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Organophosphate esters (OPEs) in Chinese foodstuffs: Dietary intake estimation via a market basket method, and suspect screening using high-resolution mass spectrometry

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ABSTRACT

Despite of the ubiquity of organophosphate esters (OPEs) in various environmental matrices, information regarding the dietary intakes of OPEs is currently limited. To better understand dietary exposure and intake, the present study investigated 11 OPE flame retardants (FRs) in 105 composite food samples divided into 9 food categories, collected in 2018 and based on the contents of a typical Chinese food market basket. Nine OPEs, including triethyl phosphate (TEP), tributyl phosphate (TNBP), tris(2-chloroethyl) phosphate (TCEP), tris(2-chloroisopropyl) phosphate (TCIPP), triphenyl phosphate (TPHP), 2-ethylhexyl-diphenyl phosphate (EHDPP), tris(2-butoxyethyl) phosphate (TBOEP), tris(2-ethylhexyl) phosphate (TEHP) and tris(methyl-phenyl) phosphate (TMPP), were measurable above the method limits of quantifications (MLOQs) in at least one of the analyzed samples. Among the 9 food categories, sweets were contaminated most severely with a mean sum (Σ) OPE concentration of 10.34 ng/g wet weight (ww). Regardless the food categories, EHDPP and TEP were the predominant OPEs with mean concentrations of 1.12 and 0.95 ng/g ww, respectively. In addition, the levels of OPEs in "processed foods" were significantly (unpaired *t*-test, $p < 0.01$) higher than those in "non-processed foods". Based on the measured OPE concentrations, we estimated daily per capita dietary intakes of ΣOPEs for Chinese adult population to be 44.3 ng/kg bw/day, that was mainly contributed by TCEP (14.3 ng/kg bw/day), TEP (12.7 ng/kg bw/day) and EHDPP (8.4 ng/kg bw/day). In addition to these 9 detected OPEs, further suspect screening in the combined extracts of foodstuffs by use of high-resolution spectrometry revealed a novel OP-FR, triphenyl phosphine oxide (TPPO). The highlight findings in this study were: 1) the amount of OPE via dietary intakes for the Chinese population is generally in the same order of magnitude as for other countries, i.e. the Swedish, Belgian and Australian adult population, and far less than the reference dosage value of each OPE (hazard index $\ll 1$); 2) the total dietary intakes of OPEs were dominated by cereals, approximately accounting for 52.2%; and 3) the first reported detection of the novel OP-FR, TPPO, in foodstuff samples.

1. Introduction

Flame retardants (FRs) are a functional accessory ingredient added into combustible materials to avoid fire or slow down the spreading of fire after ignition (Pantelaki and Voutsa, 2019). In recent decades, several traditional FRs, such as polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs), have been listed as Persistent Organic Pollutants (POPs) and phased out of production (UNEP, 2017). As an important class of promising substitutes for regulated FRs, organophosphate esters (OPEs) have emerged and largely used as FRs and plasticizers (Ding et al., 2018; Iqbal et al., 2017). They have been categorized as emerging environmental contaminants attracting more and more public attention in recent years (Iqbal et al., 2017).

Nowadays, OPEs are extensively utilized in various commercial products like electronics, furniture, paint, plastics and textiles (Brandsma et al., 2013; Wei et al., 2015). Most OPEs are generally added into host materials via physical mixing rather than being chemically bonded to polymers. Thus, it is easy for OPEs to be released

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from products containing OPEs and into the environment by volatilization, leaching, abrasion and dissolution during the entire life cycle (Pang et al., 2017). There are a handful of studies verifying that OPEs are ubiquitous in air, surface water, dust, sediment and soil (Chen et al., 2019; Giulivo et al., 2017; Kim and Kannan, 2018; Lee et al., 2018; Li et al., 2014; Persson et al., 2018; Sha et al., 2018; Wang et al., 2018; Yadav et al., 2019; Zha et al., 2018). Humans can be exposed to OPEs via air inhalation, dust ingestion, dermal absorption and dietary intake, etc. (Poma et al., 2017), and they have also been found in human hair, nail, urine and breast milk (He et al., 2018a; Liu et al., 2016; Liu et al., 2015; Sundkvist et al., 2010).

There are some adverse health impacts for animals caused by exposure to OPEs (Page-Lariviere et al., 2018; Shen et al., 2019). For instance, Li et al. (2019b) reported that zebrafish larvae exposed to TCIPP and TCEP can lead to neurotoxicity, which might be ascribed to their similar structures with neurotoxic organophosphorus pesticides (Dishaw et al., 2011). It was confirmed that aryl-OPEs (e.g. TPHP) had more serious heart developmental toxicity than alkyl-OPEs for zebrafish embryos (Du et al., 2015).

Food can be contaminanted with OPEs via biological magnification in food chains (Zhang et al., 2016) and during food production, processing (e.g. packing, caning) or storage (Ding et al., 2018; Poma et al., 2018). There are only few a studies referring to the detection of OPEs in foodstuffs (He et al., 2018b; Li et al., 2019a; Poma et al., 2017; Poma et al., 2018; Zhang et al., 2016). Although the concentrations of OPEs measured in food samples have been reported to be low, high per capita dietary consumption of OPEs via foodstuffs increases the exposure risk via dietary intake (Poma et al., 2017; Wei et al., 2015). Thus, there is an urgent need for the monitoring of OPE contamination in foodstuffs, especially in China which is s populous country that uses and consumes large amounts of FRs (Li et al., 2019a).

In the present study, a total of 11 OPEs including triethyl phosphate (TEP), tributyl phosphate (TNBP), tris(2-chloroethyl) phosphate (TCEP), tris(2-chloroisopropyl) phosphate (TCIPP), tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), triphenyl phosphate (TPHP), 2-ethylhexyl-diphenyl phosphate (EHDPP), tripropyl phosphate (TPrP), tris(2-butoxyethyl) phosphate (TBOEP), tris(2-ethylhexyl) phosphate (TEHP), and tris(methyphenyl) phosphate (TMPP) were examined in foodstuffs sampled from Chinese supermarkets, whereby the per capita exposure to OPEs via the diet as well as an assessment risk were estimated and discussed. Additionally, n = 83 OPEs or organophosphate substances that were previously considered as FRs were further screened for in the combined extracts of foodstuffs by use of high-resolution mass spectrometry (QToF-MS).

2. Materials and methods

2.1. Materials

Standards of the 11 target OPEs and 4 internal standards, d_{15}-TEP, d_{15}-TPHP, d_{12}-TCEP, and d_{15}-TDCIPP, were purchased from Sigma-Aldrich (St. Louis, MO, U.S.A.), AK Scientific (Union City, CA, U.S.A.), or TCI America (Portland, OR, U.S.A.). More information details and mass spectrometry (MS) quantitation parameters can be found in Table S1. All solvents were high performance liquid chromatography (HPLC) grade: dichloromethane (DCM) and methyl alcohol (MeOH) were purchased from Tedia (Fairfield, OH, USA); n-hexane (HEX) was purchased from LiChrosolv (Darmstadt, Germany). Sodium chloride (NaCl) and anhydrous magnesium sulfate ($MgSO_4$) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Sodium sulfate (Na_2SO_4) was purchased from Nanjing Chemical Reagent Co., Ltd. (Nanjing, Jiangsu, China). Primary secondary amine (PSA) bonded silica was purchased from Supelco (Bellefonte, PA, USA). Ultra-pure water produced with an EPED-E2-10TJ system (Yipuyida, Nanjing, Jiangsu, China).

All glassware used in sample preparation and Na_2SO_4 were treated at 450 °C and 600 °C, respectively, for eight hours in muffle furnace prior to use. The weighing spoon used in the weigh process was rinsed with MeOH, DCM and HEX in turn to remove any target organic contamination.

Table 1
Description and per capita daily consumption of the analytical food categories selected according to Jiangsu Statistics Yearbook 2016.

Number	Food categories	Food items	Consumption of food Category homogenate (g ww/day)
1	Cereals (n = 15)	Rice (3), Wheat flour (3), Potato (9)	334.3
2	Vegetables (n = 18)	Chinese cabbage (3), Tomato (9), Shii-take (3), Fresh black fungus (3)	285.1
3	Meat (n = 6)	Pork (3), Beef (3),	71.4
4	Poultry (n = 6)	Chicken (3), Duck (3)	27.2
5	Aquatic products (n = 6)	Carp (3), Clam (3)	47.7
6	Eggs (n = 18)	Fresh egg (9), Salted duck egg (9)	27.9
7	Milk (n = 6)	Milk (3), Yogurt (3)	45.0
8	Fruits (n = 24)	Apple (9), Banana (9), Walnut (3), Sunflower seed (3)	110.7
9	Sweets (n = 6)	White granulated sugar (3), Monocrystal rock candy (3)	17.6

2.2. Sample collection and preparation

According to the Jiangsu Statistics Yearbook 2016, which was regularly updated by Jiangsu Province's Bureau of Statistics (JPBS, 2016), a total of 105 individual samples, falling into 3 food market baskets and 9 food categories covering about 95% total per capita food consumption, were selected and purchased from 3 chain hypermarkets with different supply channels in Nanjing (China) during March and April 2018, as shown in Table 1. The edible parts of food samples were immediately homogenized after collection and then stored in brown glass jar capped with aluminum foil and a polyethylene (PE) screw cap at −20 °C until further pretreatment.

The preparation method of food samples was modified based on an OPE method developed previously by Chu and Letcher. (2015). In brief, about 1 g of homogenized food sample in wet weight (ww) was weighed into a borosilicate glass disposable culture tube (16 × 100 mm). 4 mL of 50/50 (v/v) DCM/HEX as the extract solvent, IS, 0.2 g NaCl and 1.5 g $MgSO_4$ were then added into a sample tube and mixed well by vortexing. The sample was extracted with ultrasound-assistance for 10 min at 20 °C, and then centrifuged. The supernatant was transferred into a clean glass centrifuge tube (10 mL). The extraction process was repeated twice and the extracts were combined. The extract was concentrated with nitrogen to dryness at 40 °C and then re-dissolved in 1 mL MeOH. The sample was subject to ultra-sonication for 10 min. Then, 0.1 g $NaSO_4$ was added into the extract and mixed well. After centrifugation, the supernatant of the MeOH phase was carefully transferred into another clean glass centrifuge tube and 300 mg of PSA bonded silica was added. This extract was subjected to dispersive solid phase extraction for 1 min, and then centrifuged. The supernatant was carefully transferred into an autosampler vial and stored at −20 °C until further instrumental analysis.

2.3. Quantification of OPEs by use of liquid chromatography-tandem mass spectrometer (LC-MS/MS)

Quantification of OPEs was carried out using a Waters XEVO-TQ-S ultra-high performance liquid chromatography-tandem mass spectrometer (UPLC-MS/MS) with a positive atmospheric pressure chemical ionization source (APCI+) (Waters Limited, Milford, USA). More details on the instrumental parameters can be found elsewhere (Chu and Letcher, 2015; Su et al., 2016). In brief, OPEs were separated by use of a Waters Cortecs™ UPLC® C18 column (1.6 μm particle size, 2.1 × 50 mm) (Waters Limited, Milford, USA). The injection volume was 5 μL. The mobile phases were water (A) and methanol at a flow rate of 0.5 mL/min. We set the gradient as follows: 95% A initially, decreased to 5% A in 3 min, and held for 8 min, and then returned to initial 95% A for 4 min. For the MS, the nebulization and desolvation gas for both was nitrogen, and the collision gas was argon. The corona voltage was 3.0 kV, and the APCI probe was operated at a temperature of 400 °C. The flow rates of desolvation and cone gas were set as 1000 and 150 L/h, respectively.

To ensure good recoveries of the target analytes, three potato/pork (from one sample supermarket) samples spiked with OPE standards were analyzed and good recoveries were observed for all investigated OPEs. For all the OPEs, standard recoveries were achieved from 40.8% to 135.9%, and the relative standard deviations (RSDs) were < 22.0% (Table 2). Some background contamination was observed for TNBP, TCEP, TCIPP, TDCIPP TPHP, EHDPP and TBOEP. Thus, for each batch of extractions, one procedural blank was also included to investigate the possible laboratory contamination during the analysis. The blank concentrations were subtracted from the values found in the samples in their batch. The MLOQs were ranged from 0.01 to 0.36 ng/g ww based on a signal-to-noise ratio (S/N) of 10 (Table S2). OPE quantification was via an IS approach.

2.4. Data analysis

Excel 2016 and GraphPad Prism 5 software were used for data calculations, statistical analyses and presentation. For the significance analysis, one-way analysis of variance (ANOVA) was used to compare three or more sets of data, and an unpaired *t*-test compared just two groups, and where the significance level was set at 0.05. For non-quantifiable OPEs, concentration values were assigned as half of the quantification levels (< MLOQ = 1/2 MLOQ).

2.5. Estimated dietary intakes (EDI) and risk assessment

The calculation of human daily intake via food ingestion was based on the following formula (Ding et al., 2018; Zhang et al., 2016):

$$\mathrm{EDI} = \frac{\sum_{i=1}^{n} c_i \times CF_i}{BW} \quad (1)$$

where EDI was the nanogram dietary intake of the target OPEs per kilogram of body weight per day (ng/kg bw/day), c_i was the mean/95th percentile concentrations of the target OPEs in each food category (ng/g); CF_i was the daily per capita consumption of the corresponding food category (g/day), which was obtained from Jiangsu Statistics Yearbook 2016 and listed in Table 1 (JPBS, 2016); BW was the average body weight (kg) of the Chinese population and here 58.7 kg was used (Yang et al., 2005).

Hazard quotient (HQ) and hazard index (HI) values were considered as critical indicators to judge whether OPEs would pose a risk to human health. Their values were calculated by the following formula (Ding et al., 2018):

$$\mathrm{HQ} = \frac{EDI}{RfD} \quad (2)$$

$$\mathrm{HI} = \sum HQ \quad (3)$$

where RfD was the reference dosage values of oral toxicity (ng/kg bw/day) for each target OPE, and they were acquired from previous literature studies where RfD was calculated via dividing the chronic no-observed adverse effect levels by a safety factor (1000) or provided by United States Environmental Protection Agency (USEPA) Integrated Risk Information System (Ding et al., 2018; He et al., 2018b; Zhang et al., 2016). When the RfD value for an individual compound was available from more than one source, the most conservative RfD value was used.

2.6. Suspect screening in the extract of foodstuffs by use of high-resolution spectrometry system

The extracts of 105 foodstuff samples were combined and further conducted for OPE suspect screening by use of a high-resolution spectrometry system, that is an Agilent 1200 LC system coupled with an 6520A QToF-MS system (Agilent Technologies, Mississauga, ON, Canada). The MS system was equipped with a positive electrospray ionization (ESI^+) source. Separation of OPE compounds was conducted on a Luna C18 column (Phenomenex, Torrance, CA, U.S.A.). Water (A) and methanol (B), both containing 2 mM of ammonium acetate, were used as mobile phases with a constant flow rate of 0.5 mL/min. The mobile phase gradient was: 0 min, 95% A; 0–5 min, 5% A; hold for 10 min; and post run for 15 min. Before the analysis, the MS system was tuned and calibrated with the resolution > 20,000 at *m/z* 322.0481 (Δ = 0.01 ppm). For each run of injections, a solution containing purine (theoretical *m/z* 121.0509) and HP-0921 (theoretical *m/z* 922.0098) were consistently transferred into high-resolution system as reference masses.

Table 2
Standard recoveries (SRs) and relative standard deviation (RSD) of target OPEs measured in spiked potato and pork samples.

OPEs	Potato (n = 3)		Pork (n = 3)	
	SR (%)	RSD (%)	SR (%)	RSD (%)
TEP	85.5–91.5	3.9	81.1–94.9	8.4
TNBP	86.4–97.3	6.5	74.1–88.8	9.4
TCEP	84.2–102.1	9.6	87.2–98.1	6.1
TCIPP	93.9–100.4	3.7	69.6–82.9	8.8
TDCIPP	77.2–87.6	6.8	80.3–85.2	3.4
TPHP	72.2–109.2	22.0	81.6–98.3	9.4
EHDPP	85.1–107.4	11.7	121.8–135.9	5.5
TPrP	57.6–68.6	9.0	67.8–86.4	12.7
TBOEP	40.8–60.8	21.3	73.3–79.9	4.7
TEHP	110.0–124.6	6.8	107.6–116.0	4.0
TMPP	98.0–128.0	14.1	106.6–112.4	2.8

3. Results and discussion

3.1. Occurrence of OPEs in Chinese foodstuffs

In our study, the measured concentrations of 9 OPEs in all food categories including TEP, TNBP, TCEP, TCIPP, TPHP, EHDPP, TBOEP, TEHP and TMPP were all above the MLOQs (Table 3a). Two other OPEs, TDCIPP and TPrP, were not detected any of the food samples, so they were not considered in the following diagrams and discussion.

To investigate the variance of TEP, TNBP, TCEP, TCIPP, TPHP, EHDPP, TBOEP, TEHP and TMPP levels among food items, food categories and sampling positions, we analyzed 23 items belonging to 9 food categories individually sampled from 3 large chain supermarkets in Nanjing. The items collected included those from the same food category within the identical supermarket, those obtained from the same supermarket, and across all the food items collected from different

Table 3a
Overall demographic data of OPEs (ng/g ww) levels in various food categories on basis of a typical Chinese food market basket.

Statistics	TEP	TNBP	TCEP	TCIPP	TPHP	EHDPP	TBOEP	TEHP	TMPP	ΣOPEs
Cereals (n = 15)										
Range[a]	< 0.07–2.7	< 0.02–0.3	< 0.03–18.5	< 0.02	< 0.10–0.4	< 0.16–5.0	< 0.02–0.1	< 0.03	< 0.01	< 0.23–21.0
Median[b]	0.04	0.09	0.02	0.01	0.05	0.08	0.01	0.015	0.005	0.92
Mean[c]	0.54	0.10	2.47	0.01	0.11	0.76	0.05	0.015	0.005	4.06
SD[d]	0.85	0.11	6.12	0	0.12	1.45	0.04	0	0	6.45
CI[e]	(0.11, 0.97)	(0.05, 0.16)	(−0.63, 5.57)	(0.01, 0.01)	(0.04, 0.17)	(0.03, 1.49)	(0.03, 0.07)	(0.015, 0.015)	(0.005, 0.005)	(0.79, 7.32)
DF[f] (%)	46.7	53.3	20.0	0	20.0	26.7	46.7	0	0	73.3
Vegetables (n = 18)										
Range	< 0.07–10.0	< 0.02–0.5	< 0.03	< 0.02	< 0.10–0.5	< 0.16	< 0.02–0.2	< 0.03	< 0.01	< 0.23–10.2
Median	0.04	0.05	0.015	0.01	0.05	0.08	0.01	0.015	0.005	0.45
Mean	0.69	0.13	0.015	0.01	0.08	0.08	0.04	0.015	0.005	1.07
SD	2.34	0.16	0	0	0.12	0	0.05	0	0	2.31
CI	(−0.39, 1.78)	(0.06, 0.21)	(0.015, 0.015)	(0.01, 0.01)	(0.02, 0.13)	(0.08, 0.08)	(0.02, 0.06)	(0.015, 0.015)	(0.005, 0.005)	(0.00, 2.14)
DF (%)	38.9	50.0	0	0	5.6	0	27.8	0	0	66.7
Meat (n = 6)										
Range	0.1–2.0	< 0.02–0.1	< 0.03	< 0.02	< 0.10–3.2	< 0.16–0.2	< 0.02–0.1	< 0.03	< 0.01	0.3–4.0
Median	0.89	0.01	0.015	0.01	0.05	0.08	0.01	0.015	0.005	2.00
Mean	0.94	0.04	0.015	0.01	0.68	0.10	0.02	0.015	0.005	1.82
SD	0.81	0.04	0	0	1.25	0.05	0.03	0	0	1.34
CI	(0.29, 1.59)	(0.00, 0.07)	(0.015, 0.015)	(0.01, 0.01)	(−0.33, 1.68)	(0.06, 0.14)	(0.00, 0.05)	(0.015, 0.015)	(0.005, 0.005)	(0.75, 2.89)
DF (%)	100	33.3	0	0	33.3	16.7	16.7	0	0	100
Poultry (n = 6)										
Range	0.3–1.9	< 0.02–0.2	< 0.03	< 0.02	< 0.10–0.3	< 0.16	< 0.02–0.1	< 0.03	< 0.01	0.6–2.1
Median	1.08	0.01	0.015	0.01	0.12	0.08	0.01	0.015	0.005	1.40
Mean	1.08	0.04	0.015	0.01	0.14	0.08	0.04	0.015	0.005	1.42
SD	0.62	0.07	0	0	0.10	0	0.04	0	0	0.65
CI	(0.58, 1.57)	(−0.02, 0.10)	(0.015, 0.015)	(0.01, 0.01)	(0.06, 0.22)	(0.08, 0.08)	(0.00, 0.07)	(0.015, 0.015)	(0.005, 0.005)	(0.89, 1.94)
DF (%)	100	16.7	0	0	50.0	0	33.3	0	0	100
Aquatic products (n = 6)										
Range	0.8–3.0	< 0.02–1.0	< 0.03	< 0.02	< 0.10–0.3	< 0.16	< 0.02–0.1	< 0.03	< 0.01	1.3–3.4
Median	1.47	0.14	0.015	0.01	0.05	0.08	0.01	0.015	0.005	1.83
Mean	1.66	0.31	0.015	0.01	0.09	0.08	0.02	0.015	0.005	2.20
SD	0.81	0.38	0	0	0.09	0	0.03	0	0	0.95
CI	(1.01, 2.31)	(0.00, 0.61)	(0.015, 0.015)	(0.01, 0.01)	(0.01, 0.16)	(0.08, 0.08)	(0.00, 0.05)	(0.015, 0.015)	(0.005, 0.005)	(1.44, 2.96)
DF (%)	100	66.7	0	0	16.7	0	16.7	0	0	100
Eggs (n = 18)										
Range	0.3–4.2	< 0.02–1.5	< 0.03	< 0.02	< 0.10–3.0	< 0.16–71.8	< 0.02–0.3	< 0.03	< 0.01	0.9–73.7
Median	1.25	0.29	0.015	0.01	0.05	0.08	0.01	0.015	0.005	2.12
Mean	1.65	0.28	0.015	0.01	0.26	4.06	0.06	0.015	0.005	6.35
SD	0.94	0.34	0	0	0.69	16.90	0.08	0	0	16.86
CI	(1.21, 2.08)	(0.13, 0.44)	(0.015, 0.015)	(0.01, 0.01)	(−0.06, 0.58)	(−3.74, 11.87)	(0.02, 0.09)	(0.015, 0.015)	(0.005, 0.005)	(−1.43, 14.14)
DF (%)	100	72.2	0	0	22.2	5.6	38.9	0	0	100
Milk (n = 6)										
Range	0.6–2.0	< 0.02–0.2	< 0.03	< 0.02	< 0.10–0.3	< 0.16	< 0.02–0.1	< 0.03	< 0.01	1.0–2.6
Median	1.14	0.09	0.015	0.01	0.12	0.08	0.05	0.015	0.005	1.51
Mean	1.29	0.10	0.015	0.01	0.14	0.08	0.05	0.015	0.005	1.70
SD	0.61	0.06	0	0	0.10	0	0.05	0	0	0.64
CI	(0.80, 1.77)	(0.05, 0.14)	(0.015, 0.015)	(0.01, 0.01)	(0.06, 0.22)	(0.08, 0.08)	(0.02, 0.09)	(0.015, 0.015)	(0.005, 0.005)	(1.18, 2.21)
DF (%)	100	83.3	0	0	50.0	0	50.0	0	0	100
Fruits (n = 24)										
Range	< 0.07–4.9	< 0.02–0.6	< 0.03	< 0.02	< 0.10–1.4	< 0.16	< 0.02–0.1	< 0.03–6.5	< 0.01–0.7	< 0.23–7.3
Median	0.14	0.10	0.015	0.01	0.05	0.08	0.01	0.02	0.01	1.17
Mean	0.79	0.14	0.015	0.01	0.20	0.08	0.05	0.71	0.07	2.07
SD	1.26	0.13	0	0	0.29	0	0.04	1.89	0.17	2.32
CI	(0.29, 1.30)	(0.08, 0.19)	(0.015, 0.015)	(0.01, 0.01)	(0.08, 0.32)	(0.08, 0.08)	(0.03, 0.06)	(−0.04, 1.47)	(0.00, 0.14)	(1.14, 3.00)
DF (%)	58.3	83.3	0	0	41.7	0	41.7	16.7	16.7	95.8
Sweet (n = 6)										
Range	< 0.07–0.2	< 0.02–0.2	< 0.03–1.1	< 0.02–13.1	< 0.10–0.3	< 0.16–26.3	< 0.02–0.1	< 0.03	< 0.01–0.1	< 0.23–26.9
Median	0.04	0.05	0.29	3.14	0.12	0.08	0.01	0.015	0.01	9.34
Mean	0.06	0.07	0.39	5.06	0.15	4.54	0.02	0.015	0.04	10.34
SD	0.07	0.07	0.41	5.74	0.12	10.67	0.04	0	0.05	9.84
CI	(0.01, 0.11)	(0.01, 0.13)	(0.07, 0.72)	(0.47, 9.65)	(0.06, 0.25)	(−4.00, 13.07)	(0.00, 0.05)	(0.015, 0.015)	(0.00, 0.07)	(2.47, 18.22)
DF (%)	16.7	50.0	66.7	66.7	50.0	33.3	16.7	0	33.3	83.3

[a] Range: concentration range.
[b] Median: median concentration.
[c] Mean: arithmetic mean concentration.
[d] SD: standard deviation.
[e] CI: confidence interval (95%).
[f] DF: detection frequency.

supermarkets. Compared with different items (mean RSD of 66%) and different sampling positions (mean RSD of 66%), the difference among food categories was relatively high (mean RSD of 107%). This indicated that the variance was at most a function of food categories. Furthermore, the significance analysis among food items, food categories and sampling positions were conducted and the outcomes are shown in Tables S3 ~ S5. The levels of ΣOPEs (sum of 9 target OPEs) measured in milk products were higher than in yogurt (unpaired *t*-test, $p < 0.05$), and the levels of ΣOPEs in sweets products were significantly higher than the other food categories (one-way ANOVA, $p < 0.01$). The contamination source is currently unknown for OPEs in sweets, but could be related with its complex food processing or packaging. Interestingly, EHDPP is traditionally proposed as an additive by the U.S. Food and Drug Administration (US-FDA), and we observed that ΣOPEs in sweets was dominated by this chemical. With respect to the rest food items/categories or sampling supermarkets, significant differences were not observed.

The detection frequencies of ΣOPEs in 9 food categories for 105 samples ranged from 66.7% in vegetables to 100% in meat, poultry, aquatic products, eggs and milk. TEP and TNBP, as the most prevalent OPEs in all samples, were detected in 67.6% and 61.9% of samples, respectively, followed by TBOEP and TPHP with the percentage of detection of ~30%, and the other targeted OPEs were detected in < 10% of the samples. These differences might be associated with MLOQs, physicochemical properties, half-lives, and degradation/metabolism of OPEs (He et al., 2018b). Moreover, the detection frequencies of the OPEs were lower as compared to halogenated FRs in foodstuffs sampled from the same area (Su et al., 2012), which was probably attributed to their low concentrations in foodstuffs or due to lower accumulation through the food chain (Van der Veen and De Boer, 2012). The conclusion that OPEs could be metabolized/excreted rapidly in organisms, with hours of half-lives for OPE parent compounds and their metabolites reinforced our statement (Greaves et al., 2016; Su et al., 2014; Van den Eede et al., 2013; Van den Eede et al., 2016).

As shown in Fig. 1, the distribution and contribution of OPEs in the analyzed foodstuffs were analyzed and calculated. For each OPE, the proportion of its total contents in all food categories was ranked in the order from highest to lowest: EHDPP (33.6%), TEP (28.5%), TCEP (11.7%), TCIPP (9.0%), TPHP (5.6%), TEHP (5.3%), TNBP (4.5%), TBOEP (1.3%) and TMPP (0.7%). For individual food categories, TEP was the most dominant OPE in the various food categories including aquatic products (1.66 ng/g ww, 75.2%), meat (0.94 ng/g ww, 51.6%), milk (1.29 ng/g ww, 75.7%), poultry (1.08 ng/g ww, 75.9%) and vegetables (0.69 ng/g ww, 65.0%). TEP (0.79 ng/g ww, 38.4%) and TEHP

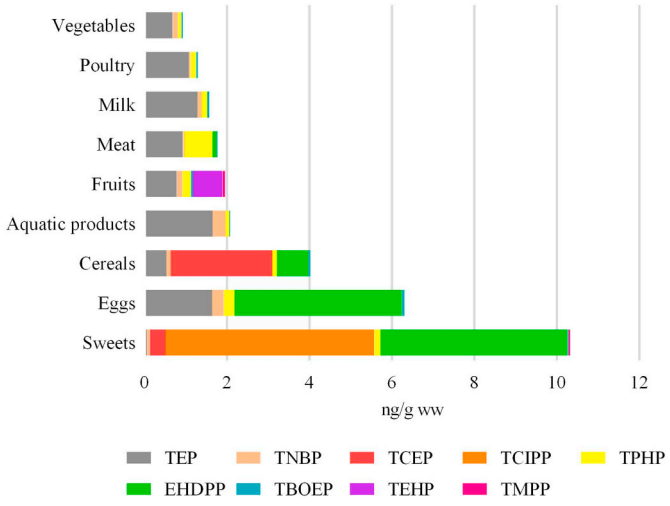

Fig. 1. Distribution of individual OPEs (mean concentration, ng/g ww) in different foodstuff categories.

(0.71 ng/g ww) were the dominant contaminants in fruits, accounting for 38.4% and 34.5% of the ΣOPE concentration, respectively. TCEP (2.47 ng/g ww) accounted for the greatest proportion of the ΣOPE concentration at 60.9%. EHDPP was mainly distributed in sweets (4.54 ng/g ww, 43.8%) and eggs (4.06 ng/g ww, 64.0%). TCIPP (5.06 ng/g ww) was also mainly found in sweets with 48.9% of the ΣOPE concentration. The distributions of the rest of the OPEs in each food categories were more homogeneous. EHDPP detected in food samples may have been derived from food packaging materials where EHDPP is an additive as reported by the U.S. Food and Drug Administration (US-FDA) (US-FDA, 2006), while TPHP is generally found in electrical equipment (e.g. cell phones), with high levels in indoor dust which can be deposited in industrial facilities (Van der Veen and De Boer, 2012; Yang et al., 2019). The source of remaining OPEs under study is not known to our knowledge.

The levels of ΣOPEs in our investigated food categories was consistent with findings from previous studies in Australia (2.46 ng/g ww in meat to 4.13 ng/g ww in vegetables) (He et al., 2018b), Belgium (0.41 ng/g ww in vegetables to 36.87 ng/g ww in cereals) (Poma et al., 2018) and Sweden (1.04 ng/g ww in fruits to 6.37 ng/g ww in cereals) (Poma et al., 2017). For all 9 of the present food categories, sweets had the highest mean concentration of ΣOPEs (10.34 ng/g ww), followed by eggs (6.35 ng/g ww), cereals (4.06 ng/g of ww), aquatic products (2.20 ng/g ww), fruits (2.07 ng/g ww), meat (1.82 ng/g ww), milk (1.70 ng/g ww), poultry (1.42 ng/g ww) and vegetables (1.07 ng/g ww) (Fig. 1). These differences might be explained by contrasting absorption of OPEs in these foods, food processing, and/or metabolic capacity of animal-based foods and plant-based foods. Moreover, the ΣOPE concentrations of most food categories were lower than those detected in Australia and Belgium (He et al., 2018b; Poma et al., 2018), while higher than those reported in Sweden (Poma et al., 2017).

Poma et al. (2017, 2018) found that the levels of OPEs in "processed foods" were higher than in "non-processed foods", implying that there is an important link of food contamination by OPEs with industrial and manipulated processing. We divided the 23 food items into two food groups as listed in Table S6. The contributions of each OPE to the total in the two groups were inhomogeneous and totally different (Table 3b). The processed food contained 16 food items, which accounted for only 36.7% of mean ΣOPEs concentration in each food item. The mean ΣOPE concentrations of processed food were significantly higher than those of non-processed food (unpaired *t*-test, $p = 0.0003$). These outcomes were consistent with the findings of Poma et al. (2017, 2018) where the most OPE contaminated food items were rice (mean: 13.01 ng/g ww, 16.2%), white granulated sugar (11.60 ng/g ww, 14.5%) and salted duck eggs (10.52 ng/g ww, 13.1%). Furthermore, foodstuffs of animal origin, including pig, beef, chicken, duck, carp, clam and fresh eggs, each contributed marginally to the overall OPE distribution (< 2.8 ng/g ww, < 3.5%). This might be associated with rapid metabolism/excretion (Greaves et al., 2016) or lower exposure and uptake in the organism.

3.2. Estimation of human dietary exposure to OPEs

On the basis of the measured concentrations of the target OPEs in 9 food categories, and based on the general Chinese dietary habits and their consumption data from the Jiangsu Statistics Yearbook 2016, we estimated EDI values of OPEs for the Chinese adult population using Eq. (1). The mean and 95th percentile concentrations of all samples in a given food category represented correspondingly the average- and high-exposure scenarios of the same food category to humans, respectively, and are listed in Table 4.

For the average adult population, the mean and 95th percentile total EDI values of OPEs were calculated to be 44.3 and 75.8 (ng/kg bw/day), respectively, which are of the same order of magnitude compared to data from previous studies on the Swedish, Belgian and Australian adult populations, where the mean intake via diet was estimated to be

Table 3b
Overall demographic data of OPEs (ng/g ww) levels in various food groups on basis of a typical Chinese food market basket.

Statistics	TEP	TNBP	TCEP	TCIPP	TPHP	EHDPP	TBOEP	TEHP	TMPP	ΣOPEs
Processed food groups										
Range	< 0.07–2.9	< 0.02–0.6	< 0.03–18.5	< 0.02–13.1	< 0.10–3.0	< 0.16–71.8	< 0.02–0.2	< 0.03	< 0.01–0.1	< 0.23–73.7
Median	0.89	0.10	0.02	0.01	0.05	0.08	0.01	0.015	0.01	2.68
Mean	1.11	0.15	1.58	1.22	0.26	4.10	0.04	0.015	0.01	8.50
SD	0.97	0.16	4.81	3.42	0.58	15.04	0.05	0	0.03	15.30
CI	(0.75, 1.48)	(0.09, 0.21)	(−0.24, 3.39)	(−0.07, 2.51)	(0.04, 0.48)	(−1.57, 9.77)	(0.03, 0.06)	(0.015, 0.015)	(0.00, 0.02)	(2.72, 14.27)
DF (%)	77.8	66.7	25.9	14.8	40.7	18.5	37.0	0	7.4	96.3
Non-processed food groups										
Range	< 0.07–10.0	< 0.02–1.5	< 0.03	< 0.02	< 0.10–3.2	< 0.16–5.0	< 0.02–0.3	< 0.03–6.5	< 0.01–0.7	< 0.23–10.2
Median	0.30	0.09	0.015	0.01	0.05	0.08	0.01	0.02	0.01	1.05
Mean	0.89	0.15	0.015	0.01	0.17	0.18	0.04	0.23	0.03	1.71
SD	1.46	0.23	0	0	0.40	0.66	0.05	1.08	0.10	1.95
CI	(0.56, 1.21)	(0.10, 0.20)	(0.015, 0.015)	(0.01, 0.01)	(0.08, 0.25)	(0.04, 0.33)	(0.03, 0.05)	(−0.01, 0.47)	(0.00, 0.05)	(1.28, 2.14)
DF (%)	64.1	60.3	0	0	24.4	3.8	34.6	5.1	5.1	100
ΣOPEs										
Range	< 0.07–10.0	< 0.02–1.5	< 0.03–18.5	< 0.02–13.1	< 0.10–3.2	< 0.16–71.8	< 0.02–0.3	< 0.03–6.5	< 0.01–0.7	< 0.23–73.7
Median	0.50	0.10	0.02	0.01	0.05	0.08	0.01	0.02	0.01	1.50
Mean	0.95	0.15	0.39	0.30	0.19	1.12	0.04	0.17	0.02	3.32
SD	1.34	0.21	2.41	1.72	0.44	7.44	0.05	0.94	0.09	8.08
CI	(0.69, 1.20)	(0.11, 0.19)	(−0.07, 0.85)	(−0.03, 0.63)	(0.10, 0.27)	(−0.31, 2.54)	(0.03, 0.05)	(0.00, 0.35)	(0.01, 0.04)	(1.78, 4.87)
DF (%)	67.6	61.9	6.7	3.8	28.6	7.6	35.2	3.8	5.7	88.6

84.7 ng/g bw day, 106.1 ng/kg bw/day for male (and 93.2 ng/kg bw/day for female) and 40.8 ng/g bw/day, respectively (Table 4) (He et al., 2018b; Poma et al., 2017; Poma et al., 2018). The contributions of all analyzed food categories and the target OPEs to mean total dietary intake is illustrated in Fig. 3 (Poma et al., 2017; Poma et al., 2018; Zhang et al., 2016). Cereals were the greatest contributor to human exposure to OPEs through dietary intake. TCEP (32.4%, 14.3 ng/kg bw/day), TEP (28.7%, 12.7 ng/kg bw/day) and EHDPP (19.1%, 8.4 ng/kg bw/day) were found to be the primary contaminants followed by TPHP (5.8%, 2.6 ng/kg bw/day), TNBP (4.6%, 2.0 ng/kg bw/day), TCIPP (3.8%, 1.7 ng/kg bw/day), TEHP (3.5%, 1.6 ng/kg bw/day), TBOEP (1.6%, 0.7 ng/kg bw/day) and TMPP (0.5%, 0.2 ng/kg bw/day). With regard to OPEs in specific food categories, cereals (TCEP 98.1%, EHDPP 51.2% and TEP 24.1%) and vegetables (TEP 26.5%) accounted for a major contribution to TCEP, TEP and/or EHDPP dietary intake. Nevertheless, Poma et al. (2018) reported that the distribution of OPEs to the total dietary intake for Belgian adults was in the order of TPHP (45%, 46.6 ng/kg bw/day) > TCIPP (18%, 18.5 ng/kg bw/day) > EHDPP (15%, 14.9 ng/kg bw/day) > TDCIPP (9%, 9.6 ng/kg bw/day) > TNBP (5%, 5.5 ng/kg bw/day) > TEHP (5%, 4.9 ng/kg bw/day) > TCEP (3%, 2.8 ng/kg bw/day) (Poma et al., 2018), and the mean EDI values of ΣOPEs from different food categories ranged from 0.7 to 23.1 ng/kg bw/day. Comparing common food categories in the present and previous studies, in our study the order was 1) cereals (52.2%), vegetables (11.7%), eggs (6.8%), meat (5.0%), aquatic products (4.0%) and milk (2.9%), whereas the order was cereals (42 and 39%), meat (6 and 7%), egg (0.1 and 0.9%), milk, vegetables and aquatic products (20%, 6% and 4%) in Belgium and Swedish studies, respectively (Poma et al., 2017; Poma et al., 2018). The contamination profile regarding both OPE pattern or food category in our study were different with those previous studies, which may be associated with various factors such as dietary habits among different regions, number and items of collected food samples and sample preparation.

3.3. Risk assessment of OPEs via dietary intakes pathway

According to the definition given by USEPA, RfD value represents the threshold limit value of a chemical compound via daily oral exposure to human body and is regarded as an important indicator of risk assessment of human exposure to noncarcinogenic toxic substances

Table 4
Estimation of daily per capita dietary intakes and risk assessment exposure to OPEs for Chinese adults.

Food categories	TEP	TNBP	TCEP	TCIPP	TPHP	EHDPP	TBOEP	TEHP	TMPP	ΣOPEs (ng/day)	EDI (ng/kg bw/day)
Cereals	180 (324)	34 (53)	826 (1862)	3.3 (3.3)	35 (57)	254 (498)	17 (23)	5.0 (5.0)	1.7 (1.7)	1356 (2447)	23.1 (41.7)
Vegetables	198 (508)	38 (60)	4.3 (4.3)	2.9 (2.9)	22 (37)	23 (23)	11 (17)	4.3 (4.3)	1.4 (1.4)	304 (610)	5.2 (10.4)
Meat	67 (114)	2.8 (5.0)	1.1 (1.1)	0.7 (0.7)	48 (120)	7.0 (10)	1.7 (3.6)	1.1 (1.1)	0.4 (0.4)	130 (206)	2.2 (3.5)
Poultry	29 (43)	1.1 (2.7)	0.4 (0.4)	0.3 (0.3)	3.7 (6.0)	2.2 (2.2)	1.1 (1.9)	0.4 (0.4)	0.1 (0.1)	39 (53)	0.7 (0.9)
Aquatic products	79 (110)	15 (29)	0.7 (0.7)	0.5 (0.5)	4.2 (7.6)	3.8 (3.8)	1.2 (2.4)	0.7 (0.7)	0.2 (0.2)	105 (141)	1.8 (2.4)
Eggs	46 (58)	7.9 (12)	0.4 (0.4)	0.3 (0.3)	7.2 (16)	113 (331)	1.6 (2.5)	0.4 (0.4)	0.1 (0.1)	177 (395)	3.0 (6.7)
Milk	58 (80)	4.4 (6.3)	0.7 (0.7)	0.4 (0.4)	6.2 (10)	3.6 (3.6)	2.4 (4.0)	0.7 (0.7)	0.2 (0.2)	76 (99)	1.3 (1.7)
Fruits	88 (144)	15 (21)	1.7 (1.7)	1.1 (1.1)	22 (35)	8.9 (9)	5.1 (6.6)	79 (163)	8.0 (15)	229 (332)	3.9 (5.7)
Sweet	1.1 (1.9)	1.2 (2.3)	6.9 (13)	89 (170)	2.7 (4.4)	80 (230)	0.4 (0.9)	0.3 (0.3)	0.6 (1.2)	182 (321)	3.1 (5.5)
ΣFood categories (ng/day)	746 (1382)	119 (192)	842 (1884)	99 (180)	152 (293)	496 (1111)	41 (62)	92 (176)	13 (21)	2599 (4605)	44.3 (78.5)
EDI[a] (ng/kg bw/day)	12.7 (23.5)	2.0 (3.3)	14.3 (32.1)	1.7 (3.1)	2.6 (5.0)	8.4 (18.9)	0.7 (1.1)	1.6 (3.0)	0.2 (0.4)	44.3 (78.5)	44.3 (78.5)
RfD[b] (ng/kg bw/day)	125,000	2400	2200	3600	7000	600	1500	35,000	1300	–	–
Hazard Quotient (‰)	1.0 (1.9)	8.4 (13.6)	65.2 (145.9)	4.7 (8.5)	3.7 (7.1)	140.7 (315.5)	4.7 (7.1)	0.4 (0.9)	1.7 (2.7)	230.5 (503.2)	— (—)

[a] EDI: estimated dietary intakes.
[b] RfD: reference does.

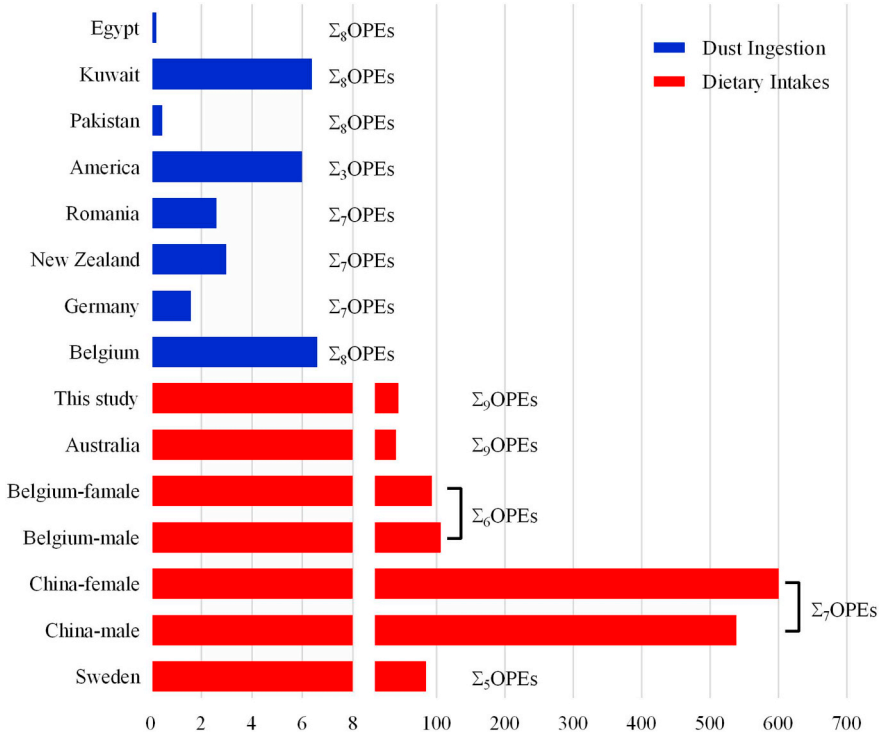

Fig. 2. Comparison of two major exposure pathways to OPEs for humans, including typical high (P50) dust ingestion and mean dietary intakes (ng/kg bw/day).

(USEPA, 2018). Regardless of mean or 95th percentile EDI values of each target OPE via diet, the values were several orders of magnitude lower than the corresponding RfD values, with HI (2.31×10^{-2} and 5.03×10^{-2}, respectively) ≪1. Moreover, in the data analysis the EDI values could be enhanced using 1/2 MLOQ instead of the detected concentrations of OPEs less than MLOQ. As such, there appears to be insignificant deleterious effects via diet ingested OPEs for Chinese adults during the entire life cycle.

Dietary intake and dust inhalation are regarded as principal routes of exposure of OPEs for the general population (Wei et al., 2015). A comparison was conducted for EDI values of the OPEs via dietary intake and via dust ingestion for adults. As depicted in Fig. 2, all the EDI values of OPEs from foodstuffs for adult population via diet were higher than those estimated typical high (P50) ranges of OPE exposure via dust ingestion for adults (Abdallah and Covaci, 2014; Ali et al., 2013; Ali et al., 2012; Brommer et al., 2012; Dirtu et al., 2012; Stapleton et al., 2009; Van den Eede et al., 2011). Dietary intake might be of equal importance with dust ingestion exposure to OPEs for humans or possibly is more important. However, in the past researchers paid more attention to dust ingestion for human exposure to OPEs due to the high concentrations of OPEs in dust (μg/g range), which were approximately 3 orders of magnitude higher than in foodstuffs (ng/g range) (He et al., 2018b; Poma et al., 2017; Poma et al., 2018; Van der Veen and De Boer, 2012). Therefore, it is important to analyze the levels of OPEs in more foodstuffs and assessment of human exposure to OPEs through dietary intake to assess the potential harm to the human health.

3.4. Suspect screening of 83 organophosphate substances in the combined foodstuff extracts

By searching the scientific literature in the Web of Science database, we found 83 OPEs or OP substances, including the 11 OPEs measured in this study, have been reported as FRs and detected somewhere in the environment (Table S7). To investigate whether other OP substances are present in the foodstuff samples, we carried out a suspect screening exercise on the combined extracts of foodstuffs by high-resolution mass spectrometry. Interestingly, in addition to 9 OPEs quantified in foodstuffs, we detected an ion of *m/z* 279.0934 in the same samples, and this ion was absent in the blank samples. This ion was presumed to be triphenyl phosphine oxide (TPPO) with a theoretical formula of $C_{18}H_{15}O_1P_1$ with $[M + H]^-$ of *m/z* 279.0933. The response intensity of the *m/z* 279.0934 ion was lower, but within an order of magnitude to the response of TPHP (Fig. 4).

TPPO does not have the basic structure of an OPE, but shares a very comparable chemical structure with TPHP. TPPO was traditionally employed as an intermediate in chemical reactions for pharmaceutical products and as a ligand for metal centers, and this chemical was recently proposed as alternative FR for brominated formulations in textile back-coatings (Bollmann et al., 2012; Van der Veen and De Boer, 2012). Extensive industrial production and usage has led to an increase detection frequency of TPPO in various environmental matrices, i.e. wastewater effluent, natural river water, indoor air (Faiz et al., 2016; Rodil et al., 2012; Schlusener et al., 2015; Wang et al., 2015; Wang et al., 2017). Our study provides the first evidence that TPPO might also exist in foodstuff samples, prompting the need for action to understand the assessment of risk to human health via food dietary intake.

4. Conclusion

Overall, 11 OPEs were analyzed in 105 foodstuff samples collected in 2018 on the basis of a typical Chinese food market basket, and 9 OPEs were detectable in at least one of analyzed samples. Regardless of the food category, the proportion of concentration of individual OPEs to the Σ9OPEs was ranked in the order from highest to lowest: EHDPP (33.6%), TEP (28.5%), TCEP (11.7%), TCIPP (9.0%), TPHP (5.6%), TEHP (5.3%), TNBP (4.5%), TBOEP (1.3%) and TMPP (0.7%), and potentially suggesting that EHDPP, TEP, and TCEP are the predominant OPEs in Chinese foodstuff samples. Different food categories exhibited different contamination profiles of OPEs, and it is worth noting that we observed statistically significant differences (unpaired *t*-test, $p = 0.0003$) for the mean ΣOPEs concentrations between processed food and non-processed food. The processed food was mainly contaminated by EHDPP. Further estimation of human dietary exposure to OPEs suggested that the mean EDI values of ΣOPEs for Chinese

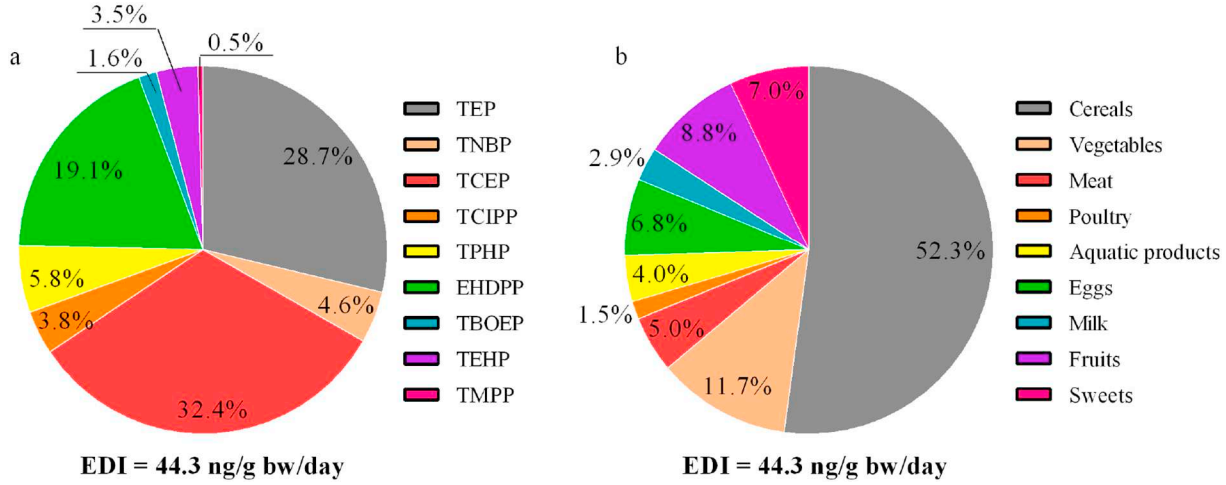

Fig. 3. Contribution of OPEs (3a) and food categories (3b) to the total estimated daily per capita dietary intakes for the Chinese adult population.

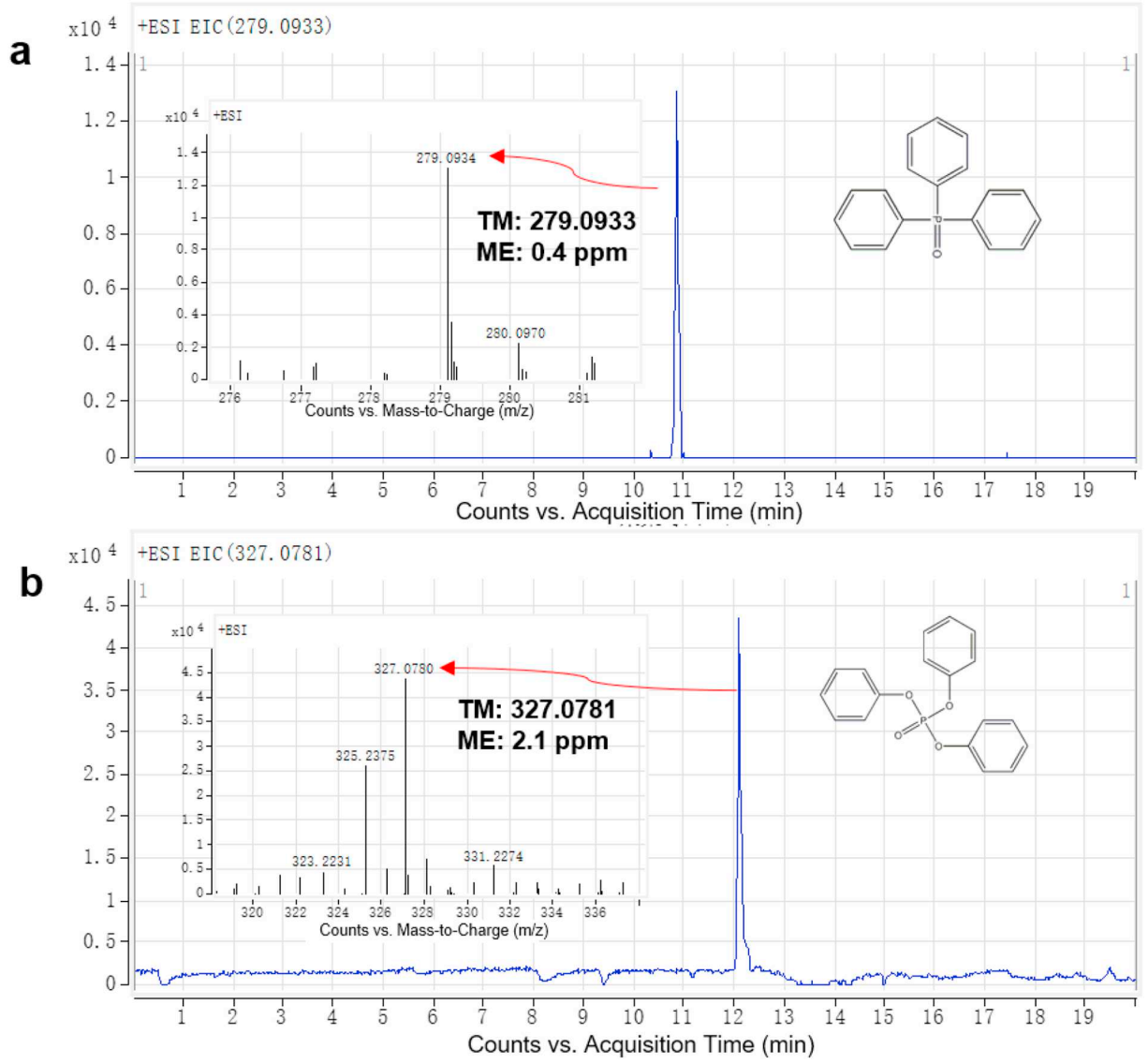

Fig. 4. Detection of triphenyl phosphine oxide (TPPO; a) and comparison with triphenyl phosphate (TPHP; b) in the same sample of extract combined with 105 foodstuff samples by use of liquid chromatography (LC)-electrospray (ESI)-time-of-flight mass spectrometry. The ESI source was operated in positive mode. "TM" means theoretical mass, and "ME" means error between theoretical and observed masses.

populations was 44.3 ng/kg bw/day, which was mainly due to the consumption of cereals (accounting for 52.2% of EDI values), followed by vegetables (11.7%), eggs (6.8%), meat (5.0%), aquatic products (4.0%) and milk (2.9%), respectively. The amount of OPE via dietary intakes for the Chinese population is far less when compared to the reference dosage value of each OPE (hazard index $\ll 1$). This indicates that any deleterious effects caused by OPEs were negligible to Chinese adults exposed through the diet. Finally, by use of high-resolution mass spectrometry, further suspect screening resulted in the detection of the novel OP-FR, TPPO, emphasizing the need for further research and monitoring programs in human foodstuff samples.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.04.055.

References

Abdallah, M.A., Covaci, A., 2014. Organophosphate flame retardants in indoor dust from Egypt: implications for human exposure. Environ. Sci. Technol. 48 (9), 4782–4789. https://doi.org/10.1021/es501078s.

Ali, N., Dirtu, A.C., Van den Eede, N., Goosey, E., Harrad, S., Neels, H., t Mannetje, A., Coakley, J., Douwes, J., Covaci, A., 2012. Occurrence of alternative flame retardants in indoor dust from New Zealand: indoor sources and human exposure assessment. Chemosphere 88 (11), 1276–1282. https://doi.org/10.1016/j.chemosphere.2012.03.100.

Ali, N., Ali, L., Mehdi, T., Dirtu, A.C., Al-Shammari, F., Neels, H., Covaci, A., 2013. Levels and profiles of organochlorines and flame retardants in car and house dust from Kuwait and Pakistan: implication for human exposure via dust ingestion. Environ. Int. 55, 62–70. https://doi.org/10.1016/j.envint.2013.02.001.

Bollmann, U.E., Moler, A., Xie, Z.Y., Ebinghaus, R., Einax, J.W., 2012. Occurrence and fate of organophosphorus flame retardants and plasticizers in coastal and marine surface waters. Water Res. 46 (2), 531–538. https://doi.org/10.1016/j.watres.2011.11.028.

Brandsma, S.H., de Boer, J., Leonards, P.E.G., Cofino, W.P., Covaci, A., Leonards, P.E.G., 2013. Organophosphorus flame-retardant and plasticizer analysis, including recommendations from the first worldwide interlaboratory study. Trends Anal. Chem. 43, 217–228. https://doi.org/10.1016/j.trac.2012.12.004.

Brommer, S., Harrad, S., Van den Eede, N., Covaci, A., 2012. Concentrations of organophosphate esters and brominated flame retardants in German indoor dust samples. J. Environ. Monit. 14 (9), 2482–2487. https://doi.org/10.1039/c2em30303e.

Chen, M., Jiang, J., Gan, Z., Yan, Y., Ding, S., Su, S., Bao, X., 2019. Grain size distribution and exposure evaluation of organophosphorus and brominated flame retardants in indoor and outdoor dust and PM10 from Chengdu, China. J. Hazard. Mater. 365, 280–288. https://doi.org/10.1016/j.jhazmat.2018.10.082.

Chu, S., Letcher, R.J., 2015. Determination of organophosphate flame retardants and plasticizers in lipid-rich matrices using dispersive solid-phase extraction as a sample cleanup step and ultra-high performance liquid chromatography with atmospheric pressure chemical ionization mass spectrometry. Anal. Chim. Acta 885, 183–190. https://doi.org/10.1016/j.aca.2015.05.024.

Ding, J., Deng, T., Xu, M., Wang, S., Yang, F., 2018. Residuals of organophosphate esters in foodstuffs and implication for human exposure. Environ. Pollut. 233, 986–991. https://doi.org/10.1016/j.envpol.2017.09.092.

Dirtu, A.C., Ali, N., Van den Eede, N., Neels, H., Covaci, A., 2012. Country specific comparison for profile of chlorinated, brominated and phosphate organic contaminants in indoor dust. Case study for Eastern Romania, 2010. Environ. Int. 49, 1–8. https://doi.org/10.1016/j.envint.2012.08.002.

Dishaw, L.V., Powers, C.M., Ryde, I.T., Roberts, S.C., Seidler, F.J., Slotkin, T.A., Stapleton, H.M., 2011. Is the PentaBDE replacement, tris (1,3-dichloro-2-propyl) phosphate (TDCPP), a developmental neurotoxicant? Studies in PC12 cells. Toxicol. Appl. Pharmacol. 256 (3), 281–289. https://doi.org/10.1016/j.taap.2011.01.005.

Du, Z., Wang, G., Gao, S., Wang, Z., 2015. Aryl organophosphate flame retardants induced cardiotoxicity during zebrafish embryogenesis: by disturbing expression of the transcriptional regulators. Aquat. Toxicol. 161, 25–32. https://doi.org/10.1016/j.aquatox.2015.01.027.

Faiz, Y., Zhao, W., Feng, J.F., Sun, C., He, H., Zhu, J.P., 2016. Occurrence of triphenylphosphine oxide and other organophosphorus compounds in indoor air and settled dust of an institute building. Build. Environ. 106, 196–204. https://doi.org/10.1016/j.buildenv.2016.06.022.

Giulivo, M., Capri, E., Kalogianni, E., Milacic, R., Majone, B., Ferrari, F., Eljarrat, E., Barcelo, D., 2017. Occurrence of halogenated and organophosphate flame retardants in sediment and fish samples from three European river basins. Sci. Total Environ. 586, 782–791. https://doi.org/10.1016/j.scitotenv.2017.02.056.

Greaves, A.K., Su, G., Letcher, R.J., 2016. Environmentally relevant organophosphate triesters in herring gulls: in vitro biotransformation and kinetics and diester metabolite formation using a hepatic microsomal assay. Toxicol. Appl. Pharmacol. 308, 59–65. https://doi.org/10.1016/j.taap.2016.08.007.

He, C., English, K., Baduel, C., Thai, P., Jagals, P., Ware, R.S., Li, Y., Wang, X., Sly, P.D., Mueller, J.F., 2018a. Concentrations of organophosphate flame retardants and plasticizers in urine from young children in Queensland, Australia and associations with environmental and behavioural factors. Environ. Res. 164, 262–270. https://doi.org/10.1016/j.envres.2018.02.040.

He, C., Wang, X., Tang, S., Thai, P., Li, Z., Baduel, C., Mueller, J.F., 2018b. Concentrations of organophosphate esters and their specific metabolites in food in Southeast Queensland, Australia: is dietary exposure an important pathway of organophosphate esters and their metabolites? Environ. Sci. Technol. 52, 12765–12773. https://doi.org/10.1021/acs.est.8b03043.

Iqbal, M., Syed, J.H., Katsoyiannis, A., Malik, R.N., Farooqi, A., Butt, A., Li, J., Zhang, G., Cincinelli, A., Jones, K.C., 2017. Legacy and emerging flame retardants (FRs) in the freshwater ecosystem: a review. Environ. Res. 152, 26–42. https://doi.org/10.1016/j.envres.2016.09.024.

Jiangsu Province's Bureau of Statistics, 2016. Jiangsu statistics yearbook 2016. http://www.jssb.gov.cn/2017nj/nj05/nj0507.htm.

Kim, U.J., Kannan, K., 2018. Occurrence and distribution of organophosphate flame retardants/plasticizers in surface waters, tap water, and rainwater: implications for human exposure. Environ. Sci. Technol. 52 (10), 5625–5633. https://doi.org/10.1021/acs.est.8b00727.

Lee, S., Cho, H.J., Choi, W., Moon, H.B., 2018. Organophosphate flame retardants (OPFRs) in water and sediment: occurrence, distribution, and hotspots of contamination of Lake Shihwa, Korea. Mar. Pollut. Bull. 130, 105–112. https://doi.org/10.1016/j.marpolbul.2018.03.009.

Li, J., Yu, N.Y., Zhang, B.B., Jin, L., Li, M.Y., Hu, M.Y., Zhang, X.W., Wei, S., Yu, H.X., 2014. Occurrence of organophosphate flame retardants in drinking water from China. Water Res. 54, 53–61. https://doi.org/10.1016/j.watres.2014.01.031.

Li, J., Zhao, L., Letcher, R.J., Zhang, Y., Jian, K., Zhang, J., Su, G., 2019a. A review on organophosphate ester (OPE) flame retardants and plasticizers in foodstuffs: levels, distribution, human dietary exposure, and future directions. Environ. Int. 127, 35–51. https://doi.org/10.1016/j.envint.2019.03.009.

Li, R., Wang, H., Mi, C., Feng, C., Zhang, L., Yang, L., Zhou, B., 2019b. The adverse effect of TCIPP and TCEP on neurodevelopment of zebrafish embryos/larvae. Chemosphere 220, 811–817. https://doi.org/10.1016/j.chemosphere.2018.12.198.

Liu, L., 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. https://doi.org/10.1016/j.chroma.2015.06.003.

Liu, L., 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 (6), 3065–3073. https://doi.org/10.1021/acs.est.5b05073.

Page-Lariviere, F., Chiu, S., Jones, S.P., Farhat, A., Crump, D., O'Brien, J.M., 2018. Prioritization of 10 organic flame retardants using an avian hepatocyte toxicogenomic assay. Environ. Toxicol. Chem. 37 (12), 3134–3144. https://doi.org/10.1002/etc.4260.

Pang, L., Yang, H., Yang, P., Zhang, H., Zhao, J., 2017. Trace determination of organophosphate esters in white wine, red wine, and beer samples using dispersive liquid-liquid microextraction combined with ultra-high-performance liquid chromatography-tandem mass spectrometry. Food Chem. 229, 445–451. https://doi.org/10.1016/j.foodchem.2017.02.103.

Pantelaki, I., Voutsa, D., 2019. Organophosphate flame retardants (OPFRs): a review on analytical methods and occurrence in wastewater and aquatic environment. Sci. Total Environ. 649, 247–263. https://doi.org/10.1016/j.scitotenv.2018.08.286.

Persson, J., Wang, T., Hagberg, J., 2018. Organophosphate flame retardants and plasticizers in indoor dust, air and window wipes in newly built low-energy preschools. Sci. Total Environ. 628–629, 159–168. https://doi.org/10.1016/j.scitotenv.2018.02.053.

Poma, G., Glynn, A., Malarvannan, G., Covaci, A., Darnerud, P.O., 2017. Dietary intake of phosphorus flame retardants (PFRs) using Swedish food market basket estimations. Food Chem. Toxicol. 100, 1–7. https://doi.org/10.1016/j.fct.2016.12.011.

Poma, G., Sales, C., Bruyland, B., Christia, C., Goscinny, S., Van Loco, J., Covaci, A., 2018. Occurrence of organophosphorus flame retardants and plasticizers (PFRs) in Belgian foodstuffs and estimation of the dietary exposure of the adult population. Environ. Sci. Technol. 52 (4), 2331–2338. https://doi.org/10.1021/acs.est.7b06395.

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 (10), 1040–1049. https://doi.org/10.1016/j.chemosphere.2011.11.053.

Schlusener, M.P., Kunkel, U., Ternes, T.A., 2015. Quaternary triphenylphosphonium compounds: a new class of environmental pollutants. Environ. Sci. Technol. 49 (24), 14282–14291. https://doi.org/10.1021/acs.est.5b03926.

Sha, B., Dahlberg, A.K., Wiberg, K., Ahrens, L., 2018. Fluorotelomer alcohols (FTOHs), brominated flame retardants (BFRs), organophosphorus flame retardants (OPFRs) and cyclic volatile methylsiloxanes (cVMSs) in indoor air from occupational and home environments. Environ. Pollut. 241, 319–330. https://doi.org/10.1016/j.envpol.2018.04.032.

Shen, J., Zhang, Y., Yu, N., Crump, D., Li, J., Su, H., Letcher, R.J., Su, G., 2019. Organophosphate ester, 2-ethylhexyl diphenyl phosphate (EHDPP), elicits cytotoxic

and transcriptomic effects in chicken embryonic hepatocytes and its biotransformation profile compared to humans. Environ. Sci. Technol. 53 (4), 2151–2160. https://doi.org/10.1021/acs.est.8b06246.

Stapleton, H.M., Klosterhaus, S., Eagle, S., Fuh, J., Meeker, J.D., Blum, A., Webster, T.F., 2009. Detection of organophosphate flame retardants in furniture foam and U.S. house dust. Environ. Sci. Technol. 43 (19), 7490–7495. https://doi.org/10.1021/es9014019.

Su, G., Liu, X., Gao, Z., Xian, Q., Feng, J., Zhang, X., Giesy, J.P., Wei, S., Liu, H., Yu, H., 2012. Dietary intake of polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) from fish and meat by residents of Nanjing, China. Environ. Int. 42, 138–143. https://doi.org/10.1016/j.envint.2011.05.015.

Su, G., Crump, D., Letcher, R.J., Kennedy, S.W., 2014. Rapid in vitro metabolism of the flame retardant triphenyl phosphate and effects on cytotoxicity and mRNA expression in chicken embryonic hepatocytes. Environ. Sci. Technol. 48 (22), 13511–13519. https://doi.org/10.1021/es5039547.

Su, G., Letcher, R.J., Yu, H., 2016. Organophosphate flame retardants and plasticizers in aqueous solution: pH-dependent hydrolysis, kinetics, and pathways. Environ. Sci. Technol. 50 (15), 8103–8111. https://doi.org/10.1021/acs.est.6b02187.

Sundkvist, A.M., Olofsson, U., Haglund, P., 2010. Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. J. Environ. Monit. 12 (4), 943–951. https://doi.org/10.1039/b921910b.

United Nations Environment Programme, 2017. The POPs. http://chm.pops.int/TheConvention/ThePOPs/TheNewPOPs/tabid/2511/Default.aspx.

United States Environmental Protection Agency, 2018. Regional screening levels (RSLs) - user's guide. https://www.epa.gov/risk/regional-screening-levels-rsls-users-guide#toxicity.

United States Food and Drug Administration, 2006. Total diet study market baskets 1991-3 through 2003-4. https://www.fda.gov/downloads/Food/FoodSafety/FoodContaminantsAdulteration/TotalDietStudy/UCM184303.pdf.

Van den Eede, N., Dirtu, A.C., Neels, H., Covaci, A., 2011. Analytical developments and preliminary assessment of human exposure to organophosphate flame retardants from indoor dust. Environ. Int. 37 (2), 454–461. https://doi.org/10.1016/j.envint.2010.11.010.

Van den Eede, N., Maho, W., Erratico, C., Neels, H., Covaci, A., 2013. First insights in the metabolism of phosphate flame retardants and plasticizers using human liver fractions. Toxicol. Lett. 223 (1), 9–15. https://doi.org/10.1016/j.toxlet.2013.08.012.

Van den Eede, N., Tomy, G., Tao, F., Halldorson, T., Harrad, S., Neels, H., Covaci, A., 2016. Kinetics of tris (1-chloro-2-propyl) phosphate (TCIPP) metabolism in human liver microsomes and serum. Chemosphere 144, 1299–1305. https://doi.org/10.1016/j.chemosphere.2015.09.049.

Van der Veen, I., De Boer, J., 2012. Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis. Chemosphere 88 (10), 1119–1153. https://doi.org/10.1016/j.chemosphere.2012.03.067.

Wang, R., Tang, J., Xie, Z., Mi, W., Chen, Y., Wolschke, H., Tian, C., Pan, X., Luo, Y., Ebinghaus, R., 2015. Occurrence and spatial distribution of organophosphate ester flame retardants and plasticizers in 40 rivers draining into the Bohai Sea, North China. Environ. Pollut. 198, 172–178. https://doi.org/10.1016/j.envpol.2014.12.037.

Wang, Y., Hou, M., Zhang, Q., Wu, X., Zhao, H., Xie, Q., Chen, J., 2017. Organophosphorus flame retardants and plasticizers in building and decoration materials and their potential burdens in newly decorated houses in China. Environ. Sci. Technol. 51 (19), 10991–10999. https://doi.org/10.1021/acs.est.7b03367.

Wang, Y., Sun, H., Zhu, H., Yao, Y., Chen, H., Ren, C., Wu, F., Kannan, K., 2018. Occurrence and distribution of organophosphate flame retardants (OPFRs) in soil and outdoor settled dust from a multi-waste recycling area in China. Sci. Total Environ. 625, 1056–1064. https://doi.org/10.1016/j.scitotenv.2018.01.013.

Wei, G., Li, D., Zhuo, M., Liao, Y., Xie, Z., Guo, T., Li, J., Zhang, S., Liang, Z., 2015. Organophosphorus flame retardants and plasticizers: sources, occurrence, toxicity and human exposure. Environ. Pollut. 196, 29–46. https://doi.org/10.1016/j.envpol.2014.09.012.

Yadav, I.C., Devi, N.L., Singh, V.K., Li, J., Zhang, G., 2019. Measurement of legacy and emerging flame retardants in indoor dust from a rural village (Kopawa) in Nepal: implication for source apportionment and health risk assessment. Ecotoxicol. Environ. Saf. 168, 304–314. https://doi.org/10.1016/j.ecoenv.2018.10.089.

Yang, X., Li, Y., Ma, G., Hu, X., Wang, J., Cui, Z., Wang, Z., Yu, W., Yang, Z., Zhai, F., 2005. Study on weight and height of the Chinese people and the differences between 1992 and 2002. 26, 489–493.

Yang, C., Harris, S.A., Jantunen, L.M., Siddique, S., Kubwabo, C., Tsirlin, D., Latifovic, L., Fraser, B., St-Jean, M., De La Campa, R., You, H., Kulka, R., Diamond, M.L., 2019. Are cell phones an indicator of personal exposure to organophosphate flame retardants and plasticizers? Environ. Int. 122, 104–116. https://doi.org/10.1016/j.envint.2018.10.021.

Zha, D., Li, Y., Yang, C., Yao, C., 2018. Assessment of organophosphate flame retardants in surface water and sediment from a freshwater environment (Yangtze River, China). Environ. Monit. Assess. 190 (4), 222. https://doi.org/10.1007/s10661-018-6587-5.

Zhang, X., Zou, W., Mu, L., Chen, Y., Ren, C., Hu, X., Zhou, Q., 2016. Rice ingestion is a major pathway for human exposure to organophosphate flame retardants (OPFRs) in China. J. Hazard. Mater. 318, 686–693. https://doi.org/10.1016/j.jhazmat.2016.07.055.