]. Briefly, target PAEs were determined using a Thermo Scientific TRACE 1300 Series gas chromatograph equipped with a Thermo Scientific TSQ 8000 Evo triple quadrupole mass spectrometer (GC-MS/MS; Thermo Fisher Scientific, San Jose, CA, USA). For separation, a capillary column (TG-5MS, 30 m × 0.25 mm × 0.25 μ m; Thermo Fisher Scientific) was used. The selective ion-monitoring (SIM) mode was also adopted. Detailed protocols for the instrumental analysis and optimized parameters of the target analytes are described in Supplementary Text 1 and Supplementary Table 3.

Quality assurance and quality control (QA/QC)

Information regarding QA/QC is described and presented in detail in Supplementary Table 4. The limits of detection (LODs) and quantitation (LOQs) of the target EDCs were $0.0001-0.735 \ \mu g \ kg^{-1}$ and $0.0004-2.45 \ \mu g \ kg^{-1}$, respectively. The recoveries of internal standards for all of the samples were 102% (TCS-d₄), 64.0% (TCC-d₄), 96.9% (MeP-d₄), 106% (PrP-d₄), 118% (HepP-d₄), 96.4% (BPA-d₁₆), 110% (BPAF-d₄), 127% (TBBPA-d₁₀), 60.8% (DMP-d₄), 66.4% (DBP-d₄), and 72.5% (DEHP-d₄), respectively. The reported concentrations of the target EDCs in the samples were corrected for the recoveries of the internal standards. To verify the accuracy of the experimental data, a procedural blank, a spiked blank, and a pair of spiked matrixes were used with every 15 samples. The blank background of PAEs (DMP: 11.9 μ g kg⁻¹; DEP: 3.21 μ g kg⁻¹; DIBP: 17.5 μ g kg⁻¹; DBP: 36.1 μ g kg⁻¹; and DEHP: 27.1 μ g kg⁻¹) was subtracted from the reported concentrations of the target compounds. The matrix-spike recoveries of 23 target EDCs were within 70%-130%, except for TCS (63.9%), TCC (55.1%), HepP (65.3%), TBBPS (49.6%), and TCBPA (148%). The data

of TCS, TCC, HepP, TBBPS, and TCBPA were semi-quantitative in this study. Randomly selected samples (n = 3) were analyzed, and the relative standard deviations of the EDCs were < 15%.

Health risk assessment

The carcinogenic properties of chemicals of interest were estimated using the ADMETlab software^[36]. The results showed that among the 28 target chemicals, nine substances, including TCS, TCC, BzP, BPF, BPS, BPAP, BPAF, BzBP, and DEHP, are carcinogenic, and the rest are non-carcinogenic compounds related to human health. The non-dietary pathways for human exposure to EDCs through soil are soil ingestion, inhalation, and dermal contact^[37]. The non-carcinogenic risks of EDCs were estimated according to the method recommended by the United States EPA^[38], which is as follows:

$$ADD_{ing} = \frac{C_{soil} \times IRS \times EF \times ED \times CF}{BW \times AT}$$
(1)

$$ADD_{inh} = \frac{C_{soil} \times Ij \times EF \times ED}{BW \times AT \times PEF}$$
(2)

$$ADD_{der} = \frac{C_{soil} \times SA \times AF \times ABS \times EF \times ED \times CF}{BW \times AT}$$
(3)

where *ADD* is the average daily dose, μ g kg⁻¹ day⁻¹; *C*_{soil} is the concentrations of EDCs in soil, μ g kg⁻¹; *IRS* is the soil ingestion rate, mg day⁻¹; *EF* is the exposure frequency, days year⁻¹; *ED* is the exposure duration, year; *CF* is the unit conversion factor, 10⁻⁶ kg mg⁻¹; *BW* is the body weight, kg; *AT* is the average time, days; *Ij* is the respiratory rate, m³ day⁻¹; *PEF* is the particulate emission factor, m³ g⁻¹; *SA* is the dermal exposure area, cm²; *AF* is the soil adherence factor, mg cm⁻² day⁻¹; and *ABS* is the dermal adsorption fraction, unitless. All of the associated parameters used in these models for adults were based on a previous work^[39], as shown in Supplementary Table 5.

$$HQ = \frac{ADD_i}{RfD_i} \tag{4}$$

$$HI = \sum HQ_s \tag{5}$$

where HQ is the hazard quotient for a certain contaminant; HI is the hazard index for multiple contaminants; RfD is defined as the daily maximum permissible level of contaminants. Humans are considered to suffer from non-carcinogenic risks if the value of HI > 1 or HQ > 1.

Statistical analysis

Origin 2022b (Origin Lab, USA) and SPSS Statistics 20.0 (IBM Corp., USA) were utilized for graphing and data analysis. The LOQ divided by $\sqrt{2}$ (LOQ/ $\sqrt{2}$) was used if the data regarding the target chemicals were below the LOQ.

RESULTS AND DISCUSSION

Concentrations, profiles and distributions of EDCs

Table 1 presents a summary of the EDC data in the soil, sediment, and sludge samples. The detection rates of TCS and TCC in all the samples were 100%. The results show that TCS and TCC are widespread in the environment. The GM concentrations of Σ (TCS + TCC) in the soil, sediment, and sludge samples were 146

Table 1. Concentrations (µg k	g ⁻ dw) of several	EDCs in soil, sediment,	and sludge samples
-------------------------------	-------------------------------	-------------------------	--------------------

	Soil (<i>n</i> = 20)			Sediment (n = 3)			Sludge (<i>n</i> = 1)		
	DR ^a	Min ^b	GM ^c	Max ^d	DR	Min	GM	Max	_
TCS	100	126	144	183	100	117	136	152	2950
ТСС	100	0.878	1.56	3.02	100	1.61	12.6	58.8	124
$\Sigma(TCS + TCC)$		127	146	186		118	159	211	3070
MeP	100	10.1	18.3	27.5	100	15.5	20.4	23.9	107
EtP	95.0	< LOQ ^e	0.623	8.14	100	0.578	0.714	0.986	0.722
PrP	100	2.28	4.91	9.04	100	3.84	5.75	8.36	6.10
BuP	100	0.390	0.610	1.21	100	0.784	0.887	1.08	0.540
HepP	100	0.122	0.176	0.306	100	0.167	0.182	0.212	< LOQ
BzP	100	0.476	0.555	0.623	100	0.483	0.843	2.32	6.47
Σ_6 parabens		17.5	26.0	39.9		23.6	29.4	35.1	121
BPF	100	2.43	6.42	12.7	100	7.93	15.5	34.9	20.2
BPA	100	15.8	25.1	46.9	100	35.4	104	233	328
BPB	0	< LOQ	1.73	< LOQ	0	< LOQ	< LOQ	< LOQ	< LOQ
BPS	100	1.22	1.57	3.10	100	2.11	13.8	80.1	3.77
BPZ	0	< LOQ	0.323	< LOQ	0	< LOQ	< LOQ	< LOQ	< LOQ
BPAP	5.00	< LOQ	0.337	0.956	0	< LOQ	< LOQ	< LOQ	14.3
BPAF	100	0.351	0.689	1.05	100	0.685	0.751	0.892	2.99
BPP	20.0	< LOQ	0.274	10.8	0	< LOQ	< LOQ	< LOQ	< LOQ
Σ_8 BPAs		23.7	38.1	60.9		54.5	153	259	372
TCBPA	75.0	< LOQ	0.931	2.02	100	1.42	1.92	2.46	709
TBBPA	90.0	< LOQ	3.15	150	100	1.10	6.89	70.8	< LOQ
TBBPS	30.0	< LOQ	1.06	2.69	66.7	< LOQ	1.97	3.47	< LOQ
Σ_3 TBBPAs		< LOQ	5.94	154		5.99	15.9	74.0	710
DMP	100	3.73	7.68	19.5	100	5.29	6.24	7.11	10.3
DEP	100	1.81	2.96	4.97	100	2.32	3.02	3.69	4.40
DIBP	100	6.99	16.6	39.2	100	3.53	15.1	37.4	56.2
DBP	100	39.7	67.4	100	100	32.6	58.0	100	207
DNHP	84.2	< LOQ	0.0283	0.567	66.7	< LOQ	0.0070	0.064	< LOQ
BzBP	89.5	< LOQ	0.121	0.508	100	0.0987	0.241	0.408	0.729
DCHP	31.6	< LOQ	0.0199	0.0461	0	< LOQ	< LOQ	< LOQ	< LOQ
DEHP	100	132	214	518	100	126	792	6400	1790
DNOP	47.4	< LOQ	0.234	1.64	0	< LOQ	< LOQ	< LOQ	46.6
$\Sigma_9 PAEs$		196	314	661		170	925	6550	2120

^aDR: Detection rate (%); ^bMin: minimum value; ^cGM: geometric mean; ^dMax: maximum value; ^e< LOQ: below the limit of quantitation.

(range: 127-186) μ g kg⁻¹ dw, 159 (118-211) μ g kg⁻¹ dw, and 3070 μ g kg⁻¹ dw, respectively. It was found that the concentration of Σ (TCS + TCC) in the sludge sample was approximately 20 times higher than those in the soil and sediment samples. As shown in Figure 1, the composition profiles of TCS and TCC in soil were similar to that in sludge, in which TCS was the most dominant congener (> 96%). However, elevated contributions of TCC were found in sediment samples, in which it accounted for 16.6% of the total concentration, which is in contrast to the contributions of TCC found in sediment in the East China Sea^[40]. Higher concentrations of TCC in sediment were found at S22 and S23 (21.1 and 58.5 μ g kg⁻¹ dw, respectively) than at S21 (1.61 μ g kg⁻¹ dw). According to the sampling information [Supplementary Figure 1], sediment 21 was collected from a pond outside the park, and sediments 22 and 23 were collected from the rivers in the industrial park. It was speculated that the industrial emissions from the industries in the park may have contributed to the increase in the level of TCS in the sediment samples.



Figure 1. Composition profiles of EDCs in soil, sediment, and sludge samples.

The distributions of five categories of EDCs in soils from the chemical park were determined [Supplementary Table 6]. Significant differences in the concentrations of TCS/TCC in soils were found at different sampling sites. The concentrations of Σ (TCS + TCC) in soils in the chemical park were found to be higher at sites S9 and S19, with concentrations of 168 and 186 µg kg⁻¹ dw, respectively. The concentrations of Σ (TCS + TCC) in soils from site S19 were the highest. According to information regarding the sample collection, S19 is a manufacturer of pharmaceutical intermediates, which may pollute the soil nearby. Wastewater has been found to be an important source of TCS and TCC to the environment^[41]. TCS and TCC may leak into the soil from pipes used to transport wastewater and from facilities that store wastewater, and the released contaminants may accumulate in the soil. The concentrations of Σ (TCS + TCC) in soil may be influenced by wastewater leaks, through volatilization and deposition to the soil or waste dumping into the soil.

The concentrations of Σ_{6} parabens in soil samples ranged from 17.5 to 39.9 µg kg⁻¹ dw, with a GM concentration of 26.0 µg kg⁻¹ dw. The concentrations of Σ_{6} parabens in sediment samples were 23.6-35.1 µg kg⁻¹ dw with a GM concentration of 29.4 µg kg⁻¹ dw. The concentration of Σ_{6} parabens in the sludge sample was 121 µg kg⁻¹ dw. The distribution of parabens in the environmental medium was similar to that of TCS and TCC, which was in the following order: sludge >> soil \approx sediment. Except for S15, the contributions of individual parabens to the total concentration of Σ_{6} parabens were in the following order: MeP (69.8%-88.6%) > PrP (7.00%-31.2%). In site S15, the contributions of MeP, ethylparaben (EtP), and PrP were 44.9%, 33.2%, and 16.9%, respectively [Supplementary Figure 2]. MeP is the most extensively used paraben in household and consumer goods, such as food ingredients, pharmaceuticals, and cosmetics^[42]. EtP is widely used in chemicals, food packaging materials, feed additives, and preservatives^[12]. A soil sample from S15 was collected from the area surrounding a chemical enterprise, which may have been affected by the chemical production. Concentrations of parabens from site S1 were higher, with a value of 39.9 µg kg⁻¹ dw [Supplementary Table 6]. Site S1 is located in a busy river transportation area with frequent human activities. The elevated levels of paraben could be attributed to human activities.

The detection frequencies of BPF, BPA, BPS, and BPAF were 100% in all of the samples. BPB and BPZ were not detected in any of the samples. The predominant bisphenol detected in the samples was BPA (71.4%, 72.0%, and 88.8%), which demonstrated a GM concentration of 25.1, 104, and 328 μ g kg⁻¹ dw in the soil, sediment, and sludge samples, respectively. The concentrations of Σ_s BPAs in soils and sediments ranged from 23.7 to 60.9 μ g kg⁻¹ dw with an average of 38.1 μ g kg⁻¹ dw and from 54.5 to 259 μ g kg⁻¹ dw with an average of 153 μ g kg⁻¹ dw, respectively. The concentration of Σ_s BPAs in the sludge sample was $372 \,\mu g \, kg^{-1} \, dw$. The distribution of BPAs in the environmental medium was as follows: sludge > sediment > soil. In this study, basically, the concentrations of Σ_s BPAs in sludge were higher than those in soil by one order of magnitude. BPA and BPF were the main contributors in all of the samples. The largest contributor was BPA, with GM concentrations of 15.8, 35.4, and 328 μ g kg⁻¹ dw in the soil, sediment and sludge samples, respectively. The GM concentrations of BPF were 6.42, 15.5, and 20.2 μ g kg⁻¹ dw, respectively. The accumulative contributions of BPA and BPF ranged from 67.7% to 96.7% in all of the samples. Additionally, BPS was also one of the major dominant analogue in the sediment samples from S23, contributing 32.0%. This pattern was similar to that in sludge samples from 30 cities in China, in which BPA, BPF, and BPS were the most dominant analogues^[43]. With regard to bisphenol analogues, higher concentrations were found in site S6 [Supplementary Table 6], which is located outside the chemical park. This indicates that the contamination of BPAs in soil perhaps has not been related to the discharge of pollutants from the chemical enterprises in the chemical park. In addition, as S6 is located in the northwest of the chemical park, wind could be one of the factors influencing the deposition of BPAs in the soil, given that the frequency of southeast wind in this area is relatively high.

TBBPS and TBBPA were not detected in the sludge samples. The total concentrations (Σ_3 TBBPAs) in the soil samples ranged from < LOQ to 154 µg kg⁻¹ dw, with a GM value of 5.94 µg kg⁻¹ dw. The concentrations of Σ_3 TBBPAs in the sediment samples ranged from 5.99 to 74.0 µg kg⁻¹ dw with a GM value of 15.9 µg kg⁻¹ dw. The concentration of Σ_3 TBBPAs in the sludge sample was 710 µg kg⁻¹ dw. In the soil and sludge samples, TBBPA was the most abundant analogue, representing 88.2% and 86.1% of the Σ_3 TBBPA concentrations, respectively. An obviously high concentration of Σ_3 TBBPAs in soil was found at S5 (154 µg kg⁻¹ dw), while the lowest concentration was at S15 (1.96 µg kg⁻¹ dw) [Supplementary Table 6]. The highest concentration of Σ_3 TBBPAs in soil was 79 times higher than the lowest concentration. The S5 sample was collected near the main sewage outlet in the WWTP. The results suggest that the WWTP may have an impact on the concentration of TBBPA in the surrounding soil. Further investigations regarding the removal of TBBPAs in this WWTP are needed.

Among nine PAEs, DMP, DEP, DIBP, DBP, and DEHP were detected in 100% of the samples. This implies that PAEs were ubiquitous contaminants in the chemical park. The concentrations of Σ_9 PAEs varied by the environmental matrices, and the highest GM concentrations of Σ_9 PAEs were obtained in the sludge samples (GM: 2120 µg kg⁻¹ dw), followed by (in decreasing order) the sediment samples (925 µg kg⁻¹ dw) and soil samples (314 µg kg⁻¹ dw). The composition profiles of PAEs in the soil, sediment, and sludge samples were similar. DEHP was the most abundant analogue in soil (68.8%), followed by DBP (21.6%) and DIBP (5.86%). Consistent with the profiles in the soil samples, DEHP, DBP, and DIBP were found to be the most dominant PAE congeners in the sediment and sludge samples; their aggregate accounted for 99.6% and 97.1% of the total PAEs, respectively. Similar results regarding the composition profiles of PAEs in soil and sediment have been reported in various previous studies^[52,44]. In addition, an elevated contribution of DNOP of 2.20% was found in sludge, which is consistent with findings that confirmed the presence of DNOP in sludge in Taiwan^[45]. No obvious differences were found regarding the PAE concentrations among the soil samples. The concentrations of PAEs in soils were found higher outside (467 µg kg⁻¹ dw) than inside the chemical park (303 µg kg⁻¹ dw) [Supplementary Table 6]. A previous study has determined concentrations

of chlorinated paraffins in the same region, and the highest concentration was found in soil near the Bingcha Canal outside the chemical park^[31]. The elevated levels of PAE in the soil outside the chemical park may be affected by human activities, such as the discharge of household waste.

In this study, the samples of sludge and sediment were mainly collected in the chemical park. The measured concentrations may reflect the pollution status of several typical EDCs in the park to some extent. However, due to the relatively small sample size, the production capacity of EDCs in chemical plants cannot be accurately assumed. More sludge or sediment samples should be supplemented for clarification in further study.

Comparison of target analyte concentrations

TCS, MeP, BPA, TBBPA, and DEHP are compounds that were found to have relatively higher concentrations and detection rates in this study, and they were selected for comparison. Their concentrations (GM/mean, median, and range) found in soil, sediment and sludge samples in other regions are listed in Table 2.

The GM concentration of TCS in soils in the chemical park (144 μ g kg⁻¹ dw) was three orders of magnitude higher than the concentrations reported in Andalusia, Spain (0.289 μ g kg⁻¹ dw)^[46] and Michigan, USA (0.068 μ g kg⁻¹ dw)^[47]. Similarly, TCS concentrations in sediments in this study (range: 117-152 μ g kg⁻¹ dw) were higher than the values in sediments from Andalusia, Spain (0.049-0.170 μ g kg⁻¹ dw)^[46] and East China Sea (not detected (nd)-0.700 μ g kg⁻¹ dw)^[40]. The concentration of TCS in sludge (2950 μ g kg⁻¹ dw) was comparable to those concentrations previously reported from China at the nationwide level (1090 μ g kg⁻¹ dw)^[48] and from 22 provinces in China (1660 μ g kg⁻¹ dw)^[34], and the concentration was higher than that in sludge from Changsha, Hunan, China (199 μ g kg⁻¹ dw)^[49]. Our results show that the concentrations of TCS detected in the chemical park are at the higher end of the concentration range reported in soil, sediment and sludge samples from other regions.

The MeP concentrations (range: 10.1-27.5 μ g kg⁻¹ dw) in soil samples in this study were slightly higher than those previously reported in Spain (nd-8.04 μ g kg⁻¹ dw)^[50]. The GM concentration of MeP in sediment (20.8 μ g kg⁻¹ dw) was comparable to those previously reported from the Yellow River (13.0 μ g kg⁻¹ dw)^[51] and the Huai River (11.6 μ g kg⁻¹ dw)^[51]. The mean concentration was higher than that in sediment from the Bohai Sea and Yellow Sea (1.99 μ g kg⁻¹ dw)^[52]. The concentration of MeP in sludge (107 μ g kg⁻¹ dw) was comparable to those previously reported from China on the nationwide scale (66 μ g kg⁻¹ dw)^[48], 22 provinces in China (59.4 μ g kg⁻¹ dw)^[34], and Changsha, Hunan, China (38.6 μ g kg⁻¹ dw)^[49].

The concentrations of BPA in soils (range: 15.8-46.9 μ g kg⁻¹ dw) were comparable to those reported in Longtang, Guangdong (0.50-325 μ g kg⁻¹ dw)^[30] and Shouguang, Shandong (0.185-18.7 μ g kg⁻¹ dw)^[29]. Higher BPA concentrations have been reported to be present in sediments from Shouguang, Shandong at levels of up to 5450 μ g kg⁻¹ dw^[29]. In this study, the BPA concentrations in sediments (range: 35.4-233 μ g kg⁻¹ dw) were about 10-fold higher than the values in sediments from the East China Sea (2.20-34.0 μ g kg⁻¹ dw)^[40]. In this study, the BPA concentration in sludge (328 μ g kg⁻¹ dw) was 70, 5, and 4 times higher than those from 30 cities in China (4.69 μ g kg⁻¹ dw)^[43], Dalian, China (63.6 μ g kg⁻¹ dw)^[53], 22 provinces, China (85.5 μ g kg⁻¹ dw)^[34], respectively.

The TBBPA levels in soils in this study (nd-150 μ g kg⁻¹ dw) were obviously lower than that reported in Qingyuan, Guangdong (84-646 μ g kg⁻¹ dw)^[54]; comparable to those reported in Ningbo, China (nd-78.6 μ g kg⁻¹ dw)^[55], Longtang, Guangdong (nd-220 μ g kg⁻¹ dw)^[30], Chongqing (nd-33.8 μ g kg⁻¹ dw)^[56],

Compounds	Sample information	Location	Sample number	GM ^ª /Mean	Median	Range	References
TCS	soil	Andalusia, Spain	2	0.289/0.290	0.290	0.270- 0.310	[46]
	soil	Michigan, USA	5	0.068/0.155	0.025	nd ^b -0.52	[47]
	soil	Jiangsu, China, a chemical park	20	144/145	-	126-183	This study
	sediment	Andalusia, Spain	4	0.090/0.104	0.098	0.049- 0.170	[46]
	sediment	East China Sea	28	-/nd	nd	nd-0.700	[40]
	sediment	Jiangsu, China, a chemical park	3	136/136	-	117-152	This study
	sludge	nationwide China	100	-/1090	770	nd-4870	[48]
	sludge	22 provinces in China	46	1280/1660	1680	107-3890	[34]
	sludge	Changsha, Hunan, China	-	-/199	200	154-275	[49]
	sludge	Jiangsu, China, a chemical park	1	2950	-	-	This study
MeP	soil	Spain	12	-	-	nd-8.04	[50]
	soil	Jiangsu, China, a chemical park	20	18.3/19.0	-	10.1-27.5	This study
	sediment	the Yellow River	74	-/13.0	12.4	7.07-27.6	[51]
	sediment	the Huai River	48	-/11.6	12.0	6.97-18.8	[51]
	surface sediment	the Bohai Sea and Yellow Sea	48	1.99/-	1.97	0.962- 5.82	[52]
	sediment	Jiangsu, China, a chemical park	3	20.4/20.8	-	15.5-23.9	This study
	sludge	nationwide China	100	-/66	46	nd-630	[48]
	sludge	22 provinces in China	46	49.0/59.4	48.8	8.51-263	[34]
	sludge	Changsha, Hunan, China	-	-/38.6	34.2	21.6-66.9	[49]
	sludge	Jiangsu, China, a chemical park	1	107	-	-	Reference: [46] [47] This study [46] [40] This study [48] [34] [49] This study [50] This study [51] [52] This study [48] [34] [49] This study [48] [34] [49] This study [48] [34] [49] This study [30] [29] This study [29] This study [29] This study [29] This study [29] This study [29] [51] [30] [29] This study [29] This study [29] [53] [34] This study [55] [30] [55] [
BPA	soil	Longtang, Guangdong, South China, a typical electronic waste recycling center	70	-	-	0.50-325	[30]
	soil	Shouguang, Shandong, China	15	-/4.61	-	0.185- 18.7	[29]
	soil	Jiangsu, China, a chemical park	20	25.1/26.2	-	15.8-46.9	This study
	sediment	Shouguang, Shandong, China	15	-/521	-	1.03- 5450	[29]
	sediment	East China Sea	28	-/13.0	14.0	2.20-34.0	[40]
	sediment	Jiangsu, China, a chemical park	3	104/134	-	35.4-233	This study
	sludge	30 cities in China	52	4.69/-	9.36	nd-152	[43]
	sludge	Dalian, China	1	63.6	-	-	[53]
	sludge	22 provinces in China	46	85.5/172	76.9	16.7-1210	[34]
	sludge	Jiangsu, China, a chemical park	1	328	-	-	This study
TBBPA	soil	Ningbo, China	90	-	9.17	nd-78.6	[55]
	soil	Longtang, Guangdong, China, a typical electronic waste recycling center	70	-	-	nd-220	[30]
	soil	Qingyuan, Guangdong, China, e-waste dismantling areas	14	-/296	-	84 646	[54]
	paddy soils	Liaohe River Basin, China	17	-	-	0.03- 4.06	[58]
	soil	Chongqing, China	81	-/2.38	-	nd-33.8	[56]
	soil	Shouguang, Shandong, China	15	-/17.9	-	0.263- 83.7	[29]
	soil	nationwide South Korea	61	-/4.4	-	nd-110	[57]
	soil	Jiangsu, China, a chemical park	20	3.15/11.7	-	nd-150	This study
	sediment	Qingyuan, Guangdong, China, e-waste dismantling areas	14	-/384	-	24.7-914	[54]
	sediment	Liaohe River Basin, China	17	-/0.59	-	0.04- 3.00	[58]

Table 2. Concentrations (μ g kg⁻¹ dw) of TCS, MeP, BPA, TBBPA, and DEHP in soil, sediment and sludge in other regions.

	sediment	Shouguang, Shandong, China	15	-/261		2.08- 1350	[29]
	sediment	East China Sea	28	-/nd	nd	nd-0.270	[40]
	sediment	Jiangsu, China, a chemical park	3	6.89/25.4	-	1.10-70.8	This study
	sludge	Catalonia, Spain	17	-/104	96.7	nd-472	[59]
	sludge	30 cities in China	52	20.5/-	24.7	nd-259	[43]
	sludge	Jiangsu, China, a chemical park	1	nd	-	-	This study
DEHP	soil	Nanjing, Jiangsu, China	61	968/983	954	570-1350	[60]
	soil	Yangtze River Delta	241	-/546	349	nd-9190	[61]
	soil	Yangtze River Delta	32	-/217	117	29.1-1170	[32]
	soil	Jiangsu, China, a chemical park	20	214/227	-	132-518	This study
	sediment	the East China Sea	19	2070/4350	3220	419- 22,160	[44]
sediment sediment		Hangzhou Bay	30	-	-	0.310- 2410	[62]
		Yangtze River Delta	32	-/1000	241	5.51- 15,800	[32]
	sediment	Jiangsu, China, a chemical park	3	792/2380	-	126-6400	This study
	sludge	22 provinces in China	46	-/14.7	10.0	0.326- 67.8	[63]
	sludge	western Taiwan	17	5880/8000	6470	1330- 22600	[45]
	sludge	Jiangsu, China, a chemical park	1	1790	-	-	This study

^aGM: Geometric mean; ^bnd: not detected.

Shouguang, Shandong $(0.263-83.7 \ \mu g \ kg^{-1} \ dw)^{[29]}$, and nationwide South Korea $(nd-110 \ \mu g \ kg^{-1} \ dw)^{[57]}$; and higher than that reported in the Liaohe River Basin $(0.03-4.06 \ \mu g \ kg^{-1} \ dw)^{[58]}$. The concentrations of TBBPA in sediments in the present study (mean: 25.4, range: 1.10-70.8 $\ \mu g \ kg^{-1} \ dw)$ were approximately 10 and 15 times lower than the values reported in Qingyuan, Guangdong (384, 24.7-914 $\ \mu g \ kg^{-1} \ dw)^{[54]}$ and Shouguang, Shandong (261, 2.08-1350 $\ \mu g \ kg^{-1} \ dw)^{[29]}$, respectively, but they were higher than those reported in the Liaohe River Basin (0.59, 0.04-3.00 $\ \mu g \ kg^{-1} \ dw)^{[58]}$ and East China Sea (nd, nd-0.270 $\ \mu g \ kg^{-1} \ dw)^{[40]}$. It is noteworthy that the sediment samples from Qingyuan, Guangdong and Shouguang, Shandong were collected from e-waste dismantling areas or BFR factories. This result shows that e-waste dismantling activity and BFR production are important sources of TBBPA. TBBPA was not detected in the sludge samples in this study. The concentrations of TBBPA in sludges from Catalonia, Spain and 30 cities in China were nd-472 and nd-259 $\ \mu g \ kg^{-1} \ dw$, respectively.

The concentrations of DEHP in soils ranged from 132 to 518 μ g kg⁻¹ dw with a mean value of 227 μ g kg⁻¹ dw, which were similar to the concentration in soils from the Yangtze River Delta (mean: 217, range: 29.1-1170 μ g kg⁻¹ dw)^[32]. Higher levels of DEHP were found in soils from Nanjing, Jiangsu (983, 570-1350 μ g kg⁻¹ dw)^[60] and the Yangtze River Delta (546, nd-9190 μ g kg⁻¹ dw)^[61]. The concentrations of DEHP in sediments (2380, 126-6400 μ g kg⁻¹ dw) were lower than the values in sediments from the East China Sea (4350, 419-22,160 μ g kg⁻¹ dw)^[44], comparable to the values from the Yangtze River Delta (1000, 5.51-15,800 μ g kg⁻¹ dw)^[32], higher than the values from Hangzhou Bay (0.310-2410 μ g kg⁻¹ dw)^[62]. In this study, the DEHP concentrations in sludge (1790 μ g kg⁻¹ dw) were higher than those found in 22 provinces in China (14.7 μ g kg⁻¹ dw)^[63], but they were lower than those found in western Taiwan (8000 μ g kg⁻¹ dw)^[45].

Non-carcinogenic risk assessment of EDCs

Humans are exposed to ubiquitous EDCs every day. It is crucial to assess the potential risk of EDCs around the Yangkou Chemical Industrial Park for local residents. In this study, the non-carcinogenic risks of EDCs

were estimated based on measured concentrations of EDCs in soil. The results of the risk assessment are shown in Table 3.

In general, the value of the non-carcinogenic risk of total EDC intake from soil was as follows: soil ingestion > dermal contact > inhalation. The total daily doses of EDCs for adults through soil inhalation were 7.20E-08 μ g kg⁻¹ day⁻¹. These values were 3-4 orders of magnitude lower than those through soil ingestion (7.25E-04) and dermal contact (2.89E-04). The total daily dose ($ADD_{soil} = ADD_{ing} + ADD_{inh} + ADD_{der}$) of EDCs from soil was 1.01E-03 μ g kg⁻¹ day⁻¹ for adults.

The GM values of non-carcinogenic exposure to EDCs for adults were (from high to low): Σ_{g} PAEs (6.02E-04 µg kg⁻¹day⁻¹), Σ (TCS + TCC) (2.79E-04), Σ_{g} BPAs (7.31E-05), Σ_{g} parabens (4.99E-05), and Σ , TBBPAs (1.14E-05). Tao *et al.* reported the non-carcinogenic risk of PAEs in agricultural soil from Yinchuan, northwest China, and the ADD values of PAEs were as follows for adults: DEHP (7.85E-04), DNOP (2.80E-04), DBP (1.50E-04), DEP (5.12E-06), DMP (3.00E-06), and BzBP (1.84E-06)^[39]. Studies have shown that foodstuff is one of the primary pathways for human exposure to several EDCs^[15,42,64]. The total daily exposure of parabens from foodstuffs was estimated as 1260 μ g kg⁻¹ day⁻¹ for adults^[42]. A previous study determined concentrations of parabens in various foodstuffs from China, and the estimated daily intake values of parabens for adults was approximately 1 µg kg⁻¹ day^{-1[65]}. Given that exposure to parabens originating from the soil in the chemical park in this study was estimated at $4.99E-05 \ \mu g \ kg^{-1} \ day^{-1}$, the contribution of soil to the total estimated daily intake of parabens was minor. These estimated ADD values of DEHP, DBP and DEP are comparable to those found in our study. According to the European Food Safety Agency (EFSA) and the results of previous studies, the *RfD* values for TCS, MeP + EtP, and PrP were 1200, 10000, and 100 μ g kg⁻¹ day⁻¹, respectively^[66]. For BPA, BPS, and BPF, the *RfD* values were 4^[67], 50^[68], and 20000 µg kg⁻¹day^{-1[69]}, respectively. The *RfD* value for TBBPA was 600 µg kg⁻¹day^{-1[70]}. The *RfD* values for DMP, DEP, DBP, BzBP, DEHP, and DNOP were 10000, 800, 100, 200, 20, and 400 µg kg-1 day-1, respectively^[37]. The calculated ADD results for target compounds [Table 3] in this study were several orders of magnitude lower compared to the reported *RfD* values.

The HQ and HI results summarized in this study are shown in Figure 2. Among the 28 EDCs, DEHP had the highest HQ, ranging from 1.27E-05 to 4.97E-05. Regarding parabens, MeP was the predominant compound, followed by PrP. However, the risk of PrP (9.97E-08) was higher than that of MeP + EtP (3.84E-09), which was attributed to the relatively high toxicity of PrP. Among the BPA analogues, BPA, BPF, and BPS were the main analogues. Similarly, the risks of BPA analogues were also related to their toxicities. Their risks were as follows: BPA > BPS > BPF. For all the samples, the non-carcinogenic risks from soil were far less than the recommended allowable level (HQs< 1, HIs< 1), indicating that the chemical park posed a low threat to the exposed population.

There are several uncertainties that may have affected the results of the risk assessment^[71]. We lacked *RfD* values for several EDCs, such as TCC, BuP, BPAF, and DIBP. These chemicals were not included in the HQ calculations, which would have led to an underestimation of the health risks. Furthermore, *ADD* calculations reflected the daily intake rather than the risk of long-term exposure. Finally, interactions between multiple pollutants were not considered in this study, and simply adding up the risks of each compound may have increased the uncertainty.

Preliminary estimation of mass inventory for EDCs

The concentrations of EDCs in soil can reflect their burden in the Yangkou Chemical Industrial Park. To assess the impact of EDCs in the Yangkou Chemical Industrial Park, the mass inventories (*I*, kg) of EDCs

Table 3. Average daily dose (ADD, $\mu g \ kg^{-1} day^{-1}$) of EDCs thr	rough soil ingestion, inhalation and dermal contact for workers
---	---

	ADD _{ing} ^a	ADD b	ADD _{der} ^c	ADD_{soil} (ing + inh + der) ^d	-
TCS	1.97E-04	1.96E-08	7.87E-05	2.76E-04	-
ТСС	2.14E-06	2.12E-10	8.53E-07	2.99E-06	
$\Sigma(TCS + TCC)$	1.99E-04	1.98E-08	7.96E-05	2.79E-04	
MeP	2.50E-05	2.49E-09	9.99E-06	3.50E-05	
EtP	8.53E-07	8.47E-11	3.40E-07	1.19E-06	
PrP	6.73E-06	6.68E-10	2.68E-06	9.41E-06	
BuP	8.35E-07	8.29E-11	3.33E-07	1.17E-06	
HepP	2.41E-07	2.39E-11	9.63E-08	3.38E-07	
BzP	7.61E-07	7.55E-11	3.04E-07	1.06E-06	
Σ_6 parabens	3.57E-05	3.54E-09	1.42E-05	4.99E-05	
BPF	8.80E-06	8.73E-10	3.51E-06	1.23E-05	
BPA	3.44E-05	3.41E-09	1.37E-05	4.81E-05	
BPB	2.37E-06	2.36E-10	9.47E-07	3.32E-06	
BPS	2.15E-06	2.13E-10	8.57E-07	3.01E-06	
BPZ	4.42E-07	4.39E-11	1.76E-07	6.19E-07	
BPAP	4.62E-07	4.59E-11	1.84E-07	6.46E-07	
BPAF	9.44E-07	9.37E-11	3.77E-07	1.32E-06	
BPP	3.76E-07	3.73E-11	1.50E-07	5.26E-07	
Σ_8 BPAs	5.23E-05	5.19E-09	2.08E-05	7.31E-05	
ТСВРА	1.28E-06	1.27E-10	5.09E-07	1.78E-06	
TBBPA	4.32E-06	4.29E-10	1.72E-06	6.04E-06	
TBBPS	1.45E-06	1.44E-10	5.78E-07	2.03E-06	
$\Sigma_3 TBBPAs$	8.13E-06	8.07E-10	3.24E-06	1.14E-05	
DMP	1.05E-05	1.04E-09	4.20E-06	1.47E-05	
DEP	4.05E-06	4.02E-10	1.62E-06	5.67E-06	
DIBP	2.27E-05	2.26E-09	9.07E-06	3.18E-05	
DBP	9.24E-05	9.17E-09	3.69E-05	1.29E-04	
DNHP	3.88E-08	3.85E-12	1.55E-08	5.43E-08	
BzBP	1.66E-07	1.65E-11	6.64E-08	2.33E-07	
DCHP	2.73E-08	2.71E-12	1.09E-08	3.82E-08	
DEHP	2.93E-04	2.91E-08	1.17E-04	4.10E-04	
DNOP	3.20E-07	3.18E-11	1.28E-07	4.48E-07	
$\Sigma_9 PAEs$	4.30E-04	4.27E-08	1.72E-04	6.02E-04	

^aADDing: Average daily dose through soil ingestion; ^bADDinh: average daily dose through soil inhalation; ^cADDder: average daily dose through dermal contact; ^dADD_{soil} (*ing* + *inh* + *der*): the total daily dose through soil ingestion, inhalation and dermal contact.

were calculated, as shown in Eq. $(6)^{[72]}$:

$$I = \sum k C_i A_i d \rho \tag{6}$$

where C_i (µg kg⁻¹ dw) is the mean concentration of EDCs in soils for the sampling area; A_i is the land area (km²), d is the thickness of the sampled soil (cm); ρ is the average density of dry soil particles (g cm⁻³); and k is the unit conversion factor. The area of the Yangkou Chemical Industrial Park is 11.6 km², with a soil depth of 20 cm, and the soil density was assumed to be 1.5 g cm⁻³.



Figure 2. Hazard indexes of EDCs.

The mass inventories of $\Sigma(TCS + TCC)$, Σ_6 parabens, Σ_8 BPAs, Σ_3 TBBPAs, and Σ_9 PAEs were estimated to be 507, 90.6, 133, 20.7, and 1090 kg, respectively. In this study, the total mass inventory of Σ_{28} EDCs was 1840 kg, which was lower than that for Σ_{10} PBDEs (8870 kg) in three districts from the Pearl River Delta^[72]. The total soil area of the Yangkou Chemical Industrial Park is only a tiny fraction of the total land area in the Yangtze River Delta, which implies that the potential inventory will be much larger than the estimated inventory.

Conclusions

The occurrence, composition profile, and distribution of 28 EDCs in soil, sediment, and sludge from the Yangkou Chemical Industrial Park were investigated. The distribution showed that the higher level of $\Sigma(TCS + TCC)$ in soil has probably been caused by a chemical plant nearby. An elevated concentration of Σ_3 TBBPAs in soil was found near the main sewage outlet of the WWTP. Nevertheless, the non-carcinogenic risk assessment results regarding soil suggested that the chemical park poses a low risk to the workers. Furthermore, more data regarding EDCs at a larger scale should be supplemented for the estimation of potential inventories.

DECLARATIONS

Authors' contributions

Conceptualization, methodology, sampling, sample analysis, and writing - original draft: Zhu Q Data analysis: Fang M Scientific drawing: Wang X Writing - review & editing, supervision, and funding acquisition: Liao C Resources and supervision: Jiang G All authors contributed extensively to conducting the experiments and revising the paper.

Availability of data and materials

Extra data is published in the Supplementary Materials.

Page 16 of 19

Financial support and sponsorship

This study was financially supported by the National Key Research and Development Program of China (2020YFA0907500 and 2019YFC1604802), the National Natural Science Foundation of China (22193051 and 22225605), and the K.C. Wong Education Foundation of China (GJTD-2020-03).

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

© The Author(s) 2023.

REFERENCES

- 1. Dodge LE, Choi JW, Kelley KE, Herńandez-D Iaz S, Hauser R. Medications as a potential source of exposure to parabens in the United States population. *Environ Res* 2018;164:580-4. DOI PubMed PMC
- 2. Halden RU, Paull DH. Co-occurrence of triclocarban and triclosan in United States water resources. *Environ Sci Technol* 2005;39:1420-6. DOI PubMed
- 3. Chen D, Kannan K, Tan H, et al. Bisphenol Analogues other than BPA: Environmental occurrence, human exposure, and toxicity-a review. *Environ Sci Technol* 2016;50:5438-53. DOI PubMed
- 4. Malkoske T, Tang Y, Xu W, Yu S, Wang H. A review of the environmental distribution, fate, and control of tetrabromobisphenol A released from sources. *Sci Total Environ* 2016;569-570:1608-17. DOI PubMed
- 5. González-toledo E, Compañó R, Granados M, Dolors Prat M. Detection techniques in speciation analysis of organotin compounds by liquid chromatography. *Trend Anal Chem* 2003;22:26-33. DOI
- 6. Liao C, Kannan K. A survey of alkylphenols, bisphenols, and triclosan in personal care products from China and the United States. *Arch Environ Contam Toxicol* 2014;67:50-9. DOI PubMed
- 7. Huang H, Du G, Zhang W, et al. The *in vitro* estrogenic activities of triclosan and triclocarban. *J Appl Toxicol* 2014;34:1060-7. DOI PubMed
- 8. Jung EM, An BS, Choi KC, Jeung EB. Potential estrogenic activity of triclosan in the uterus of immature rats and rat pituitary GH3 cells. *Toxicol Lett* 2012;208:142-8. DOI PubMed
- 9. Dann AB, Hontela A. Triclosan: environmental exposure, toxicity and mechanisms of action. *J Appl Toxicol* 2011;31:285-311. DOI PubMed
- 10. Halden RU, Lindeman AE, Aiello AE, et al. The florence statement on triclosan and triclocarban. *Environ Health Perspect* 2017;125:064501. DOI PubMed PMC
- 11. Giulivo M, Lopez de Alda M, Capri E, Barceló D. Human exposure to endocrine disrupting compounds: Their role in reproductive systems, metabolic syndrome and breast cancer. A review. *Environ Res* 2016;151:251-64. DOI PubMed
- 12. Wang W, Kannan K. Fate of parabens and their metabolites in two wastewater treatment plants in New York State, United States. *Environ Sci Technol* 2016;50:1174-81. DOI PubMed
- 13. Zhang L, Dong L, Ding S, et al. Effects of n-butylparaben on steroidogenesis and spermatogenesis through changed E□ levels in male rat offspring. *Environ Toxicol Pharmacol* 2014;37:705-17. DOI PubMed
- 14. SCCS. Clarification on Opinion SCCS/1348/10 in the light of the Danish clause of safeguard banning the use of parabens in cosmetic products intended for children under three years of age. Scientific Committee on Consumer Safety (SCCS) 2011. Available from: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_069.pdf [Last accessed on 23 Feb 2023].
- 15. Błędzka D, Gromadzińska J, Wąsowicz W. Parabens. From environmental studies to human health. *Environ Int* 2014;67:27-42. DOI PubMed
- 16. Official Journal of the European Union. Regulation (EC) no 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products. 2009;L342:59-209. Available from: https://eur-lex.europa.eu/legal-content/en/ALL/?uri=CELEX:32009R1223 [Last accessed on 23 Feb 2023].
- 17. Seachrist DD, Bonk KW, Ho SM, Prins GS, Soto AM, Keri RA. A review of the carcinogenic potential of bisphenol A. *Reprod Toxicol* 2016;59:167-82. DOI PubMed PMC
- 18. Xu W. The development status and trend of BPA industry. Chem Ind 2021; 39: 28-36 (in Chinese). Available from: https://

- The European Commission. Commission directive 2011/8/EU of 28 January 2011 amending directive 2002/72/EC as regards the restriction of use of bisphenol A in plastic infant feeding bottles. Off J Eur Union 10-05-2013 2011. Available from: https://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:006:0011:0014:EN:PDF [Last accessed on 23 Feb 2023].
- Government of Canada. Order amending schedule I to the hazardous products act (Bisphenol A), Part II, 144,7. Government of Canada. 2010. Available from: https://publications.gc.ca/gazette/archives/p2/2010/2010-03-31/pdf/g2-14407.pdf [Last accessed on 23 Feb 2023].
- 21. Rochester JR, Bolden AL. Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol A substitutes. *Environ Health Perspect* 2015;123:643-50. DOI PubMed PMC
- 22. Ding K, Zhang H, Wang H, et al. Atomic-scale investigation of the interactions between tetrabromobisphenol A, tetrabromobisphenol S and bovine trypsin by spectroscopies and molecular dynamics simulations. *J Hazard Mater* 2015;299:486-94. DOI PubMed
- 23. Liu K, Li J, Yan S, Zhang W, Li Y, Han D. A review of status of tetrabromobisphenol A (TBBPA) in China. *Chemosphere* 2016;148:8-20. DOI PubMed
- 24. Lyche JL, Rosseland C, Berge G, Polder A. Human health risk associated with brominated flame-retardants (BFRs). *Environ Int* 2015;74:170-80. DOI PubMed
- 25. Yang R, Liu S, Liang X, et al. TBBPA, TBBPS, and TCBPA disrupt hESC hepatic differentiation and promote the proliferation of differentiated cells partly via up-regulation of the FGF10 signaling pathway. *J Hazard Mater* 2021;401:123341. DOI PubMed
- 26. Net S, Sempéré R, Delmont A, Paluselli A, Ouddane B. Occurrence, fate, behavior and ecotoxicological state of phthalates in different environmental matrices. *Environ Sci Technol* 2015;49:4019-35. DOI PubMed
- 27. Specht IO, Toft G, Hougaard KS, et al. Associations between serum phthalates and biomarkers of reproductive function in 589 adult men. *Environ Int* 2014;66:146-56. DOI PubMed
- USEPA. Toxic and priority pollutants under the clean water act. Available from: https://www.epa.gov/eg/toxic-and-priority-pollutantsunder-clean-water-act [Last accessed on 23 Feb 2023].
- 29. Lan J, Shen Z, Gao W, Liu A. Occurrence of bisphenol-A and its brominated derivatives in tributary and estuary of Xiaoqing River adjacent to Bohai Sea, China. *Mar Pollut Bull* 2019;149:110551. DOI PubMed
- 30. Huang DY, Zhao HQ, Liu CP, Sun CX. Characteristics, sources, and transport of tetrabromobisphenol A and bisphenol A in soils from a typical e-waste recycling area in South China. *Environ Sci Pollut Res Int* 2014;21:5818-26. DOI PubMed
- 31. Huang D, Gao L, Qiao L, et al. Concentrations of and risks posed by short-chain and medium-chain chlorinated paraffins in soil at a chemical industrial park on the southeast coast of China. *Environ Pollut* 2020;258:113704. DOI PubMed
- 32. Zhu Q, Xu L, Wang W, Liu W, Liao C, Jiang G. Occurrence, spatial distribution and ecological risk assessment of phthalate esters in water, soil and sediment from Yangtze River Delta, China. *Sci Total Environ* 2022;806:150966. DOI PubMed
- 33. Zhu Q, Wang M, Jia J, Hu Y, Wang X, Liao C, Jiang G. Occurrence, distribution, and human exposure of several endocrine-disrupting chemicals in indoor dust: a nationwide study. *Environ Sci Technol* 2020;54:11333-43. DOI PubMed
- 34. Zhu Q, Jia J, Wang Y, et al. Spatial distribution of parabens, triclocarban, triclosan, bisphenols, and tetrabromobisphenol A and its alternatives in municipal sewage sludges in China. *Sci Total Environ* 2019;679:61-9. DOI PubMed
- Zhu Q, Jia J, Zhang K, Zhang H, Liao C, Jiang G. Phthalate esters in indoor dust from several regions, China and their implications for human exposure. Sci Total Environ 2019;652:1187-94. DOI PubMed
- **36**. Dong J, Wang NN, Yao ZJ, et al. ADMETlab: a platform for systematic ADMET evaluation based on a comprehensively collected ADMET database. *J Cheminform* 2018;10:29. DOI PubMed PMC
- 37. Wang J, Chen G, Christie P, Zhang M, Luo Y, Teng Y. Occurrence and risk assessment of phthalate esters (PAEs) in vegetables and soils of suburban plastic film greenhouses. *Sci Total Environ* 2015;523:129-37. DOI PubMed
- USEPA. Supplemental guidance for developing soil screening level for superfund sites. OSWER 9355.4-24. Office of Solid Waste and Emergency Response, Washington. 2001. Available from: https://epa-sdcc.ornl.gov/pdfs/SSG_nonrad_supplemental.pdf [Last accessed on 23 Feb 2023].
- 39. Tao H, Wang Y, Liang H, Zhang X, Liu X, Li J. Pollution characteristics of phthalate acid esters in agricultural soil of Yinchuan, northwest China, and health risk assessment. *Environ Geochem Health* 2020;42:4313-26. DOI PubMed
- 40. Xie J, Zhao N, Zhang Y, Hu H, Zhao M, Jin H. Occurrence and partitioning of bisphenol analogues, triclocarban, and triclosan in seawater and sediment from East China Sea. *Chemosphere* 2022;287:132218. DOI PubMed
- 41. Lozano N, Rice CP, Ramirez M, Torrents A. Fate of Triclocarban, Triclosan and Methyltriclosan during wastewater and biosolids treatment processes. *Water Res* 2013;47:4519-27. DOI PubMed
- 42. Soni MG, Carabin IG, Burdock GA. Safety assessment of esters of p-hydroxybenzoic acid (parabens). *Food Chem Toxicol* 2005;43:985-1015. DOI PubMed
- 43. Song S, Song M, Zeng L, et al. Occurrence and profiles of bisphenol analogues in municipal sewage sludge in China. *Environ Pollut* 2014;186:14-9. DOI PubMed
- 44. Zhang ZM, Yang GP, Zhang HH, Shi XZ, Zou YW, Zhang J. Phthalic acid esters in the sea-surface microlayer, seawater and sediments of the East China Sea: spatiotemporal variation and ecological risk assessment. *Environ Pollut* 2020;259:113802. DOI PubMed

- 45. Wang MH, Chen CF, Albarico FPJB, Chen CW, Dong CD. Occurrence and distribution of phthalate esters and microplastics in wastewater treatment plants in Taiwan and their toxicological risks. *Chemosphere* 2022;307:135857. DOI PubMed
- 46. Azzouz A, Ballesteros E. Combined microwave-assisted extraction and continuous solid-phase extraction prior to gas chromatographymass spectrometry determination of pharmaceuticals, personal care products and hormones in soils, sediments and sludge. *Sci Total Environ* 2012;419:208-15. DOI PubMed
- 47. Cha J, Cupples AM. Determination of triclocarban and triclosan in biosolid and soil samples by application of pressurized liquid extraction and liquid chromatography with tandem mass spectrometry. *Geosystem Engineering* 2012;15:280-91. DOI
- 48. Chen J, Meng XZ, Bergman A, Halden RU. Nationwide reconnaissance of five parabens, triclosan, triclocarban and its transformation products in sewage sludge from China. *J Hazard Mater* 2019;365:502-10. DOI PubMed
- **49**. Mao H, Li H, Li Y, Li L, Yin L, Yang Z. Four typical personal care products in a municipal wastewater treatment plant in China: Occurrence, removal efficiency, mass loading and emission. *Ecotoxicol Environ Saf* 2020;188:109818. DOI PubMed
- 50. Pérez RA, Albero B, Miguel E, Sánchez-Brunete C. Determination of parabens and endocrine-disrupting alkylphenols in soil by gas chromatography-mass spectrometry following matrix solid-phase dispersion or in-column microwave-assisted extraction: a comparative study. *Anal Bioanal Chem* 2012;402:2347-57. DOI PubMed
- Feng J, Zhao J, Xi N, Guo W, Sun J. Parabens and their metabolite in surface water and sediment from the Yellow River and the Huai River in Henan Province: Spatial distribution, seasonal variation and risk assessment. *Ecotoxicol Environ Saf* 2019;172:480-7. DOI PubMed
- Liao C, Shi J, Wang X, Zhu Q, Kannan K. Occurrence and distribution of parabens and bisphenols in sediment from northern Chinese coastal areas. *Environ Pollut* 2019;253:759-67. DOI PubMed
- 53. Sun X, Peng J, Wang M, et al. Determination of nine bisphenols in sewage and sludge using dummy molecularly imprinted solid-phase extraction coupled with liquid chromatography tandem mass spectrometry. *J Chromatogr A* 2018;1552:10-6. DOI PubMed
- 54. Wang J, Liu L, Wang J, et al. Distribution of metals and brominated flame retardants (BFRs) in sediments, soils and plants from an informal e-waste dismantling site, South China. *Environ Sci Pollut Res Int* 2015;22:1020-33. DOI PubMed
- 55. Tang J, Feng J, Li X, Li G. Levels of flame retardants HBCD, TBBPA and TBC in surface soils from an industrialized region of East China. *Environ Sci Process Impacts* 2014;16:1015-21. DOI PubMed
- 56. Lu JF, He MJ, Yang ZH, Wei SQ. Occurrence of tetrabromobisphenol a (TBBPA) and hexabromocyclododecane (HBCD) in soil and road dust in Chongqing, western China, with emphasis on diastereoisomer profiles, particle size distribution, and human exposure. *Environ Pollut* 2018;242:219-28. DOI PubMed
- Jeon JW, Kim CS, Kim HJ, Lee CH, Hwang SM, Choi SD. Spatial distribution, source identification, and anthropogenic effects of brominated flame retardants in nationwide soil collected from South Korea. *Environ Pollut* 2021;272:116026. DOI PubMed
- Li F, Jin J, Tan D, et al. Hexabromocyclododecane and tetrabromobisphenol A in sediments and paddy soils from Liaohe River Basin, China: levels, distribution and mass inventory. *J Environ Sci (China)* 2016;48:209-17. DOI PubMed
- 59. Gorga M, Martínez E, Ginebreda A, Eljarrat E, Barceló D. Determination of PBDEs, HBB, PBEB, DBDPE, HBCD, TBBPA and related compounds in sewage sludge from Catalonia (Spain). *Sci Total Environ* 2013;444:51-9. DOI PubMed
- 60. Ma TT, Wu LH, Chen L, Zhang HB, Teng Y, Luo YM. Phthalate esters contamination in soils and vegetables of plastic film greenhouses of suburb Nanjing, China and the potential human health risk. *Environ Sci Pollut Res Int* 2015;22:12018-28. DOI PubMed
- 61. Sun J, Pan L, Zhan Y, et al. Contamination of phthalate esters, organochlorine pesticides and polybrominated diphenyl ethers in agricultural soils from the Yangtze River Delta of China. *Sci Total Environ* 2016;544:670-6. DOI PubMed
- 62. Wang LY, Gu YY, Zhang ZM, et al. Contaminant occurrence, mobility and ecological risk assessment of phthalate esters in the sediment-water system of the Hangzhou Bay. *Sci Total Environ* 2021;770:144705. DOI PubMed
- 63. Zhu Q, Jia J, Zhang K, Zhang H, Liao C. Spatial distribution and mass loading of phthalate esters in wastewater treatment plants in China: An assessment of human exposure. *Sci Total Environ* 2019;656:862-9. DOI PubMed
- 64. Geens T, Aerts D, Berthot C, et al. A review of dietary and non-dietary exposure to bisphenol-A. *Food Chem Toxicol* 2012;50:3725-40. DOI PubMed
- 65. Liao C, Chen L, Kannan K. Occurrence of parabens in foodstuffs from China and its implications for human dietary exposure. *Environ Int* 2013;57-58:68-74. DOI PubMed
- 66. Liao C, Chen L, Kannan K. Occurrence of parabens in foodstuffs from China and its implications for human dietary exposure. *Environ Int* 2013;57-58:68-74. DOI PubMed
- 67. Silano V, Bolognesi C, Castle L, et al; Panel on Food Contact Materials; Enzymes; Flavourings and Processing Aids (CEF). A statement on the developmental immunotoxicity of bisphenol A (BPA): answer to the question from the Dutch Ministry of Health, Welfare and Sport. *EFSA J* 2016;14:e04580. DOI PubMed PMC
- Fitzgerald R, Loveren HV, Civitella C, Castoldi AF, Bernasconi G; European Food Safety Authority (EFSA). Assessment of new information on Bisphenol S (BPS) submitted in response to the Decision 1 under REACH Regulation (EC) No 1907/2006. EFS3 2020:17. DOI
- Higashihara N, Shiraishi K, Miyata K, Oshima Y, Minobe Y, Yamasaki K. Subacute oral toxicity study of bisphenol F based on the draft protocol for the "Enhanced OECD Test Guideline no. 407". Arch Toxicol 2007;81:825-32. DOI PubMed
- Wikoff D, Thompson C, Perry C, et al. Development of toxicity values and exposure estimates for tetrabromobisphenol A: application in a margin of exposure assessment. *J Appl Toxicol* 2015;35:1292-308. DOI PubMed PMC

- 71. Li X, Zhong Y, He W, et al. Co-exposure and health risks of parabens, bisphenols, triclosan, phthalate metabolites and hydroxyl polycyclic aromatic hydrocarbons based on simultaneous detection in urine samples from guangzhou, south China. *Environ Pollut* 2021;272:115990. DOI PubMed
- 72. Zou MY, Ran Y, Gong J, Mai BX, Zeng EY. Polybrominated diphenyl ethers in watershed soils of the Pearl River Delta, China: occurrence, inventory, and fate. *Environ Sci Technol* 2007;41:8262-7. DOI PubMed