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Analysis of polybrominated diphenyl ethers, hexabromocyclododecanes, and legacy and emerging phosphorus flame retardants in human hair

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HIGHLIGHTS

- A method for the analysis of PBDEs, HBCDs, PFRs, and ePFRs in hair was proposed.
- BDE 209 was the major PBDE congener, and γ-HBCDD dominated the HBCDDs in human hair.
- TPHP was the most abundant PFRs/ePFRs, followed by EHDPP, TDCIPP, and TCIPP.
- This is the first report on V6, iDDPHP, BDP, and RDP levels in human hair.
- PFRs/ePFRs constitute the major compounds in hair samples of the workers.

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ABSTRACT

Human hair has been identified as a non-invasive alternative matrix for assessing the human exposure to specific organic contaminants. In the present study, a solvent-saving analytical method for the simultaneous determination of 8 polybrominated diphenyl ethers (PBDEs), 3 hexabromocyclododecanes (HBCDDs), 12 phosphorus flame retardants (PFRs), and 4 emerging PFRs (ePFRs) has been developed and validated for the first time. Hair sample preparation protocols include precleaning with Milli-Q water, digestion with HNO_3/H_2O_2 (1:1, v/v), liquid–liquid extraction with hexane:dichloromethane (4:1, v/v), and fractionation and cleanup on a Florisil cartridge. The method was validated by using two levels of spiked hair samples of 3 replicates for each spiking group. Limits of quantification (LOQs) were 0.12–22.4 ng/g for all analytes, average values of accuracies were ranging between 88 and 115%, 82–117%, 81–128%, and 81–95% for PBDEs, HBCDDs, PFRs, and ePFRs, respectively; and precision was also acceptable (RSD < 20%) for all analytes. Eventually, this method was applied to measure the levels of the targeted analytes in hair samples of e-waste dismantling workers (n = 14) from Qingyuan, South China. Median values ranged between 3.00 and 18.1 ng/g for PBDEs, 0.84–4.04 ng/g for HBCDDs, 2.13–131 ng/g PFRs, and 1.49–29.4 ng/g for ePFRs, respectively. PFRs/ePFRs constitute the major compounds in human hair samples, implying the wide use of PFRs/ePFRs as replacements of PBDEs and HBCDDs, as well the potential high human exposure risks of PFRs/ePFRs. Overall, this work will allow to a comprehensive assessment of human exposure to multiple groups of FRs using hair as a non-invasive bioindicator.

1. Introduction

Polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecanes (HBCDDs) are two major classes of legacy brominated flame retardants (BFRs) that have been widely added in products such as electronic appliances, textiles, furniture, and

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plastics to improve the fire resistance (Covaci et al., 2011; de Wit, 2002). Due to the increasing evidence of their toxicity, persistence, and other ecological and health concerns, commercial PBDE and HBCDD mixtures have been listed as persistent organic pollutants (POPs) by the Stockholm Convention and been gradually banned for production and use globally (UNEP, 2017). Nevertheless, PBDEs and HBCDDs were constantly detected in the environment because of their historically widespread usages (Tay et al., 2019). As a result, humans are continuously exposed to PBDEs and HBCDDs through pathways such as indoor dust ingestion, air inhalation, and contaminated food consumption (Tao et al., 2016; Tay et al., 2018, 2019).

In addition, the restrictions and phase-out of PBDEs and HBCDDs have resulted in an increase in the production and use of phosphorus flame retardants (PFRs) as alternatives (van der Veen and de Boer, 2012; Wei et al., 2015). Like BFRs, PFRs have been frequently detected in indoor dust and air (Araki et al., 2014; Yang et al., 2014), sediment (Cristale and Lacorte, 2013), water (Rodil et al., 2012), biota samples (Chen et al., 2012; Liu et al., 2018), and human milk and blood (Kim et al., 2014; Li et al., 2017). The ubiquitous occurrence of PFRs is currently of environmental and human health concerns because of their potential toxic effects (van der Veen and de Boer, 2012; Wei et al., 2015). Moreover, several emerging PFRs (ePFRs) were recently identified in commercial applications, including 2,2-bis(chloromethyl)-propane-1,3-diyltetrakis(2-chloroethyl) bisphosphate (V6), isodecyl diphenyl phosphate (iDDPHP), bisphenol A bis(diphenyl phosphate) (BDP), resorcinol bis (diphenyl phosphate) (RDP) (Christia et al., 2019; Tan et al., 2018). A few studies have reported the occurrence of ePFRs in house dust and car dust(Brandsma et al., 2013; Christia et al., 2019; Tan et al., 2018), however, investigations on the fate and human exposure risks of ePFRs remain overall limited so far.

Human biomonitoring (HBM) is a reliable method to directly assess the human exposure to BFRs and PFRs by measuring the concentrations of BFRs/PFRs or their metabolites in human samples (Poon et al., 2014). Although blood/serum and other tissues are ideal matrices for HBM purpose, they are often rejected by participants due to the invasive nature of sample collection. This problem is especially significant for the most sensitive populations, such as the elderly, children, and pregnant women (Liu et al., 2015). With the advantages of being easy and inexpensive to collect, convenient to transport and store, and short-term and long-term exposure tracings, human hair has been identified as a suitable non-invasive alternative matrix for HBM studies (Qiao et al., 2019). Several recent studies have reported the application of human hair as alternative non-invasive indicator to assess human exposure to flame retardants, including PBDEs (Liu et al., 2015; Zheng et al., 2014), HBCDDs (Malarvannan et al., 2013), and PFRs (Liu et al., 2015; Qiao et al., 2019). However, the methods described in literature focused on determination of both PBDEs and HBCDDs (Malarvannan et al., 2013), or both PBDEs and PFRs (Liu et al., 2015; Qiao et al., 2019), whilst no method is currently available for determination of all three groups of chemicals, probably due to their specific physical-chemical properties and thus not easy to cleanup and fractionation in a single method. In a recent study by Liu et al. (2015), a method has been developed to simultaneously measure PBDEs, PFRs, and alternative flame retardants (AFRs) using gas chromatography mass spectrometry (GC-MS); however, large amounts of solvent volume were needed for the method they used, and HBCDDs and ePFRs were not included in that study. Moreover, to our knowledge, no study has reported the ePFR levels in human hair to date. Therefore, it is essential to establish an appropriate analytical method that will permit a rapid, simultaneous, solvent-saving, and selective determination of multiple groups of chemicals, such as BFRs (including PBDEs and HBCDDs), PFRs and ePFRs.

Consequently, the main objective of this study was to develop an analytical method based on GC-MS and liquid chromatography tandem mass spectrometry (LC-MS/MS), for the analysis of PBDEs, HBCDDs, and PFRs/ePFRs in low sample amounts of human hair and with low volume of solvent consumption. The proposed method was validated by using spiked replicate hair samples. Eventually, levels of the targeted analytes were measured in human hair samples collected from workers at an e-waste site in Qingyuan city, South China, to test the applicability of the developed method.

2. Materials and methods

2.1. Chemicals and materials

Standards of three HBCDD diastereoisomers (α-, β-, γ-HBCDDs), eight PBDEs (BDEs 28, 47, 99, 100, 153, 154, 183, and 209), twelve PFRs (triphenyl phosphate (TPHP), triisopropyl phosphate (TiPP), tripropyl phosphate (TPP), triethyl phosphate (TEP), tri-n-butyl phosphate (TNBP), tris(2-butoxyethyl) phosphate (TBOEP), tris(2-ethylhexyl) phosphate (TEHP), 2-ethylhexyl diphenyl phosphate (EHDPP), tris(chloroethyl) phosphate (TCEP), tris(2-chloroisopropyl) phosphate (TCIPP), tris(1,3-dichloroisopropyl) phosphate (TDCIPP), tricresyl phosphate (TMPP)), and four ePFRs (V6, iDDPHP, BDP and RDP) were purchased from AccuStandard Inc. (New Haven, CT, USA). D_{15}-TPHP, d_{15}-TDCIPP, d_{12}-TCEP, and d_{18}-TCIPP served as internal standards (ISs) for quantification of PFRs/ePFRs and were acquired from Cambridge Isotope Laboratories Inc. (Andover, MA, USA). A labelled mixture (consisting of α-, β-, and γ-$^{13}C_{12}$-HBCDD) served as ISs for HBCDD analysis, BDEs 118 and 128 were used as ISs for PBDEs, and BDEs 77 and 181 were used as recovery standards (RS) for PBDEs, were purchased from AccuStandard, Inc.. Labelled tetrabromobisphenol A ($^{13}C_{12}$-TBBPA) and d_{27}-TNBP were purchased from Cambridge Isotope Laboratories, Inc., and were used as RSs for HBCDDs and PFRs/ePFRs, respectively. Detailed information of the analytes is provided in Table S1 in the Supplementary Information (SI).

All solvents were chromatography grade: dichloromethane (DCM), 1-chlorobutane, n-Hexane (n-Hex), ethyl acetate (EtAc), and methanol were purchased from Merck KGaA (Darmstadt, Germany). Florisil® ENVI cartridges (500 mg, 3 mL) were acquired from Supelco (Bellefonte, PA, USA).

2.2. Sample collection

Fourteen e-waste dismantling workers (ages 20–50) were selected from an e-waste recycling site in Longtang Town of Qingyuan city from Guangdong province, South China in August 2015. The workers should have inhabited in the e-waste area for more than five years, and have not had hair care, such as hair coloring or perming, within two years. The details of the sample region have been described in our previous studies (Qiao et al., 2019; Zheng et al., 2017a). Written informed consent was obtained from all the participants, and they were clearly informed about the scope and nature of the study. Stainless steel scissors pre-cleaned with isopropyl alcohol were used to cut the hair near scalp. Hair sample was wrapped in aluminum foil, sealed in a polythene zipper bag, and kept at −20 °C in the laboratory prior to chemical analysis.

2.3. Sample preparation

The newly developed analytical procedure was based on a combination of previous reported protocols for analysis of PBDEs and PFRs (Liu et al., 2015; Qiao et al., 2019), and described as below (Fig. 1). Hair sample was rinsed twice with Milli-Q water at 40 °C in a shaking incubator (1 h for each washing process), to remove

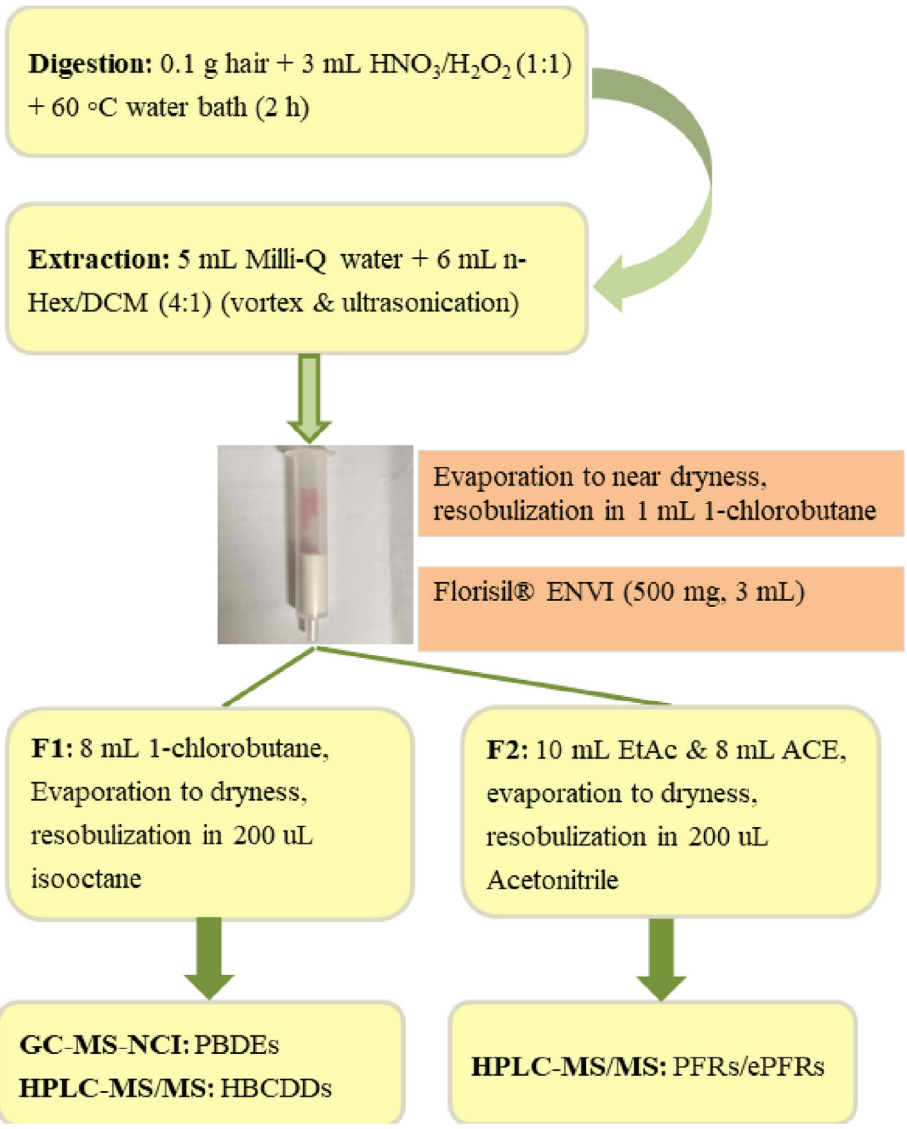

Fig. 1. Workflow chart for the sample preparation and analysis procedure.

external contamination. This method has been proven to be efficient removal of external contamination without destroying the hair cuticle or extracting analytes from the hair matrix (Zheng et al., 2013). Then, hair sample was freeze-dried, cut into small pieces (2–3 mm), and homogenized. Approximately 100 mg of hair was weighed into a 50-mL Teflon tube, 3 mL of HNO_3 (65%)/H_2O_2 (1:1, v/v) was added to digest hair, and known amounts of ISs (BDE 118 and BDE 128 each at 20 ng; $^{13}C_{12}$-HBCDDs at 5 ng; d_{15}-TPHP, d_{15}-TDCIPP, d_{12}-TCEP, and d_{18}-TCIPP each at 10 ng) was spiked. The digestion process was carried out in a 60 °C water bath for 2 h. After the addition of 5 mL of Milli-Q water, the digested mixture was liquid-liquid extracted twice with 6 mL n-Hex: DCM solution (4:1, v/v). The extracts were centrifuged at 4000 rpm for 10 min, and the supernatants were combined into a pre-cleaned glass tube, evaporated to near dryness, reconstituted in 1 mL of 1-chlorobutane, and vortexed for 1 min. Afterwards, the extract was transferred onto a Florisil® ENVI cartridge (500 mg, 3 mL) conditioned consecutively with 6 mL Actone, 6 mL EtAc, and 6 mL 1-chlorobutane. The first fraction (F1, containing PBDEs and HBCDDs) was achieved by eluting with 8 mL 1-chlorobutane and the second fraction (F2, containing PFRs/ePFRs) with 10 mL EtAc and 8 mL Acetone. Both F1 and F2 were concentrated to near dryness under a gentle nitrogen stream. F1 was reconstituted in 180 μL of isooctane, spiked with 20 μL of RSs (BDEs 77 and 181), and 100 μL concentrated sulfuric acid was added to remove the impurity (e.g. lipids and pigments). The extracts were stored at −20 °C for 24 h, and then were centrifuged at 10000 rpm for 5 min to remove the H_2SO_4 residues. The supernatant was collected and transferred to an amber injection vial. After analyzing PBDEs by GC-MS, F1 was concentrated to near dryness again, redissolved in 180 μL of ACN, and spiked with 20 μL RS ($^{13}C_{12}$-TBBPA) prior to be analyzed for HBCDDs using LC-MS/MS. F2 was reconstituted in 180 μL ACN and spiked with 20 μL RS (d_{27}-TNBP), and transferred to an amber injection vial for the analysis of PFRs/ePFRs using LC-MS/MS.

2.4. Instrumental analysis

Chromatographic analysis of the target analytes was performed following the methodology reported in previous studies (Christia et al., 2019; Qiao et al., 2019; Zheng et al., 2017b).

PBDEs were measured by an Agilent 7890B GC couple to an Agilent 5977A MS (Santa Clara, CA, USA) in electron capture

negative ionization (ECNI) source and the selected ion monitoring (SIM) mode. A DB-5HT capillary column (15 m × 0.25 mm i.d., 0.10 μm film thickness, J&W Scientific; CA, USA) was used for separation. The injection volume was 1 μL at the splitless mode. Helium was used as the carrier gas at a flow rate of 1.5 mL/min, and methane was used as chemical ionization moderating gas. PBDE congeners were monitored with ions *m/z* 79 and 81, with exception for BDE 209, for which ions *m/z* 487 and 489 were used. The GC-oven temperature was set to rise from 110 °C to 200 °C at 20 °C/min (holding for 4.5 min), then to rise to 310 °C at 10 °C/min (holding for 15 min).

An Agilent 1260 Infinity liquid chromatography (LC) (Santa Clara, CA, USA) system couple to AB SCIEX API 4000 tandem mass spectrometry (MS/MS) (Applied Biosystems, Foster City, CA, USA) was used for the analysis of HBCDDs and PFRs/ePFRs. A CORTECS-C18 column (4.6 × 100 mm, 2.7 μm; Waters, Milford, MA, USA) was used for the separation of HBCDD diastereoisomers. The mobile phases were (A) MeOH and (B) ultrapure water. The gradient of separation was 90% A in 0–4.5 min, 90–100% A in 4.5–5.5 min, 100% A in 5.5–6.5 min, 100–90% A in 6.5–10 min. Total duration of each run was 10 min, the injection volume was 10 μL, and the flow rate 0.70 mL/min. Source parameters were set as: column temperature at 40 °C, gas temperature at 550 °C, gas flow at 10 mL/min, entrance potential at −10 V, collision cell exit potential −15 V, and ionspary voltage at −4500 V, ion source mode at negative electrospray ionization (ESI-).

A Kinetex EVO-C18 column (100 × 2.1 mm, 5 μm; Phenomenex, Torrance, CA, USA) was used for the separation of PFRs/ePFRs. The mobile phases were (A) MeOH and (B) ultrapure water 5 mM ammonium acetate. The gradient of separation was 35% A in 0–0.1 min, 35–95% A in 0.1–9 min, 95–100% A in 9–13 min, 100% A in 14 min, 100–35% A in 14–15 min, and 35% A in 15–20 min. Total duration of each run was 20 min. The injection volume was 5 μL, and the flow rate 0.25 mL/min. Source parameters were set as: column temperature at 40 °C, gas temperature at 550 °C, gas flow at 10 mL/min, entrance potential at 10 V, collision cell exit potential 5 V, and ionspary voltage at 4000 V, ion source mode at positive electrospray ionization (ESI+). Detailed chromatographic information for HBCDDs and PFRs/ePFRs is reported in Table S2.

2.5. Quality control

Quality control (QC) for analysis of the fourteen hair samples was performed by the regular analysis of three procedural blank samples in the same batch to track the potential background contamination. The values of the chemicals in the blank samples were subtracted from the hair sample values. Instrumental QC was performed by regular injection of solvent blanks and standard solutions (relative standard deviation (RSD) less than 15%). Recoveries of ISs for PBDEs, HBCDDs, and PFRs/ePFRs in hair samples were in a range of 89 ± 11% to 118 ± 15%, further revealed the reliability of our newly developed method.

3. Results and discussion

3.1. Method development

3.1.1. Instrumental method optimization

The instrumental methods for the targeted analytes were modified according the methodology reported in previous studies (Christia et al., 2019; Qiao et al., 2019; Zheng et al., 2017b). Individual standards of analytes were used to set optimal values of *m/z* ions for analysis of PBDEs in GC-MS with SIM mode, and of multiple reaction monitoring (MRM) transitions with the corresponding fragmentor voltage and collision energy for analysis of HBCDDs and PFRs/ePFRs in LC-MS/MS with ESI(−) and ESI(+) mode, respectively (Table S1).

3.1.2. Hair sample digestion

For extraction of POPs in hair, the most frequently used method is to incubate hair samples with 3–4 M HCl or 10% HNO_3 overnight at 40 °C, and extracted the samples with Hex:DCM (4:1, v/v) (Kucharska et al., 2015a; Malarvannan et al., 2013; Qiao et al., 2019). However, 3–4 M HCl or 10% HNO_3 were unable to completely digest the hair samples to generate homogeneous sample solutions and to liberate the target compounds, which was essential for the efficient extraction of targeted analytes from hair. In a recent study by Liu et al. (2015), hair samples were completely digested by 2 mL HNO_3/H_2O_2 (1:1, v/v) at 60 °C for 2 h, generating a homogeneous mixture; good recoveries for targeted compounds (PBDEs, AFRs, and PFRs) were achieved after dilution of the mixture with HPLC grade water and extraction with Hex:DCM (4:1, v/v). Therefore, in the present study, digestion and extraction procedure were adopted to the methodology by Liu et al. (2015), and all hair samples were digested completely. However, as large amount of volume (10 mL per time, extracted 3 times) of organic solvents was used in the study by Liu et al. (2015), we reduced the volume of Hex:DCM (4:1, v/v) to 6 mL per time for the extraction procedure, which was conducted for 2 times. The recoveries for targeted chemicals were observed as 79–117% (Fig. S1), suggesting that the target chemicals were not destroyed by the sample digestion using acid, and good recoveries were achieved by using less volume of solvents in comparison with the previous study (Liu et al., 2015).

3.1.3. Clean-up

Florisil column was commonly used for the clean-up and simultaneous analysis of PBDEs and PFRs in human hair (Kucharska et al., 2015b; Liu et al., 2015; Qiao et al., 2019). In the study by Liu et al. (2015), a column containing 6 g of 2.5% water deactivated Florisil was used for clean-up, and chromatograms of the fractions were clean enough for determination of all three classes of targeted analytes, *i.e.* PBDEs, AFRs, and PFRs; however, large volume of solvent was needed for this method, with 35 mL hexane, 35 mL Hex:DCM (1:1, v/v), and 40 mL DCM:ACE (1:1, v/v) were used for eluting of F1 (containing PBDEs and most AFRs), F2 (containing AFRs), and F3 (containing PFRs), respectively. In our recent study using packed Florisil cartridge (500 mg, 3 mL) to fractionate PBDEs, AFRs, and PFRs, only 8 mL Hex (F1, containing PBDEs and AFRs) and 8 mL EtAc (F2, containing PFRs) were needed (Qiao et al., 2019). Therefore, in the present study, Florisil cartridge was selected for clean-up and fractionation of hair samples according to our previous study (Qiao et al., 2019).

Two different solvents, *i.e.* Hex and 1-chlorobutane, were tested for eluting both PBDEs and HBCDDs in F1; whilst for F2, the volume of EtAC was increased from 8 mL to 10 mL and additional 8 mL Acetone was used according to the methodology of Christia et al. (2019) to ensure the complete elution of ePFRs in this fraction. Moreover, most lipids eluted in F1 on Florisil cartridges, which would interfere in the chromatograms on GC-MS (Xu et al., 2015), and thus an aliquot of concentrated sulfuric acid was added for clean-up of F1, as both PBDEs and HBCDDs are acid resistant. Procedure blanks, native spiked blanks, and native spiked matrix (a homogenates hair sample) each in triplicates were tested for the extraction procedure and these two clean-up protocols. The results of the recoveries of targeted chemicals indicated that Hex was unable to elute HBCDD isomers completely in F1, especially for β-HBCDD (Fig. S1). On the other hand, however, clean chromatograms and acceptable recoveries were achieved for HBCDDs using 1-chlorobutane (Fig. S1). As for PBDEs and PFRs/ePFRs, acceptance for recoveries of targeted chemicals was obtained for both

protocols. Based on these results, 1-chlorobutane and EtAc were selected for the elution for F1 and F2, respectively, for subsequential experiments in the present study. The optimal protocol for hair sample treatment is described in "*Sample preparation*" in Section 2.3, and the chromatograms of PFRs/ePFRs in spiked matrix samples are given in Fig. S2.

3.2. Method validation

Owing to the lack of suitable standard reference material for hair analysis, the performance of the developed method was validated by experiments of spiked matrices (a real hair sample) and blanks. A scalp hair sample collected from Guangzhou city was used. This sample was rinsed with Milli-Q water in a shaking incubator (1 h, 40 °C, twice) and further pre-cleaned with 30 mL of Acetone (1 h, 40 °C, twice) to reduce the potential contamination of target analytes in the matrix, as which would affect the results for the spiking experiments. After being freeze-dried, the hair sample was cut into small pieces, and thoroughly mixed. This precleaned hair sample was then divided into 9 aliquots (each at 100 mg) in Teflon-tubes, and 3 mL HNO_3/H_2O_2 (1:1, v/v) was added to each tube. Afterwards, 3 of these samples were spiked at low-level mass (LL, 4.0 ng) of the target analytes, 3 at high-level mass (HL, 20 ng), and the remaining 3 replicates were used as non-spiked controls. The laboratory background contamination was determined by three procedural solvent blanks. Finally, the measured average levels of target analytes in solvent blanks and non-spiked controls (Table S3) were subtracted from the spiked sample results. Calculation of the validation parameters was based on the US Food and Drugs Administration (FDA) guideline for Bioanalytical Method Validation (referred as Guideline hereinafter) (Guidance for Industry, 2018). The performance of the developed method was evaluated by the linearity of the calibration curves, the limits of detection and quantification (LOD/LOQ), and the accuracy and precision of each individual analyte, which were described in detail as below.

3.2.1. Linearity of the calibration curves

Based on the three standard mixtures, three calibration curves of the target analytes were prepared: PBDE standard mixture (BDEs 28, 47, 99, 100, 153, 154, 183, and 209) for use in GC-ECNI-MS; HBCDD standard mixture (α-HBCDD, β-HBCDD, γ-HBCDD), and PFR/ePFR standard mixture (TPHP, TiPP, TPP, TEP, TNBP, TBOEP, TEHP, EHDPP, TCEP, TCIPP, TDCIPP, TMPP, V6, iDDPHP, BDP, and RDP), respectively, for use in LC-ESI-MS/MS. The calibration curves were set at 9 levels for all target analytes, which covered a wide range of concentrations (Table 1). According to the Guideline, the concentration-response relationship for the calibration curves should be fit in with the simplest regression model, and non-zero calibrators should be ±15% of nominal (theoretical) concentrations (Guidance for Industry, 2018). The calibration curves were best fitted to a linear model for all three mixtures, and the linearity was estimated by the coefficient of determination (R^2). Good correlations were obtained for all targeted analytes with $R^2 \geq 0.995$ (Table 1), and thus a good linearity within the stated ranges can be assured, indicating the acceptance criteria was achieved.

3.2.2. Limits of detection and quantification (LOD/LOQ)

LODs and LOQs were calculated to check the sensitivity of the developed method. The LODs for targeted analytes were calculated from the lowest level of the calibration curve, based on a signal/

Table 1
Validation results for the developed method.

Target analyte	Linearity (R^2)	Calibration curve interval (ng)	LOD (ng/g)	LOQ (ng/g)	LL spiking (n = 3)				HL spiking (n = 3)			
					Spiked mass (ng)	SD (%)	RSD (%)	Accuracy (%)	Spiked mass (ng)	SD (%)	RSD (%)	Accuracy
PBDEs												
BDE28	0.998	0.05–150	0.06	0.17	4.0	2	13	100	20	6	7	109
BDE47	0.999		0.08	0.25	4.0	3	14	99	20	5	6	91
BDE99	0.999		5.56	16.7	4.0	2	9	108	20	5	6	99
BDE100	0.999		3.94	11.8	4.0	1	6	96	20	6	8	104
BDE153	0.995		7.48	22.4	4.0	0.5	2	101	20	6	7	94
BDE154	0.998		0.11	0.33	4.0	0.8	6	91	20	9	11	88
BDE183	0.998		0.09	0.28	4.0	1	5	113	20	8	7	102
BDE209	0.998		0.08	0.24	4.0	5	13	98	20	16	7	115
HBCDDs												
α-HBCDD	0.998	0.05–150	0.04	0.12	4.0	2	10	103	20	5	5	94
β-HBCDD	0.999		0.23	0.69	4.0	0.7	4	107	20	4	4	90
γ-HBCDD	0.999		0.08	0.23	4.0	2	6	117	20	4	2	82
PFRs												
TPHP	0.996	0.05–150	0.30	0.91	4.0	3	3	95	20	4	6	92
TiPP	0.999		0.11	0.32	4.0	1	12	82	20	1	4	86
TPP	0.999		0.96	2.89	4.0	1	5	81	20	5	7	85
TEP	0.999		0.15	0.44	4.0	5	16	88	20	15	18	91
TNBP	0.998		3.62	10.9	4.0	5	12	86	20	4	3	95
TBOEP	0.999		1.03	3.08	4.0	1	10	97	20	4	6	105
TEHP	0.999		0.67	2.00	4.0	6	8	128	20	8	6	116
EHDPP	0.996		1.74	5.21	4.0	9	17	86	20	11	10	96
TCEP	0.999		3.47	10.4	4.0	3	4	93	20	1	2	84
TCIPP	0.996		1.11	3.33	4.0	4	8	94	20	3	3	99
TDCIPP	0.999		5.59	16.7	4.0	2	2	98	20	10	9	95
TMPP	0.999		0.12	0.36	4.0	9	17	102	20	6	7	103
ePFRs												
V6	0.998	0.05–150	0.36	1.09	4.0	2	14	81	20	16	17	95
iDDPHP	0.999		0.16	0.48	4.0	2	12	82	20	4	14	82
BDP	0.997		0.11	0.33	4.0	4	11	89	20	10	13	85
RDP	0.999		0.14	0.42	4.0	2	9	92	20	9	11	93

LL, low spike level, HL, high spike level.

noise ratio of 3 (S/N = 3). The analyte response at the LOQ should be more than five times the analyte response of the zero calibrator (Guidance for Industry, 2018). The LOQs were estimated as the mean value of target analytes detected in procedure blanks plus three times of standard deviations. For the analytes with negligible levels in procedural blanks, LOQs were calculated as a signal to noise ratio of 10 (S/N = 10) generated from the lowest calibration point. Determined LOQ range was 0.24–22.4 ng/g for PBDEs, 0.12–0.69 ng/g for HBCDDs, 0.32–16.7 ng/g for PFRs, and 0.33–1.09 ng/g for ePFRs, respectively. The LOQs for each individual analyte are given in Table 1.

3.2.3. Accuracy and precision

Accuracy was estimated as the recovery of each targeted analyte individual in the native spiked samples, which were calculated as the percentage of the determined amount (corrected by those in procedure blank samples) relative to the spiked amount for each analyte. Precision, also referred as the intra-day repeatability, of the analytical method, was calculated as the RSD of three replicate analyses in repeatable conditions. The accuracy of each analyte should be of ±20% of nominal concentration (i.e. recovery should be 80–120%), and the RSD should be less than 20%, according to the Guideline (Guidance for Industry, 2018).

Generally, most of the analytes in both LL and HL groups showed acceptable accuracies and precisions based on the validation results (Table 1). The average accuracies for PBDEs, HBCDDs, PFRs, and ePFRs, were in a range of 91–113% (RSD < 14%), of 103–117% (RSD < 10%), of 81–128% (RSD < 17%), and of 81–92% (RSD < 14%), respectively, in LL; and were in a range of 88–115% (RSD < 11%), of 82–94% (RSD < 5%), of 84–116% (RSD < 18%), and of 82–95% (RSD < 17%), respectively, in HL. The recoveries of ISs in the spiked matrix samples ranged from 91 ± 15% to 110 ± 21% for PBDEs, from 80 ± 9% to 102 ± 10% for HBCDDs, and from 81 ± 19% to 92 ± 17% for PFRs/ePFRs, respectively (Fig. 2).

3.3. Method application

To examine the applicability of our developed method, the simultaneous occurrence of PBDEs, HBCDDs, PFRs and ePFRs in scalp hair samples collected from fourteen e-waste dismantling workers were analyzed.

Table 2 reports the descriptive statistics for targeted compounds related to the 14 hair samples, and Fig. 3 and Table S4 in the SI present the contribution patterns and the concentration levels of target analytes detected in samples, respectively. All the eight PBDE congeners were detected in hair samples, among which BDEs 28, 47 and 209 were detected in all samples (DF = 100%), and relatively high DFs were found also for BDE 99 (DF = 79%) and BDE 154 (DF = 93%) (Table 2). The concentrations of $\sum_8$PBDEs ranged between 15.0 and 252 ng/g, with a median concentration of 40.2 ng/g. These values were higher than those reported in human hair samples from the Pearl River Delta in South China (1.49–7.45 ng/g, median 3.40 ng/g) (Kang et al., 2011), but were lower than those reported in hair from e-waste dismantling workers in 2009 (12.4–845 ng/g, median 126 ng/g) (Zheng et al., 2011) and in 2011 (33.0–1284 ng/g, median 106 ng/g) (Zheng et al., 2014) from the same areas as the present study, and were also lower than those of e-waste dismantling workers from Taizhou, Eastern China in 2007 (21.5–1020 ng/g, median 157 ng/g) (Ma et al., 2011). The decrease trend of ∑PBDE levels in hair of the e-waste dismantling workers could be attributed to the gradually phase-out of PBDE technical mixtures, and the legislation and regulation on primitive e-waste dismantling activities since 2013 (Huang et al., 2018). BDE 209 and BDE 99 were the most abundant PBDE congeners, with concentration ranges 7.56–140 and n.d. (not detected)–41.0 ng/g (dw), respectively, and accounting for 43 ± 14% and 19 ± 15% of total PBDEs, respectively (Fig. 3a). BDE 209 was also found as the dominated PBDE congener in hair of e-waste dismantling workers in previous studies (Ma et al., 2011; Zheng et al., 2011), which could

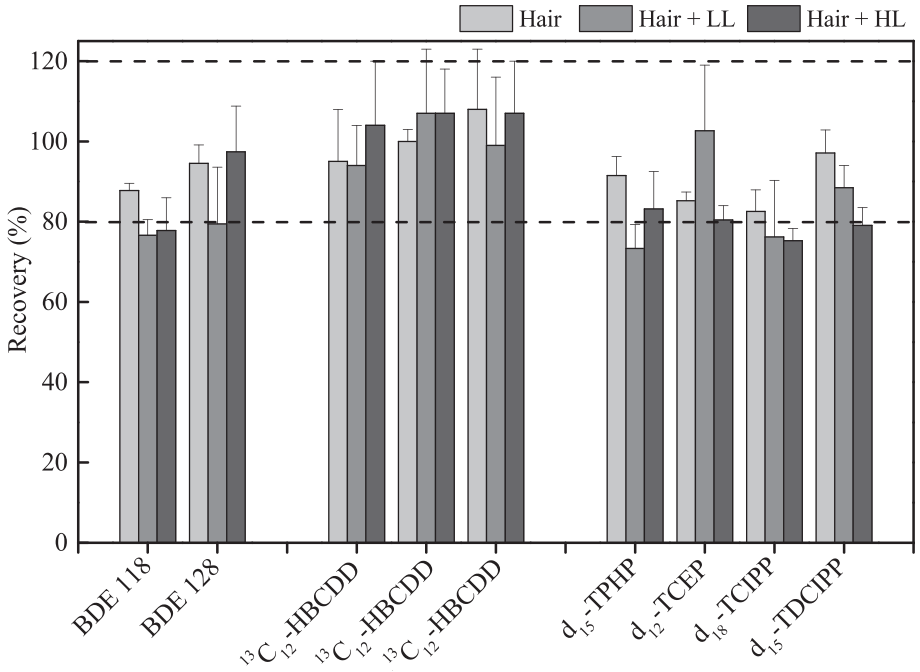

Fig. 2. The recoveries of ISs for each group of compounds in the spiked matrix samples. Dashed lines indicate acceptable range (80–120%) for recoveries. LL, low spike level; HL, high spike level.

Table 2
Levels of targeted compounds in 14 hair samples collected from Qingyuan, China (ng/g).

Targeted Analyte	DF[a] (%)	Mean	SD[b]	Median	Min	Max
PBDEs						
BDE 28	100	5.51	5.60	3.00	1.81	21.3
BDE 47	100	6.89	3.44	5.91	2.38	14.5
BDE 99	79	18.7	12.6	14.4	n.d.[c]	41.0
BDE 100	14	4.57	0.35	4.57	n.d.	4.82
BDE 153	21	16.8	12.9	10.1	n.d.	31.6
BDE 154	93	4.59	3.88	3.74	n.d.	12.2
BDE 183	14	18.1	2.27	18.1	n.d.	19.8
BDE 209	100	30.7	35.4	14.9	7.56	140
$\sum_8$ PBDEs		67.5	61.4	40.2	15.0	252
HBCDDs						
α-HBCDD	50	2.81	2.51	1.18	n.d.	7.23
β-HBCDD	43	0.92	0.35	0.84	n.d.	1.52
γ-HBCDD	50	5.06	4.17	4.04	n.d.	13.6
$\sum_3$ HBCDDs		7.57	4.64	6.24	n.d.	14.6
PFRs						
TPHP	100	240	253	131	44.7	830
TiPP	86	2.23	0.63	2.13	1.11	3.30
TPP	93	7.37	4.55	6.10	2.58	19.2
TEP	93	9.09	5.43	8.24	3.70	24.2
TBOEP	100	2.86	2.21	2.35	1.37	10.2
TEHP	100	66.3	39.7	66.0	20.0	145
EHDPP	100	159	190	77.6	19.9	710
TCEP	93	72.8	175	25.4	6.12	652
TCIPP	100	167	298	74.8	9.95	1160
TDCIPP	93	149	199	49.0	21.3	630
TMPP	100	92.8	194	36.3	3.47	750
$\sum_{11}$ PFRs		950	767	816	162	3220
ePFRs						
V6	21	4.34	3.10	3.62	1.67	7.74
iDDPHP	100	32.0	19.2	29.4	8.09	76.3
BDP	100	4.94	4.86	4.22	1.16	21.0
RDP	57	2.09	1.47	1.49	0.46	4.43
$\sum_4$ ePFRs		39.1	22.6	34.1	9.42	90.3
$\sum_{15}$ (PFRs + ePFRs)		990	772	854	171	3280

[a] DF, detection frequency.
[b] SD, standard deviation.
[c] n.d., not detected.

be attributed to the extensive use of Deca-BDE in electronic components (Ma et al., 2011; Zheng et al., 2011).

HBCDDs were detected in 43–50% of hair samples, and the concentrations of $\sum_3$HBCDDs ranged from n.d. to 14.6 ng/g (median 6.24 ng/g) (Table 2), with γ-HBCDD (n.d.–13.6 ng/g, median 4.04 ng/g) as the predominant diastereomer, followed by α-HBCDD (n.d.–7.23 ng/g, median 1.18 ng/g) and β-HBCDD (n.d.–1.52 ng/g, median 0.84 ng/g) (Fig. 3b). Few previous studies have reported the HBCDD concentrations in human hair. The concentrations of $\sum_3$HBCDDs ranging from 0.3 to 5.4 ng/g (median 0.93 ng/g) were reported in Philippines, and α-HBCDD was the predominant diastereomer (Malarvannan et al., 2013). In a recent study by Barghi et al. (Barghi et al., 2018), the $\sum_3$HBCDD concentrations ranged from n.d. to 3.24 ng/g for hair samples collected from South Korea, with γ-HBCDD as the dominant diastereomer, followed by α-HBCDD and β-HBCDD, which was consistent with the results of the present study. Generally, the reported HBCDD concentrations in the present study were higher than those obtained in previous studies as we sampled from a high exposure area, i.e. an e-waste recycling site. To our knowledge, no study has reported the levels and compositions of HBCDs in human tissues of workers form this e-waste recycling area. Nevertheless, some studies have reported α-HBCD as the dominant congener in human serum and milk samples (Thomsen et al., 2007; Rawn et al., 2014; Ryan and Rawn, 2014), which was probably attributed to the lower metabolic rate of α-HBCD, and the bioisomerization from γ-HBCD to α-HBCD in the human body. These results were contrast to those for hairs reported in the present study, implying that endogenous exposure might not be the major sources for HBCDs observed in hair samples of the workers. However, further studies are needed to confirm this hypothesis.

Additionally, elven PFRs and four ePFRs were frequently detected in hair samples (Table 2), with concentrations of $\sum_{11}$PFRs and $\sum_4$ePFRs ranged from 162 to 3220 ng/g (median 816 ng/g), and from 9.42 to 90.3 ng/g (median 34.1 ng/g), respectively. The concentrations of $\sum_{11}$PFRs observed in the present study were significantly higher than those (10.1–604 ng/g, median 148 ng/g) in hair samples from university students in Guangzhou, South China (Qiao et al., 2016), but were lower than those in hair samples from the USA (210–10800 ng/g, median 1530 ng/g) (Liu et al., 2016) and Norway (<1–3744 ng/g) (Kucharska et al., 2015a). Among the four ePFRs, iDDPHP and RDP were detected in all the hair samples (DF = 100%), and the DFs for V6 and RDP were 21% and 57%, respectively. RDP, iDDPHP and BDP were suggested as appropriate alternatives for Deca-BDE, as well as coapplied with TPHP in some cases; whilst V6 was suggested as a substitute for Penta-BDE, TDCIPP, and TCIPP (Ballesteros-Gómez et al., 2016; van der Veen and de van der Veende Boer and AuthorAnonymous, 2012). The relatively high DFs for ePFRs in hair samples of the workers implying the wide use of these novel chemicals in the electronic products dismantled in this area. To our knowledge, this is the first study that reported ePFR concentrations in hair samples, which prevents a comparison of the concentrations found in this study with similar literature outcomes. TPHP (26 ± 8.3%) was the most abundant chemical for PFRs/ePFRs, followed by EHDPP (18 ± 10%), TDCIPP (14 ± 7.3%), and TCIPP (12 ± 8.9%) (Fig. 3c) in hairs of the e-waste dismantling workers. The composition profiles of PFRs/ePFRs found in our study were different from those reported in hair in previous studies (Kucharska et al., 2015a; Liu et al., 2016; Qiao et al., 2016). TPHP, TCIPP, and TEHP were the most abundant chemicals in hairs of university students from South China (Qiao et al., 2016), while the predominant PFRs in hair samples from the USA were TPHP and TDCIPP (Liu et al., 2016). Kucharska et al. (2015a) found that TBOEP, TPHP, and TCEP dominated PFRs in Norwegian hair samples. The distinct composition profiles of PFRs could be attributed to the diverse application of PFRs in household products (Qiao et al., 2016).

Moreover, among the three investigated groups of chemicals in the present study, the contributions of PFRs/ePFRs (80–98%) generally exceed those of PBDEs (1.8–19%) and HBCDDs (0–4.4%) (Fig. 4), implying the wide use of PFRs/ePFRs as replacements of BFRs such as PBDEs and HBCDDs, as well as the high risks for human exposure of PFRs/ePFRs, and further studies for a comprehensive evaluation is urgently needed.

4. Conclusions

In the present study, a robust and sensitive analytical method was developed and validated for the simultaneous determination of 8 PBDE congeners, 3 HBCDD diastereoisomers, 12 PFRs, and 4 ePFRs in human hair samples. The method using a simple digestion and extraction procedure, enabled to separate the targeted analytes into two fractions (F1, PBDEs and HBCDDs; F2, PFRs/ePFRs) on a Florisil cartridge, and only low volumes of solvent were consumed in comparison with previously published methods. The feasibility and robustness of the method were confirmed by application to hair samples collected from 14 e-waste dismantling workers in South China. Eight PBDE congeners were detected in the hair samples, and BDE 209 was the predominant congener. The DFs for HBCDDs in the hair samples were 43–50%, with γ-HBCDD

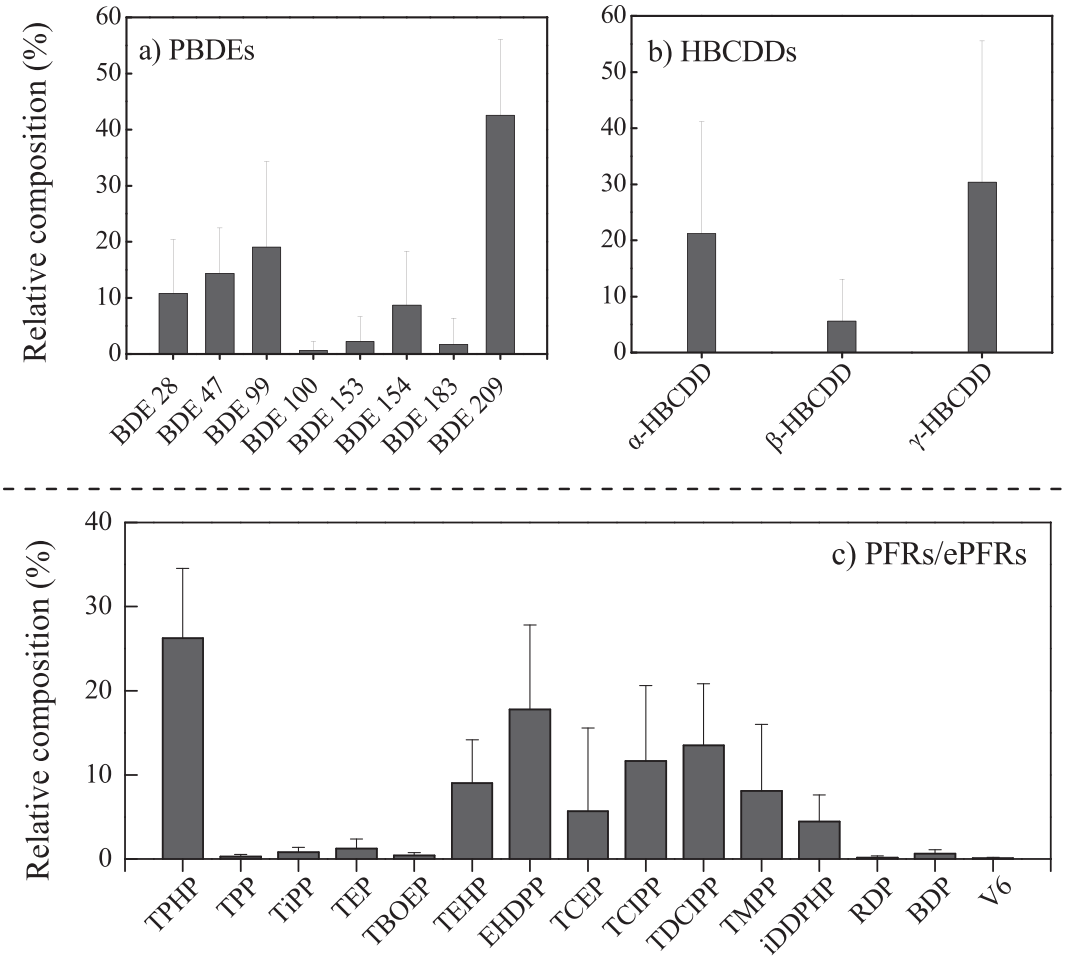

Fig. 3. Contribution of the targeted analytes in each group in 14 hair samples from an e-waste site, South China.

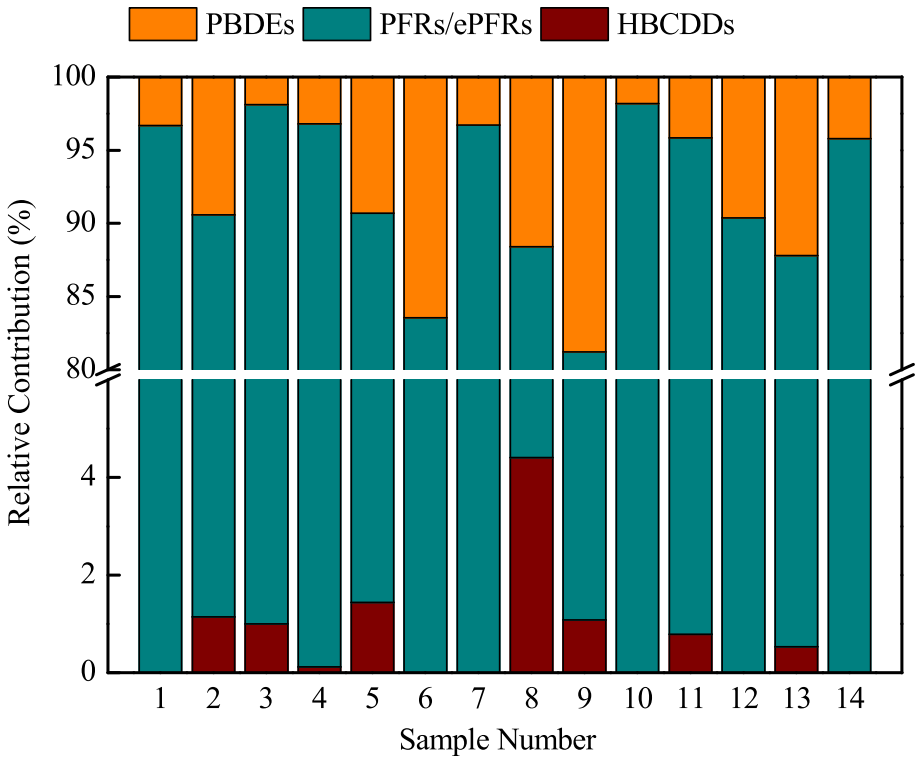

Fig. 4. Contribution of per compound group in each hair sample from an e-waste site, South China.

dominated the three diastereomers. Elven PFRs and four ePFRs were detected in the hair samples, and TPHP was the most abundant chemical for PFRs/ePFRs, followed by EHDPP, TDCIPP, and TCIPP. PFRs/ePFRs were the major compounds in human hair samples, implying the wide use of PFRs/ePFRs as replacements of BFRs such as PBDEs and HBCDDs. To our knowledge, this is the first study that reported ePFR concentrations in hair samples. Overall, this work will permit a comprehensive assessment of human exposure to multiple groups of legacy and emerging FRs using hair as a non-invasive bioindicator and a single sample preparation procedure.

Author's contributions

Bin Tang: Investigation, Writing - original draft Preparation, Visualization, Formal analysis, Shi-Mao Xiong, Methodology, Validation, Investigation, Writing - original draft Preparation, Jing Zheng, Conceptualization, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition, Mei-Huan Wang, Investigation, Writing - review & editing, Feng-Shan Cai, Investigation, Writing - review & editing, Wei-Keng Luo, Data curation, Visualization, Writing - review & editing, Rong-Fa Xu, Data curation, Writing - review & editing, Yun-Jiang Yu, Writing - review & editing, Supervision.

Declaration of competing interest

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

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2020.127807.

References

Araki, A., Saito, I., Kanazawa, A., Morimoto, K., Nakayama, K., Shibata, E., Tanaka, M., Takigawa, T., Yoshimura, T., Chikara, H., Saijo, Y., Kishi, R., 2014. Phosphorus flame retardants in indoor dust and their relation to asthma and allergies of inhabitants. Indoor Air 24, 3–15.

Ballesteros-Gómez, A., Aragón, Á., Van den Eede, N., de Boer, J., Covaci, A., 2016. Impurities of resorcinol bis(diphenyl phosphate) in plastics and dust collected on electric/electronic material. Environ. Sci. Technol. 50, 1934–1940.

Barghi, M., Shin, E.-s., Choi, S.-D., Dahmardeh Behrooz, R., Chang, Y.-S., 2018. HBCD and TBBPA in human scalp hair: evidence of internal exposure. Chemosphere 207, 70–77.

Brandsma, S.H., Sellström, U., de Wit, C.A., de Boer, J., Leonards, P.E.G., 2013. Dust measurement of two organophosphorus flame retardants, resorcinol bis (diphenylphosphate) (RBDPP) and bisphenol A bis (diphenylphosphate) (BPA-BDPP), used as alternatives for BDE-209. Environ. Sci. Technol. 47, 14434–14441.

Chen, D., Letcher, R.J., Chu, S., 2012. Determination of non-halogenated, chlorinated and brominated organophosphate flame retardants in herring gull eggs based on liquid chromatography-tandem quadrupole mass spectrometry. J. Chromatogr. A 1220, 169–174.

Christia, C., Tang, B., Yin, S.S., Luo, X.J., Mai, B.X., Poma, G., Covaci, A., 2019. Simultaneous determination of legacy and emerging organophosphorus flame retardants and plasticizers in indoor dust using liquid and gas chromatography-tandem mass spectrometry: method development, validation, and application. Anal. Bioanal. Chem. 411, 7015–7025.

Covaci, A., Harrad, S., Abdallah, M.A., Ali, N., Law, R.J., Herzke, D., de Wit, C.A., 2011. Novel brominated flame retardants: a review of their analysis, environmental fate and behaviour. Environ. Int. 37, 532–556.

Cristale, J., Lacorte, S., 2013. Development and validation of a multiresidue method for the analysis of polybrominated diphenyl ethers, new brominated and organophosphorus flame retardants in sediment, sludge and dust. J. Chromatogr. A 1305, 267–275.

de Wit, C.A., 2002. An overview of brominated flame retardants in the environment. Chemosphere 46, 583–624.

Guidance for Industry, 2018. Bioanalytical Method Validation Guidance for Industry. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and RESEARCH (CDER), Center for Veterinary Medicine (CVM).

Huang, C.C., Zeng, Y.H., Luo, X.J., Tang, B., Liu, Y.E., Ren, Z.H., Mai, B.X., 2018. Level changes and human dietary exposure assessment of halogenated flame retardant levels in free-range chicken eggs: a case study of a former e-waste recycling site. South China. Sci. Total Environ 634, 509–515.

Kang, Y., Wang, H.S., Cheung, K.C., Wong, M.H., 2011. Polybrominated diphenyl ethers (PBDEs) in indoor dust and human hair. Atmos. Environ. 45, 2386–2393.

Kim, J.W., Isobe, T., Muto, M., Tue, N.M., Katsura, K., Malarvannan, G., Sudaryanto, A., Chang, K.H., Prudente, M., Viet, P.H., Takahashi, S., Tanabe, S., 2014. Organophosphorus flame retardants (PFRs) in human breast milk from several Asian countries. Chemosphere 116, 91–97.

Kucharska, A., Cequier, E., Thomsen, C., Becher, G., Covaci, A., Voorspoels, S., 2015a. Assessment of human hair as an indicator of exposure to organophosphate flame retardants. Case study on a Norwegian mother-child cohort. Environ. Int. 83, 50–57.

Kucharska, A., Covaci, A., Vanermen, G., Voorspoels, S., 2015b. Non-invasive biomonitoring for PFRs and PBDEs: new insights in analysis of human hair externally exposed to selected flame retardants. Sci. Total Environ. 505, 1062–1071.

Li, P., Jin, J., Wang, Y., Hu, J., Xu, M., Sun, Y., Ma, Y., 2017. Concentrations of organophosphorus, polybromobenzene, and polybrominated diphenyl ether flame retardants in human serum, and relationships between concentrations and donor ages. Chemosphere 171, 654–660.

Liu, L.Y., He, K., Hites, R.A., Salamova, A., 2016. Hair and nails as noninvasive biomarkers of human exposure to brominated and organophosphate flame retardants. Environ. Sci. Technol. 50, 3065–3073.

Liu, L.Y., Salamova, A., He, K., Hites, R.A., 2015. Analysis of polybrominated diphenyl ethers and emerging halogenated and organophosphate flame retardants in human hair and nails. J. Chromatogr. A 1406, 251–257.

Liu, Y.E., Huang, L.Q., Luo, X.J., Tan, X.X., Huang, C.C., Corella, P.Z., Mai, B.X., 2018. Determination of organophosphorus flame retardants in fish by freezing-lipid precipitation, solid-phase extraction and gas chromatography-mass spectrometry. J. Chromatogr. A 1532, 68–73.

Ma, J., Cheng, J., Wang, W., Kunisue, T., Wu, M., Kannan, K., 2011. Elevated concentrations of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans and polybrominated diphenyl ethers in hair from workers at an electronic waste recycling facility in Eastern China. J. Hazard Mater. 186, 1966–1971.

Malarvannan, G., Isobe, T., Covaci, A., Prudente, M., Tanabe, S., 2013. Accumulation of brominated flame retardants and polychlorinated biphenyls in human breast milk and scalp hair from the Philippines: levels, distribution and profiles. Sci. Total Environ. 442, 366–379.

Poon, S., Wade, M.G., Aleksa, K., Rawn, D.F., Carnevale, A., Gaertner, D.W., Sadler, A., Breton, F., Koren, G., Ernest, S.R., Lalancette, C., Robaire, B., Hales, B.F., Goodyer, C.G., 2014. Hair as a biomarker of systemic exposure to polybrominated diphenyl ethers. Environ. Technol. 48, 14650–14658.

Qiao, L., Zheng, X.B., Zheng, J., Chen, S.J., Zhong, C.Q., Chen, J.H., Yang, Z.Y., Mai, B.X., 2019. Legacy and currently used organic contaminants in human hair and hand wipes of female E-waste dismantling workers and workplace dust in South China. Environ. Sci. Technol. 53, 2820–2829.

Qiao, L., Zheng, X.B., Zheng, J., Lei, W.X., Li, H.F., Wang, M.H., He, C.T., Chen, S.J., Yuan, J.G., Luo, X.J., Yu, Y.J., Yang, Z.Y., Mai, B.X., 2016. Analysis of human hair to assess exposure to organophosphate flame retardants: influence of hair segments and gender differences. Environ. Res. 148, 177–183.

Rawn, D.F.K., Ryan, J.J., Sadler, A.R., Sun, W., Weber, D., Laffey, P., Haines, D., Macey, K., Van Oostdam, J., 2014. Brominated flame retardant concentrations in sera from the Canadian health measures survey (CHMS) from 2007 to 2009. Environ. Int. 63, 26–34.

Rodil, R., Quintana, J.B., Concha-Grana, E., Lopez-Mahia, P., Muniategui-Lorenzo, S., Prada-Rodriguez, D., 2012. Emerging pollutants in sewage, surface and drinking water in Galicia (NW Spain). Chemosphere 86, 1040–1049.

Ryan, J.J., Rawn, D.F.K., 2014. The brominated flame retardants, PBDEs and HBCD, in Canadian human milk samples collected from 1992 to 2005; concentrations and trends. Environ. Bar Int. 70, 1–8.

Tan, H., Chen, D., Peng, C., Liu, X., Wu, Y., Li, X., Du, R., Wang, B., Guo, Y., Zeng, E.Y., 2018. Novel and traditional organophosphate esters in house dust from South China: association with hand wipes and exposure estimation. Environ. Sci. Technol. 52, 11017–11026.

Tao, F., Abdallah, M.A., Harrad, S., 2016. Emerging and legacy flame retardants in UK indoor air and dust: evidence for replacement of PBDEs by emerging flame retardants? Environ. Sci. Technol. 50, 13052–13061.

Tay, J.H., Sellstrom, U., Papadopoulou, E., Padilla-Sanchez, J.A., Haug, L.S., de Wit, C.A., 2018. Assessment of dermal exposure to halogenated flame retardants: comparison using direct measurements from hand wipes with an indirect estimation from settled dust concentrations. Environ. Int. 115, 285–294.

Tay, J.H., Sellstrom, U., Papadopoulou, E., Padilla-Sanchez, J.A., Haug, L.S., de Wit, C.A., 2019. Serum concentrations of legacy and emerging halogenated flame retardants in a Norwegian cohort: relationship to external exposure. Environ. Res. 178, 108731.

Thomsen, C., Molander, P., Daae, H.L., Janak, K., Froshaug, M., Liane, V.H., Thorud, S., Becher, G., Dybing, E., 2007. Occupational exposure to hexabromocyclododecane at an industrial plant. Environ. Sci. Technol. 41, 5210–5216.

UNEP, 2017. Stockholm Convention text and annexes as amended in 2017. Available at. http://chm.pops.int/Implementation/Alternatives/AlternativestoPOPs/ChemicalslistedinAnnexA/tabid/5837/Default.aspx.

van der Veen, I., de Boer, J., 2012. Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis. Chemosphere 88, 1119–1153.

Wei, G.L., Li, D.Q., Zhuo, M.N., Liao, Y.S., Xie, Z.Y., Guo, T.L., Li, J.J., Zhang, S.Y., Liang, Z.Q., 2015. Organophosphorus flame retardants and plasticizers: sources, occurrence, toxicity and human exposure. Environ. Pollut. 196, 29–46.

Xu, F., Garcia-Bermejo, A., Malarvannan, G., Gomara, B., Neels, H., Covaci, A., 2015. Multi-contaminant analysis of organophosphate and halogenated flame retardants in food matrices using ultrasonication and vacuum assisted extraction, multi-stage cleanup and gas chromatography-mass spectrometry. J. Chromatogr. A 1401, 33–41.

Yang, F., Ding, J., Huang, W., Xie, W., Liu, W., 2014. Particle size-specific distributions and preliminary exposure assessments of organophosphate flame retardants in office air particulate matter. Environ. Sci. Technol. 48, 63–70.

Zheng, J., Chen, K.H., Luo, X.J., Yan, X., He, C.T., Yu, Y.J., Hu, G.C., Peng, X.W., Ren, M.Z., Yang, Z.Y., Mai, B.X., 2014. Polybrominated diphenyl ethers (PBDEs) in paired human hair and serum from e-waste recycling workers: source apportionment of hair PBDEs and relationship between hair and serum. Environ. Sci. Technol. 48, 791–796.

Zheng, J., He, C.T., Chen, S.J., Yan, X., Guo, M.N., Wang, M.H., Yu, Y.J., Yang, Z.Y., Mai, B.X., 2017a. Disruption of thyroid hormone (TH) levels and TH-regulated gene expression by polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), and hydroxylated PCBs in e-waste recycling workers. Environ. Int. 102, 138–144.

Zheng, J., Luo, X.J., Yuan, J.G., Wang, J., Wang, Y.T., Chen, S.J., Mai, B.X., Yang, Z.Y., 2011. Levels and sources of brominated flame retardants in human hair from urban, e-waste, and rural areas in South China. Environ. Pollut 159, 3706–3713.

Zheng, X., Qiao, L., Sun, R., Luo, X., Zheng, J., Xie, Q., Sun, Y., Mai, B., 2017b. Alteration of diastereoisomeric and enantiomeric profiles of hexabromocyclododecanes (HBCDs) in adult chicken tissues, eggs, and hatchling chickens. Environ. Sci. Technol. 51, 5492–5499.

Zheng, J., Yan, X., Chen, S.J., Peng, X.W., Hu, G.C., Chen, K.H., Luo, X.J., Mai, B.X., Yang, Z.Y., 2013. Polychlorinated biphenyls in human hair at an e-waste site in China: composition profiles and chiral signatures in comparison to dust. Environ. Int. 54, 128–133.