A review on organophosphate Ester (OPE) flame retardants and plasticizers in foodstuffs: Levels, distribution, human dietary exposure, and future directions

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ABSTRACT

Given the ongoing studies on the adverse effects of organophosphate ester (OPE) flame retardants and plasticizers on human health, there is an increasing scientific interest in the risk of exposure to OPEs via dietary intake. Using peer-reviewed literature published up to 2018, this review surveyed and compiled the available and reported data on the concentrations and distributions of 30 OPEs based on their occurrence in various food samples from around the world. Regardless of sampling locations or food categories, 22 OPEs were detectable in at least one of analyzed sample, and there were clear variations in OPE levels among samples from different locations or food categories. For instance, cereals and fats/oils were the most contaminated by OPEs in China and Belgium, whereas fats/oils and desserts were the main polluted products in Sweden. In contrast, vegetables, fruits, fluid dairy products, and cereals were reported as the primary categories of food polluted by OPEs in Australia. Animal-based food categories such as eggs, fish and meat were the least contaminated, whereas the highest median OPE concentrations were found in meat and fish from the United State. The levels and distribution patterns of OPEs in foodstuffs demonstrated a tremendous difference even when collected from the same country and the same food item. Rice from China had the highest tris(2-chloroethyl) phosphate (TCEP, mean: 29.8 ng/g dw) levels, whereas 2-ethylhexyl-diphenyl phosphate (EHDPP, mean: 4.17 ng/g ww), triphenyl phosphate (TPHP, mean: 26.14 ng/g ww), tris(2-chloroisopropyl) phosphate (TCIPP, mean: 0.87 ng/g ww) and tributyl phosphate (TNBP, median: 0.55 ng/g ww) concentrations were the highest in the same food category from Sweden, Belgium, Australia, and the United States, respectively. These discrepancies may be due to a variety of reasons such as differences in OPE physico-chemical properties, extent of usage, uptake, metabolic pathways, industrial food manufacturing processes, OPE level differences as a function of habitat, and accumulation and degradability of OPEs in different species. It is worth noting that, due to its worldwide usage in food packaging materials, EHDPP was more prominently found in processed food compared to non-processed food. Based on reported OPE levels in various foods, this review conducted a preliminary assessment of human exposure to OPEs through dietary intake, which suggested that the OPE estimated daily intake (EDI) for humans was around 880 ng/kg bw/day (95th percentile). This value was well below the corresponding OPE health reference dose given by the U.S. EPA (≥15,000 ng/kg bw/day). Even so, dietary exposure to OPEs via food intake may be not negligible based on some important factors such as dilution effects, cooking processes, and the contribution of as yet unknown means of OPE exposure. Overall, this review highlights several gaps in our understanding of OPEs in foodstuffs: 1) the investigation of contamination levels of OPEs in foodstuffs should be extended to other regions, especially North America and European countries, where OPEs are widely used and frequently detected in environmental samples, and 2) newly identified OPE derivatives/by-products, e.g., OP diesters and hydroxylated metabolites, which have been reported as end-products of OPE enzymatic metabolism or degradation through aqueous hydrolysis, and which may co-exist with parent OPEs, could also be screened with precursor OPEs in foodstuffs in future studies.

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1. Introduction

Organophosphate ester (OPE) flame retardants and plasticizers, are being increasingly used as replacements for brominated flame retardants (BFRs), which are being gradually phased out due to the increasing concerns about their potential toxicity, with their production increasing from ~0.3 to 1.0 million tons (Ltd, 2018; van der Veen and de Boer, 2012). These OPEs include tributyl phosphate (TBNP), tris (methyl-phenyl) phosphate (TMPP) and tris(2-ethylhexyl) phosphate (TEHP), which are listed as high-production volume (HPV) chemicals (U.S. EPA, 2014). OPEs are widely utilized in various industrial products, such as plastics, building materials, textiles, furniture, electronics and vehicle parts (Marklund et al., 2003; Wei et al., 2015). OPEs are added into polymer materials via physical mixing rather than chemically bonding, allowing them to be released into the surrounding environments by volatilization, leaching, abrasion and dissolution (Pang et al., 2017). As such, OPEs have been detected in various environments, including indoor air (ΣOPEs: 2.96–635 ng/m^3 in bulk air; sampling site: Albany area, New York, U.S.); indoor dust (16.2–224 μg/g; sampling site: Albany area, New York, U.S.); water (up to 1600 ng/L in drink water; sampling site: Korea), soil (37.7–2100 ng/g; sampling site: Jianghai district, Tianjin, China) and sediment (983–7460 ng/g; sampling site: Bagmati River, Kathmandu Valley, Nepal) samples (Lee et al., 2016; Kim et al., 2019; Pantelaki and Voutsas, 2019; Wang et al., 2018; Yadav et al., 2018). Moreover, OPE contamination levels in the environment are likely to continue rising as a result of their growing usage (Ding et al., 2018). Because of the frequent occurrence of OPEs in the environment, humans can be exposed to OPEs via several routes, such as ingestion (and inhalation) of indoor dust and ingestion of contaminated food or drinking water (Li et al., 2014; Xu et al., 2017). A handful of studies have already reported the presence of OPEs in human hair, nails, urine, and breast milk (He et al., 2018; Liu et al., 2015; Sundkvist et al., 2010; Zhang et al., 2016).

Prolonged exposure and the accumulation of OPEs in the human body may elicit various adverse effects, including kidney toxicity, neurotoxicity, reproductive toxicity, carcinogenicity and endocrine disruption (Kanazawa et al., 2016; Li et al., 2017; Meeker and Stapleton, 2010; Yuan et al., 2018). The European Union (EU) introduced regulations and criteria starting in 2008 for the hazard classification and labelling of certain OPEs (Regulation (EC) No 12/72/2008). According to the EU’s approved harmonised classification and labelling, many OPEs constitute health and/or environmental hazards. However, the high human consumption of OPEs continues to increase without any imposed regulations (Reemtsma et al., 2008; Zhang, 2014).

Previous studies have focused primarily on dust ingestion for human exposure to OPEs due to the high concentrations of OPEs in dust (μg/g range), which were reported to be approximately three orders of magnitude higher than in foodstuffs (ng/g range) (Wei et al., 2015). Nevertheless, the average consumption of foodstuff for humans was estimated to be 0.02 to 2 kg/d, which is substantially greater than that of dust (20 mg/d for adults) (Jones-Otazo et al., 2005; Poma et al., 2017). It was inferred that dietary intake might be of equal or greater importance relative to dust ingestion for human exposure to OPEs. A few recent surveys have corroborated this fact, although reports on OPE content in food are sparse (Poma et al., 2017; Zhang et al., 2016).

OPE contaminants enter the human diet primarily via two routes. First, crops (e.g., rice, vegetables, and fruits), livestock (e.g., pigs, cattle, and chicken) and aquatic products (e.g., fish and mussels) can absorb OPEs via the soil and water, resulting in OPEs being subsequently biomagnified in the food chain (Zhang et al., 2016). Second, foodstuffs can be contaminated by OPEs during production, industrial processing (e.g., packing, canning, and drying) and storage, due to their presence in several materials used in food processing (Ding et al., 2018; Poma et al., 2018; Wang et al., 2018).

Using the published and peer-reviewed literature up to 2018, this paper reviewed OP triesters reported in foodstuffs from around the world. Furthermore, the degree of human dietary exposure to OPEs from foodstuffs was estimated. Regardless of the sampling sites, currently available data was collected for 30 OPE congeners, i.e., tris(2-chloroethyl) phosphate (TCEP), tripropyl phosphate (TPP), tris(2-chloroisopropyl) phosphate (TCIPP), tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), triphenyl phosphate (TPH), TNBP, TMPP, TEHP, 2-ethylhexyl-diphenyl phosphate (EHDP), tris(2-butoxyethyl) phosphate (TBOEP), triethyl phosphate (TEP), tris(chloropropyl) phosphate (TCP), TCPP mixture (ZTCP, TCPP is the major component), tris(1,3-dichloropropyl) phosphate (T13DCIPP), tris(2,3-dibromopropyl) phosphate (TDBBP), tri-o-tolyolphosphate (ToTP), dibutyl phenyl phosphate (DBPhP), butyl diphenyl phosphate (BdPhP), trimethyl phosphate (TMP), trisobutyl phosphate (TIBP), tripentyl phosphate (TpeP), tri(n-propyl) phosphate (TnPP), trim-tolyl phosphate (TmTP), tri-p-tolyl phosphate (TpTP), tris(2-isopropylphenyl) phosphate (Ti2IPP), tris(3,5-dimethylphenyl) phosphate (T35DMPPP), tris(p-butylphenyl) phosphate (TBPP), cresyl diphenyl phosphate (CDPP), isodecyl diphenyl phosphate (IDDP) and triisopropyl phosphate (TIPP).

2. Methodology

Our search for scientific literature used the most common database, Web of Science, and covered all original studies published up to 2018 using “organophosphorus flame retardant” (or “OPFRs”) and “food” as the search terms. Then the searched papers were categorized according the following inclusion criteria: 1) the studies must be in English, 2) they must refer to edible food such as foodstuffs from markets, the edible parts of wild fish, and eggs from free-range chicken of private owners. In view of the limited data on OPEs in foodstuffs worldwide, special caution should be exercised when comparing data from different foods found worldwide and the assessment of exposure via the diet due to differences in the presented concentrations, including ng/g wet weight (ww), dry weight (dw), or lipid weight (lw), ng/L and ng/kg. For many reports, there was a lack of information on the lipid and water content of food samples. As such, it was difficult to interconvert the data into ww, dw or lw. This review mainly inter-compared data with the same concentrations, and/or roughly compared between dw, lw and ww concentrations using the reported lipid and water content of the corresponding food category.

3. Levels of OPEs in food matrices

This study summarized the contamination levels reported for 30 OPEs in a variety of food samples consisting of non-processed and processed food from supermarkets, specialized fish stores and/or freshwaters/oceans in different regions around the world. The structures, names, abbreviations, CAS numbers and properties of these 30 OPEs are provided in Table 1. The OPE data were divided into the following groups based on the type of food: cereals and derived products, fats and oils, meat products, fish and derived products, dairy products, eggs, vegetables and fruits, and other foods including wines, desserts, and beverages, among others. The OPE concentrations (range, geometric mean and/or median) in each food group are summarized in Tables S1–S6 of the Supporting information. The summarized OPE data demonstrated that 13 OPEs, i.e., TCEP, TPP, T13CIPP, TDCIPP, TPH, TNBP, EHPD, TBOEP, TEHP, TMPP, TIBP, TMP, and TEP, were the most prevalent pollutants reported in foodstuffs, and there were clear variations in their concentrations among food items and geographical sampling locations. Nine OPEs, including TCPP, T35DMPPP, TBPP, TDBBP, and Ti2IPP, have not been discussed in the search terms. Then the searched papers were categorized according the following inclusion criteria: 1) the studies must be in English, 2)
Table 1
The structure, names, abbreviations, CAS number, and properties of the 30 organophosphate ester (OPE) flame retardants and plasticizers found in the published literature up to 2018.

| Structure | Name                                      | Abbreviation | CAS number | Lg Kow<sup>a</sup> | BCF<sup>b</sup> |
|-----------|-------------------------------------------|--------------|------------|--------------------|-----------------|
|           | Tris(2-chloroethyl) phosphate              | TCEP         | 115-96-8   | 1.44               | 3.465           |
|           | Tripropyl phosphate                       | TPrP         | 513-08-6   | 1.87               | 5.317           |
|           | Tris(2-chloroisopropyl) phosphate         | TCIPP        | 13674-84-5 | 2.59               | 12.81           |
|           | Tris(chloropropyl) phosphate              | TCPP         | 1067-98-7  | 3.11               | 49.14           |
|           | Tris(1,3-dichloro-2-propyl) phosphate     | TDCIPP       | 13674-87-8 | 3.65               | 100.6           |
|           | Tris(1,3-dichloropropyl) phosphate        | T13DCIPP     | 40120-74-9 | 3.65               | 126.3           |
|           | Triphenyl phosphate                       | TPHP         | 115-86-6   | 4.59               | 73.18           |
|           | Tributyl phosphate                        | TNBP         | 126-73-8   | 4.00               | 69.65           |
|           | Tris(methyl-phenyl) phosphate             | TMPP         | 1330-78-5  | 5.11               | 1280            |
|           | 2-ethylhexyl-diphenyl phosphate           | EHDPP        | 1241-94-7  | 5.73               | 269.2           |
|           | Tris(2-butoxyethyl) phosphate             | TBOEP        | 78-51-3    | 3.75               | 54.19           |
| Structure | Name                                      | Abbreviation | CAS number | \( \text{Lg } K_{ow} \) | \( \text{BCF} \) |
|-----------|-------------------------------------------|--------------|------------|-------------------------|-------------|
|           | Tris(2-ethylhexyl) phosphate               | TEHP         | 78-42-2    | 9.49                    | 1.219       |
|           | Triethyl phosphate                        | TEP          | 78-40-0    | 0.80                    | 1.4         |
|           | Tris(2,3-dibromopropyl) phosphate         | TDBPP        | 126-72-7   | 4.29                    | 17.68       |
|           | Tri-\( \alpha \)-tolyl phosphate         | ToTP         | 78-30-8    | 5.11                    | 1280        |
|           | Dibutyl phenyl phosphate                  | dBPbP        | 2528-36-1  | 4.27                    | 111.4       |
|           | Butyl diphenyl phosphate                  | BdBPbP      | 2752-95-6  | 4.41                    | 99.15       |
|           | Trimethyl phosphate                       | TMP          | 512-56-1   | −0.65                   | 0.9002      |
|           | Triisobutyl phosphate                     | TiBP         | 126-71-6   | 3.60                    | 64.15       |
|           | Tripentyl phosphate                       | TPnP         | 2528-38-3  | 5.29                    | 268.2       |
|           | Tri(n-propyl) phosphate                   | TnPnP       | 513-08-6   | 1.87                    | 5.317       |
|           | Tri-\( \eta \)-tolyl phosphate           | TmTP         | 563-04-2   | 6.34                    | 2809        |

(continued on next page)
concentration of 1.23 ng/g ww in smoked salmon from Belgium and a concentration from nd to 3.49 ng/g ww in free range chicken eggs from Qingyuan, China (Xu et al., 2015; Zheng et al., 2016). The levels of the three TPePs, i.e., ToTP, dBPhP, and BdPhP, and those of CDPP and IDPP in foodstuffs were discussed in three papers; the highest mean concentrations of TPeP (83 ng/g ww) were observed in bumpnose trevally (Carangoides hedlandensis) in Manila Bay, Philippines (Kim et al., 2011a, 2011b); concentration ranges of ToTP, dBPhP, and BdPhP were nd–2.5, nd–3300 and nd–2000 ng/g ww, respectively in perch from freshwater in Sweden (Sundkvist et al., 2010); and the levels of CDPP and IDPP were low but detectable in meat, fish and seafood, dairy products, and cereal products, although not detectable in oil samples in the United States (Wang et al., 2018).

Table 1 (continued)

| Structure | Name | Abbreviation | CAS number | Lg $K_{ow}$ | BCF |
|-----------|------|--------------|------------|-------------|-----|
| Tri-p-tolyl phosphate | TpTP | 78-32-0 | 6.34 | 2809 |
| Tris(2-isopropylphenyl) phosphate | T2IPPP | 64532-95-2 | – | – |
| Tris(3,5-dimethylphenyl) phosphate | T35DMPP | 25653-16-1 | 7.98 | 157.7 |
| Tris(p-t-butylphenyl) phosphate | TBPP | 78-33-1 | 10.43 | 23.29 |
| Triisopropyl phosphate | TiPP | 513-02-0 | 2.12 | 8.581 |
| Cresyl diphenyl phosphate | CDPP | 26444-49-5 | 5.25 | 213.5 |
| Isodecyl diphenyl Phosphate | IDPP | 29761-21-5 | 7.28 | 288.4 |

$^a$ Data was calculated by use of EPI (Estimated Program Interface) Suite.

$^b$ The sum of tris(2-chloroisopropyl) phosphate (TCIPP) and tris(chloropropyl) phosphate (TCPF).

3.1. Cereals and derived products

Cereals and derived products such as rice, grains, wheat, potato, flour and bread are important economic and nutritious staple foods that are consumed by billions of people around the world (Zhang et al., 2016). To our knowledge, there are five studies reporting on OPE concentrations in cereals or derived products (Table S1 and Fig. 1). Among the four countries of sampling origin, cereals from the Albany area in the United States had the smallest median ΣOPE concentrations (1.94 ng/g ww, range: 0.60–91.3 ng/g ww), while Chinese rice had the greatest ΣOPE concentrations worldwide, with a mean of 69.9 ng/g dw, and ranging from 0.38 to 287 ng/g dw in the major rice cultivation provinces of Sichuan, Chongqing, Hubei, and Guangxi (Poma et al., 2017, 2018; Wang et al., 2018; Zhang et al., 2016).
For Chinese cereals and derived products, the maximum concentrations of $\Sigma$OPEs in samples were found near OPE manufacturing factories located in Hubei province. The three relatively industrialized provinces included Sichuan, Chongqing, and Hubei, which exhibited greater $\Sigma$OPE concentrations in rice compared to the rural and agricultural area of Guangxi (Zhang et al., 2016). This suggested a significant influence of social-economic development factors on regional OPE pollution levels.

$\Sigma$OPE concentrations in Chinese rice samples were dominated by TCEP (mean: 29.8 ng/g dw), TPrP (mean: 20.4 ng/g dw), and TCIPP (mean: 24.0 ng/g dw), and this pattern was different from the $\Sigma$OPEs found in cereals from Sweden, Belgium, Australia, and the United States, which were dominated by EHDPP (mean: 4.17 ng/g ww), TPHP (mean: 26.14 ng/g ww), and TCIPP and TNBP (mean: 0.87 and 0.66 ng/g ww in Australia; median: 0.55 and 0.23 ng/g ww in the United State), respectively (He et al., 2018; Poma et al., 2017, 2018; Wang et al., 2018).

For specific foodstuffs, different countries exhibited different patterns of OPE contamination. For example, TNBP and TEHP were detectable in potatoes from Belgium, but not detectable in potato samples from Sweden. Regardless of the sampling countries, the concentrations of EHDPP were significantly greater than any of the other investigated OPEs in Sweden and Belgium, as a result of the worldwide usage of

Fig. 1. Mean contamination levels and congener compositions of organophosphate ester (OPE) flame retardants and plasticizers in cereals and fats/oils from markets in different countries. The concentration units are expressed as ng/g ww (A) or ng/g dw (B) depending on the specific literatures. Detailed data are compiled in the Table S1 of supporting information.

Fig. 2. Mean contamination levels and congener compositions of organophosphate ester (OPE) flame retardants and plasticizers in meat from markets in different countries. The concentration units are expressed as ng/g ww (A) or ng/g dw (B) depending on the specific literatures. Detailed data are compiled in the Table S2 of supporting information.
EHDPP in food packaging materials (Poma et al., 2017). The differences observed in OPE levels among sampling countries could be due to other reasons such as the uptake and metabolic pathways, the history of local OPE usage, or even manufacture processing. Although 15 OPEs, including TCEP, TPbP, TCIPp, TDCIPp, TNPb, TMPP, EHDPP, TBOEP, TEHP, TEP, TIPb, CDPP, and IDPP, but not IDPP, were detected in cereals from the Albany area in the United States, their median concentrations were below the method detection limits (MDLs) (Wang et al., 2018). Collectively, the comparison for \( \Sigma \)OPE levels in various cereals and derived products among different countries generally demonstrated the greatest levels of \( \Sigma \)OPEs in rice from China. With the exclusion of Chinese rice, cereals and derived products from Belgium exhibited the greater concentrations of \( \Sigma \)OPE compared to Sweden, Australia, the United States, or China. The major OPE congeners in this category of foodstuff were TCEP, TPHP, or EHDPP for rice from China, grains from Belgium, or potatoes from Sweden and Belgium, respectively.

### 3.2. Fats and oils

Information on OPE concentrations in fats and oils was limited to samples from Sweden, Belgium and the United States, and the limited reporting demonstrated that fats and oils from Belgium have higher levels of \( \Sigma \)OPEs compared to Sweden and the United States (Table S1 and Fig. 1) (Poma et al., 2017, 2018; Wang et al., 2018). All the investigated OPE congeners exhibited greater concentrations in fat and oil samples from Belgium compared to those from Sweden and the United States, where one exception was TPHP in fats from Belgium. TPHP was generally not detectable in Belgian samples, but showed a greater mean concentration of 4.74 ng/g ww in Swedish samples (Poma et al., 2017, 2018). Regardless of whether the samples were from Belgium or Sweden, TCIPp was the most abundant compound in fats and oils, and the mean TCIPp concentrations in Belgian samples was as high as 38.87 ng/g ww (Poma et al., 2017, 2018). Overall, fat and oil products were more OPE-contaminated compared to all other foodstuff groups, and EHDPP and TCIPp were the major contributors to the levels of OPEs in fats and oils from these countries. OPE contamination in these samples could result from raw materials in various animal tissues or oilseeds, or industrial processing during extraction, manipulation, and/or alteration of fats and oil products (e.g., packaging, canning, and drying), however a recent study indicated that food processing did not introduce OPEs in fats/oils (Ding et al., 2018; Wang et al., 2018).

### 3.3. Meat and its derived products

To date, OPEs have been frequently detected in various meats and meat products from Sweden, China, Belgium, and Australia; these foods exhibited different patterns of OPE congeners, as shown in Table S2 and Fig. 2. The median \( \Sigma \)OPE concentrations (6.76 ng/g ww) reported for meat samples from the United States were comparable to those reported for meat samples from Australia (2.29 ng/g ww); however, they were higher than the values reported for meat samples from China (0.41 ng/g ww) (He et al., 2018; Wang et al., 2018; Zhang et al., 2016). EHDPP had the highest mean concentrations (0.64 ng/g ww) in Swedish meat samples as a result of cross-contamination from food packaging materials (Poma et al., 2017), whereas TBOEP concentrations were highest in meat from the United States (Wang et al., 2018). TCIPp and TNbP were the most abundant, with mean values of 0.36 and 0.27 ng/g ww, respectively, in the meat samples from Australia (He et al., 2018). In Chinese beef, chicken, and pork samples, TEHP and TCEP were the primary OPEs with mean concentrations of 3.07 and 0.74 ng/g dw, respectively (Zhang et al., 2016). Overall, in meat or its derived products from Sweden and Australia, EHDPP and TCIpP were the most prominent OPE congeners, respectively, whereas TEHP and TCEP were the most abundant OPE congeners in meat samples from China.

There is evidence that samples from the same country could have different levels of contamination and composition patterns of OPEs, such as OPEs in Belgian meats as reported by Xu et al. (2015) and Poma et al. (2018). The levels of 9 OPEs in lean pork, bacon, and chicken thighs were below the LOQs expected for TNbP and EHDPP in lean pork, with concentrations of 1.26 and 0.30 ng/g ww, respectively, and TPHP in bacon, with a level of 0.82 ng/g ww (Xu et al., 2015). A follow-up survey covering more types of meats, such as horse, duck, rabbit, crayfish, and turkey meat, was conducted. The result showed that TPHP concentration was higher relative to other OPEs in Belgian samples with a mean concentration of 1.52 ng/g ww, followed by TDIpP.

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**Fig. 3.** Mean contamination levels and congener compositions of organophosphate ester (OPE) flame retardants and plasticizers in aquatic products from markets in different countries. The concentrations are reported as ng/g ww (A) or ng/g lw (B) depending on the literature report. Detailed data are compiled in the Table S3 of supporting information.
EHDPP, TEHP, TCIPP, TNBP, and TCEP in decreasing order; however, the levels of these OPEs did not appear to be significantly different (Poma et al., 2018). The presence of TPHP could be due to its wide-spread application in electrical industrial equipment and its high indoor dust concentration which may be found in industrial facilities (Poma et al., 2018).

3.4. Aquatic food products

A number of studies have reported on OPEs in aquatic-derived food products including various fish species, e.g., salmon (Salmo salar), herring (Clupeidae), perch (Perca fluviatilis), eelpout (Zoarces viviparus), crucian (Carassius auratus), and carp (Cyprinus carpio) (Campone et al., 2010; Gao et al., 2014; He et al., 2018; Kim et al., 2011a, 2011b; Malarvannan et al., 2015; Poma et al., 2017, 2018; Sundkvist et al., 2010; Xu et al., 2015; Wang et al., 2018; Zhao et al., 2018). Typically, OPEs could be bioaccumulated by fishes via two pathways: dietary intake or ingestion across gill membranes. Due to their hydrophobic properties, OPE burdens in fish tissue were reported to be generally three orders of magnitude greater than the surrounding water (Gao et al., 2014). Table S3 and Fig. 3 present the reported concentration values of OPEs in fish food samples collected worldwide, which are primarily from Sweden, Belgium, China, Philippines, Australia, and the United States.

The concentrations of OPEs in fish could reflect the contamination levels of OPEs in local/regional source waters. The median concentrations of ΣOPE (7.11 ng/g ww) in fish and seafood from the United States were comparable to those in the same food category from Australia (3.13 ng/g ww) (He et al., 2018; Wang et al., 2018). The current results demonstrated that OPE concentrations can vary greatly among fish depending on sampling sites/locations. For example, all OPEs were not detectable in fish samples from markets in Stockholm and Uppsala, Sweden (Campone et al., 2015; Poma et al., 2017). However, in fish samples from the Swedish part of the Baltic Sea, a mean EHDPP concentration as high as 14,000 ng/g lw was reported for eelpout (Sundkvist et al., 2010). The reasons for this high concentration of EHDPP in eelpout could be due to the following: (1) the nearby releases of wastewater from a sewage treatment plant (STP) serving two plastic goods factories in Sweden; (2) animal habit, i.e., eelpout is a Benthic (bottom) feeding fish, meaning that eelpouts would be more readily exposed to OPE-contaminated sediments (Sundkvist et al., 2010).

A recent study compared OPE contamination patterns in perch from OPE-contaminated lakes and reference lakes. TBOEP and TCIPP were only detected at levels ranging between 240 and 1000 and 49–140 ng/g lw, respectively, in fish samples downstream of STPs, which were as-associated with extremely low STP removal or degradation rates (Kim et al., 2011a, 2011b). Moreover, TBOEP residues in herring, perch, eelpout, and salmon from Sweden were not detected (Sundkvist et al., 2010), whereas up to 50 ng/g lw of TBOEP was reported in fish from Manila Bay, and the highest median concentration of TBOEP (0.62 ng/g ww) was found in fish from the Albany area in the United States (Kim et al., 2011a, 2011b; Wang et al., 2018). This is likely due to the large-scale usage of TBOEP in the Philippines and the resulting wastewaters are released into the bay where elevated TBOEP levels have been reported (Kim et al., 2011a, 2011b; Sundkvist et al., 2010).

Three studies investigated OPE concentrations in fish and fish-derived products from Belgium. Processed fish foods, i.e., smoked salmon and canned tuna, purchased from Antwerp supermarkets were found to have low concentrations of various OPEs, ranging from below the LOQs to 1.37 ng/g ww. Only TCEP (1.09 ng/g ww), TNBP (1.37 ng/g ww), and ΣTCIPP (1.23 ng/g ww) were found in smoked salmon (Xu et al., 2015). The levels of OPEs in the muscle of yellow eels (Valamugil buchanani) collected from 26 locations of Flanders (Belgium) annually between 2000 and 2009 were determined (Malarvannan et al., 2015). The concentrations of ΣOPEs varied between 7.1 ng/g lw and 329 ng/g lw, with a median value of 44 ng/g lw. The discrepancies in OPE levels among fish from 26 sampling locations are likely due to the diversity of the sampling locations, which varied from small rural creeks to highly industrialized areas. The highest ΣOPE level was 329 ng/g lw in samples collected in the Antwerp region in 2000 and could be attributed to the high number of textile and industrial plants upstream of the sampling site. Conversely, yellow eels collected from Nieuwpoort, which is in the rural countryside and has with fewer industrial activities, contained the lowest concentration of OPEs (7.1 ng/g lw) (Malarvannan et al., 2015). A recent study investigated the levels of seven OPEs, including TNBP, TCEP, TCIPP, TDCIPP, TPHP, EHDPP, and TEHP, in two groups, including unprocessed fish (fresh and frozen fish) and processed fish (prepared, canned, fried and marinated fish) from Belgium (Poma et al., 2018). All seven OPEs were detected in both groups (Table S4). The total distribution of OPEs in the two groups showed a clear dominance of OPEs in processed food (66%) versus non-processed food (34%), which supported the hypothesis that OPE contamination may occur during the industrial processing and manipulation of food products.

In Nanjing (China), TPrP and TNBP were found to be the most abundant OPEs in various fish species including hairtail (Trichiurus haumela), croaker (Pseudosciaena crocea), crucian, perch (Lateolabrax japonicas) and grass carp (Ctenopharyngodon idellus). The TNBP concentration was the highest in hairtail, with a mean of 145.4 ng/g ww. Among the investigated chlorinated OPEs, TCEP and TCIPP were detected in all fish samples due to their lipophilic properties and their persistence and presence in air, water, and soil (Gao et al., 2014). A recent study measured the concentrations of 14 OPEs in the muscle of 11 fish species (99 samples in total) from Taihu Lake (China), a body of water that has suffered severe eutrophication and contamination with organic chemicals (Zhao et al., 2018). Seven fish species, including ricerfied eel (Monopterus albus), crucian (Carassius auratus), pipefish (Tylosurus crocodilus), carp (Carassius carpio), whitefish (Alburnus), redfin culter (Cultrichthys erythrophthalmus), and wolfish (Anarhichys...
ocellaus), had the highest concentration of TCEP (mean: 2.9, 1.9, 2.5, 11, 3.4, 4.9 and 0.92 ng/g ww respectively); two fish species, silver fish (Protosalanx hyalocranius abbott) and catfish (Silurus asotus), had the highest concentration of TiBP (mean: 9.0 and 3.9 ng/g ww respectively); and two species, white bait (Hemisalanx prognathous) and yellow-head catfish (Peleobagrus fulvidraco), had the highest concentration of TPHP (mean: 0.59 and 1.2 ng/g ww respectively). The concentration range of lipid weight-based ΣOPEs was 92–999 ng/g lw, comparable to that observed in 20 fish species from Manila Bay, Philippines (Kim et al., 2011a, 2011b; Zhao et al., 2018). In eel from Taihu Lake, ΣOPEs ranged from 232 ng/g lw to 649 ng/g lw, one order of magnitude higher than that (7.0–330 ng/g lw) of the same species from Belgium (Malarvannan et al., 2015; Zhao et al., 2018).

In addition to fish, the occurrence of OPEs has also been reported in other aquatic food products, such as mussels, clams, snails, prawns, and shrimp, in Sweden, Belgium, and China (Campone et al., 2010; Sundkvist et al., 2010; Poma et al., 2018; Xu et al., 2015; Zhao et al., 2018). In Belgium, all mussel and crustacean samples had low concentrations of each OPE, with the exception of TPHP (Poma et al., 2018; Xu et al., 2015). TPHP was the highest, at a mean concentration of 6.3 ng/g ww in mussel samples, while TCIPP was the highest (mean: 9.9 ng/g ww) in fresh mussels (Lamellibranchia) from Taihu Lake (China) (Zhao et al., 2018). The occurrence of 8 OPEs (i.e., TCEP, TCIPP, TDCIPP, TPHP, TNBP, TMPP, EHDPP, and TBOEP) in blue mussels (Mytilus edulis) from Sweden was also studied (Sundkvist et al., 2010). Six OPEs, not including TDCIPP or TBOEP, were detected, of which TCIPP was by far the most abundant OPE, with a concentration ranging from 130 to 1300 ng/g lw and a mean of 715 ng/g lw. Compared to the fish products, including herring and salmon, from the same area, the levels of OPEs, especially TCIPP, in mussels were higher. This could be due to two reasons. TCIPP is classified as not readily biodegradable in relation to non-chlorinated OPEs such as TPHP and TNBP, which have half-lives of a few days in river water (Sundkvist et al., 2010). TCIPP was imported to Sweden as an important component of bulk chemicals according to the National Chemical Inspectorate of Sweden in 2004 (KemI, 2004). TCIPP was also found to be highest in freshwater shrimp (Macrobrachium nipponense) (mean: 6.2 ng/g ww) from Taihu Lake, China, while TEHP and TIBP concentrations were highest in clams (Lamellibranchia) and snails (Bellamya purificata), and white shrimp (Exopalaemon modestus) from the same region, respectively (Zhao et al., 2018). Collectively, the OPE levels in aquatic food products such as fish, mussels, prawns, and shrimp, were compared to those of other food categories, with concentrations from nd to 14,000 ng/g lw. However, for the same water, different fish species generally exhibited similar OPE contamination patterns. The levels and distribution patterns of each OPE in fish were substantially different even when collected from the same country or the same fish species at various growth stages, which may be attributable to differences in OPE physico-chemical properties, resistance to hydrolysis in aqueous environments, production and the extent of usage, as well as the accumulation and enzymatic degradability of the fish species to OPEs.

### 3.5. Dairy food products

The levels of OPEs in fluid dairy products, including milk, sour milk, yogurt and lactobacillus beverages, and in solid dairy products, including hard, processed, or cottage cheese; cream; butter; sour cream; and milk powder, were reported for Sweden, China, Belgium, Australia and the United State (Table S4 and Fig. 4). Regardless of the sampling countries, these data generally demonstrated that solid dairy products exhibit greater OPE concentrations compared to fluid dairy products. The pattern of OPE congeners in Uppsala (Sweden) samples exhibited a mean concentration order from highest to lowest as follows: EHDPP > TDCIPP ≥ TCEP ≥ TPHP > TCIPP (Poma et al., 2017). TPHP was the most prominent in both solid and fluid dairy products from Belgium (Poma et al., 2018), and TDCIPP at a mean concentration of 296 ng/L was detected as an ascendant OPE in dairy samples from Tianjin, China (Zhang et al., 2016). TNBP and TCIPP were the

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**Fig. 4.** Mean contamination levels (ng/g) and congener compositions of organophosphate ester (OPE) flame retardants and plasticizers in eggs and dairy products from markets in different countries. The concentrations are reported as ng/g ww (A) in these samples with an exception of dairy products, where the unit is ng/L (B). Detailed data are compiled in the Table S4 of supporting information.
predominant OPE compounds found in dairy products from Australia (TNBP: 0.95 ng/g ww (mean), 0.26 ng/g ww (median); TCIPP: 0.89 ng/g ww (mean), 0.58 ng/g ww (median)) and the United States (TNBP: 0.21 ng/g ww (median); TCIPP: 0.23 ng/g ww (median)) (He et al., 2018; Wang et al., 2018). Similar to the low OPE concentrations (median: 2.57 ng/g ww) reported for dairy products from Australia, dairy products containing milk, yogurt, cheese, and butter from the United States presented low OPE concentrations (1.22 ng/g ww) (He et al., 2018; Wang et al., 2018). As for different brands of milk powder and liquid milk purchased from supermarkets in Guangdong province (China), only TEP was detected in one brand of milk powder at a contamination level of hundreds of ng/kg (Guo et al., 2016; Wu et al., 2017). These results suggest that EHDPP, TPHP, TDCIPP, TNBP, TBOEP, or TEP are the most abundant compounds in dairy products depending on the sampling countries. Regardless of the sample type, both cheese and milk from Belgium exhibited greater concentrations of ΣOPEs. Here, we emphasize that human exposure to OPEs from dairy products cannot be ignored, since the sum of OPE concentrations in dairy samples from certain cities, such as Tianjin in China, reached the μg/L level, showing high contamination levels.

### 3.6. Eggs

The summarized results of OPE concentrations in eggs collected worldwide are given in Table S4 and Fig. 4. Eggs from Qingyuan (China) exhibited the greatest median concentration of OPEs, especially for TCEP and TPHP which were detected in 100% of the sampled eggs. This could due to the proximity of a local e-waste recycling facility. However, the ΣOPE levels for eggs collected at e-waste sites and the control site were reported to not be significantly different, e-waste recycling activities may only have a weak influence in terms of contamination. Chlorinated OPEs (TCEP, TCIPP and TDCIPP) had an over 50% detection frequency in eggs from Qingyuan (Zheng et al., 2016). The TCIPP and TCEP were both detected at a higher mean concentration of 0.43 and 0.19 ng/g ww compared with detected TNBP (mean: 0.17 ng/g ww) in eggs from Australia (He et al., 2018). The fact that chlorinated OPEs are more bioaccumulative or persistent than non-chlorinated OPEs could explain this phenomenon.

The levels of EHDPP (mean value of 0.91 ng/g ww) in fresh eggs from Sweden were several times higher than other targeted OPEs in the country or reported OPEs in Belgium and Australia (He et al., 2018; Poma et al., 2017, 2018). Two studies reported OPE concentrations in eggs from Belgium, where TPHP was found to be the major OPE, with a concentration of 0.27 ng/g ww in free range chicken eggs collected in 2013, and where the concentrations of other OPEs were generally below LOQs as reported by Xu et al. (2015). Longitudinal changes in the OPE levels in eggs collected from Belgium at a time interval of two and three years showed that all the concentrations of seven detectable OPEs (including TCEP, TCIPP, TDCIPP, TPHP, EHDPP, and TEHP) in eggs sampled in 2015 and 2016 fell, and were less than or equal to 0.15 ng/g ww (Poma et al., 2018). The results may be related to organizations exercising more strict management of OPE use and application (Regulation (EC) No 1272/2008). Overall, compared with the reported OPEs in eggs, TCEP concentrations in egg samples from Qingyuan, China were highest, with a median of 1.08 ng/g ww, while EHDPP concentrations in samples from Sweden were highest, with a mean of 0.91 ng/g ww.

### 3.7. Vegetables and fruits

Compared with aquatic food products or meat samples, considerably fewer reported studies have measured OPEs in vegetables and fruits, and a limited number of reports have demonstrated that the concentrations of OPEs in this category of samples were lowest among all investigated foodstuffs (Figs. 1 to 5). The sampling countries involved were limited to China, Sweden, Belgium and Australia. For individual OPEs, vegetables from Tianjin, China had generally higher OPE concentrations, especially those of TEHP (mean: 12.7 ng/g dw), by one or two orders of magnitude than samples from Sweden, Belgium and Australia. This was explained by the fact that higher levels of OPEs are found in water and soil from China compared to the other three countries and that most OPEs have excellent aqueous solubility, which
resulted in a greater accumulation of OPEs in vegetables through water and soil (Zhang et al., 2016). Vegetable samples purchased from different regions had different distributions of OPEs. Vegetables from Belgium and Australia had an overwhelming dominance of TPHP (mean: 2.01 ng/g ww) and TCPP (mean: 1.91 ng/g ww), respectively, the concentrations of which were one to two orders of magnitude higher than those of other detectable OPEs (He et al., 2018; Poma et al., 2018). The mean concentration of TCEP (0.41 ng/g ww), TDCIPP (0.37 ng/g ww), EHDPP (0.28 ng/g ww) and TCIPP (0.18 ng/g ww) in vegetables from Uppsala (Sweden) were at the same level and were significantly higher than the mean concentration of TPHP (0.07 ng/g ww) (Poma et al., 2017). In addition, leafy vegetables, such as crown-daisy chrysanthemum (Glebionis coronaria), pakchoi cabbage (Brassica rapa) and Chinese chives (Allium tuberosum) were more seriously contaminated with OPEs relative to stem or root vegetables, most likely due to leafy vegetables being more vulnerable to the deposition of organic pollutants due to a larger waxy and cuticle surface area (Zhang et al., 2016). Overall, regardless of the sampling cities, the contamination levels of OPEs in vegetable samples were generally low and at the ppb level (ng/g ww).

Aside from vegetables, fruits are also regarded as potential carriers of OPEs via their shoots. The occurrence of common OPEs in fresh fruits (i.e., banana, apple, pear, orange, mandarin, strawberry, and grape) and derived products (i.e., jam, nuts, juice, cordials, and fresh or frozen canned products) was investigated (He et al., 2018; Poma et al., 2017; Zhang et al., 2016). Generally, and similar to vegetables, higher concentrations of OPEs, except TCIPP, were found in fruits from China, most likely due to the high OPE contamination in the water, soil, and atmosphere in China (Zhang et al., 2016). The highest concentration of TCIPP (mean: 1.29 ng/g ww) was observed in fruits from Australia (He et al., 2018). EHDPP (mean: 0.47 ng/g ww) was the major component of OPEs in fruits from Uppsala, possibly due to its widespread application in fruit packaging materials (Poma et al., 2017). In contrast, the primary OPEs in fruits from Tianjin were chlorinated OPEs, in particular TDCIPP, with a mean concentration of 5.05 ng/g dw, where TDCIPP had a higher fruit-shoot concentration factor (FSCF) of 0.77 in strawberry fruit relative to other OPEs such as TCEP and TCIPP (Hyland et al., 2015).

3.8. Other foods

This category of other foods includes wines, sugar/sweets, pastries and desserts, beverages, animal feed and baby food (Table S6 and Fig. 6).

Five OPEs (TNBP, TBOEP, TPHP, TCIPP, and TCEP) in alcoholic drinks from the Henan Province in China were screened and were found to contain ΣOPE concentrations ranging from 290 to 850 ng/L, 1000 to 3050 ng/L and 860 to 1470 ng/L in white wine, red wine, and beer, respectively (Pang et al., 2017). The occurrence of OPEs in various beverages including juice, tea, liquor, carbonated drinks, energy drinks, and soda water from another Chinese city, Tianjin, was also reported. TCEP, TPHP, TCIPP, TDCIPP, TBOEP, and TEHP were detected at total concentrations ranging from 65 to 4569 ng/L, where TCEP, TPHP, and TEHP were the main contributors to the ΣOPE concentrations. In other types of beverages, including soft drinks, mineral water, and beer (up to 3.5 vol%) from Uppsala, five OPEs (TCEP, TCIPP, TCPP, TPHP and EHDPP) were detected at mean concentrations ranging from 0.20 to 1.50 ng/g ww, of which the mean concentrations of EHDPP (1.50 ng/g ww) and TDCIPP (0.86 ng/g ww) were comparable and higher than those of TPHP, TEHP, and TCIPP. The distribution of OPEs in beverages, including beer, coffee, juice, tea, and tap water obtained from Australia was different from that found in Sweden. The TCIPP and TNBP concentrations were much higher than those detected for TCEP, TDCIPP, TPHP, and TBOEP.

In pastries and desserts collected from markets in Sweden and Belgium, EHDPP was the most abundant OPE with median concentrations of 9.25 and 8.72 ng/g ww respectively. The OPEs in pastries and desserts from these two countries were not significantly different, except for the unique occurrence of TNBP and TEHP in desserts from Belgium. Similar to pastries and desserts, the rest of the items, namely sugar/sweets, animal feed and baby food, the most abundant OPE was EHDPP, with median concentrations of 3.71, 12.29 and 0.59 ng/g ww, respectively (Poma et al., 2017; 2018). Overall, the pattern of OPE concentrations varied as a function of the sampling countries. For example, ΣOPE concentrations in samples from Sweden and Belgium were dominated by EHDPP, whereas ΣOPE concentrations appeared to be dominated by TEHP and TCEP in samples from China.

| OPE | Sweden(Pastries) | Belgium(Pastries) | Sweden(Beverages) | Belgium(Beverages) | Sweden(Other food) | Belgium(Other food) | Belgium(Baby food) | China(Beverages) |
|-----|------------------|-------------------|------------------|-------------------|--------------------|--------------------|-------------------|---------------------|
| TCEP | 0.15             | 0.05              | 0.20             | 0.03              | 0.15               | 0.05               | 0.15              | 0.05                |
| TCIPP | 0.15            | 0.05             | 0.20            | 0.03            | 0.15           | 0.05            | 0.15            | 0.05              |
| TDCIPP | 0.15        | 0.05           | 0.20        | 0.03        | 0.15       | 0.05       | 0.15       | 0.05              |
| TPHP | 0.15             | 0.05             | 0.20             | 0.03             | 0.15               | 0.05               | 0.15              | 0.05                |
| TNBP | 0.15             | 0.05             | 0.20             | 0.03             | 0.15               | 0.05               | 0.15              | 0.05                |
| TMPP | 0.15             | 0.05             | 0.20             | 0.03             | 0.15               | 0.05               | 0.15              | 0.05                |
| EHDPP | 0.15            | 0.05             | 0.20            | 0.03            | 0.15           | 0.05            | 0.15            | 0.05              |
| TBOEP | 0.15           | 0.05           | 0.20           | 0.03           | 0.15           | 0.05           | 0.15           | 0.05              |
| TEHP | 0.15             | 0.05             | 0.20             | 0.03             | 0.15               | 0.05               | 0.15              | 0.05                |
| TPrP | 0.15             | 0.05             | 0.20             | 0.03             | 0.15               | 0.05               | 0.15              | 0.05                |

Fig. 6. Mean contamination levels (ng/g) of organophosphate ester (OPE) flame retardants and plasticizers in other food from markets in different regions. The concentrations are reported as ng/g ww (A) for most of samples with an exception of beverages where the concentration unit is ng/L (B). Detailed data are compiled in the Table S6 of supporting information.
3.9. Comparison among various food categories

The total average concentrations of OPEs in various types of food sampled from different foodstuff markets are shown in Fig. 7. Cereals and fats/oils were the most contaminated by OPEs in China and Belgium (Poma et al., 2018; Zhang et al., 2016), while fats/oils and desserts were the main polluted products in Sweden (Poma et al., 2017). In contrast, the four food categories, i.e. vegetables, fruits, fluid dairy products and cereals, were the primary target of contamination by OPEs in Australia (He et al., 2018). Irrespective of the sampling sites, except for the United States, animal-based foods, e.g. meats, fish and eggs, seemly to have lower mean OPE contents than plant-based food, e.g., cereals and vegetables. However, the highest median OPE concentrations were found in meat and fish products from the United States (Wang et al., 2018). This is likely due to several factors such as the food type, the analytical and sampling methods, the sampling sites, and the OPE pollution levels. For example, processed food with more complex production processes (e.g. fats, cheese, desserts, meat, and milk) were more seriously contaminated by OPEs compared with the non-processed food that nearly maintained their natural state (e.g., vegetables, eggs, meat and milk). The OPE contents of food were also significantly affected by being their proximity to OPE manufacturing facilities. Rapid metabolism/excretion of OPEs in biota very likely contributed to their low levels in fresh fish and meat products (Su et al., 2014). Additionally, OPE concentrations were not significantly different between high lipid content food (such as fish, milk and meat) and less fatty ones (such as cereals, vegetables and potatoes), suggesting that the accumulation of OPEs is lipid-independent (Poma et al., 2018).

4. Daily intake estimation for OPEs

Because of the frequent occurrence of OPEs in various foodstuffs, humans are being exposed to OPEs via their dietary intake. Based on our review, the measurable levels of OPEs in food samples from various years were highly variable among different sampling locations and even within countries, indicating that the risk of exposure to OPEs is also variable. Table 2 shows the estimated daily intake of OPE (EDI, ng/kg bw/day) for adults (including men and women), infants (< 1 years old; yr), toddlers (1 to < 6 yr), children (6 to < 11 yr in the United States; 3 to 12 yr in China), and teenagers (11 to < 21 yr) from various countries via foodstuff ingestion based on the measured concentrations of targeted compounds in various food samples by means of market basket surveys or duplicate diets. For the high-exposure scenario, the highest median EDI (95th percentile) value of ΣOPE for toddlers was up to
Table 2

Oral reference dose (RfD) and estimated daily intake (EDI) values (ng/kg bw/day) of organophosphate ester (OPE) flame retardants and plasticizers for residents in different regions.

| OPFRs       | TCEP | TCPP | TDCIPP | TPHP | TNBP | TMP | EHDP | TBQEP | THP | TEP | TCP | TMP | TiBP | SOPEs | References                  |
|-------------|------|------|--------|------|------|-----|------|-------|-----|-----|-----|-----|-----|------|------|
| RfD values  |      |      |        |      |      |     |      |       |     |     |     |     |     |      | USEPA                        |
| Tianjin (China) |      |      |        |      |      |     |      |       |     |     |     |     |     |      | Zhang et al. (2016)          |
| Mean        | 22,000 | 80,000 | 15,000 | 70,000 | 24,000 | 13,000 | 15,000 | 15,000 | 35,000 | 125,000 | 80,000 | na a | – | na |
| Male        | 162 | 72 | 37 | 68 | – | – | – | – | 39 | 160 | – | – | – | 539 |
| Female      | 182 | 82 | 42 | 77 | – | – | – | – | 44 | 174 | – | – | – | 601 |
| 95th percentile | 236 | 105 | 103 | 114 | – | – | – | – | 60 | 282 | – | – | – | 818 |
| Uppsala (Sweden) |      |      |        |      |      |     |      |       |     |     |     |     |     |      | Xu et al. (2017)             |
| Mean        | 6.0 | 8.5 | 11.9 | 9.7 | – | – | – | – | 48.6 | – | – | – | – | – |
| Female      | 182 | 82 | 42 | 77 | – | – | – | – | 44 | 174 | – | – | – | 601 |
| 95th percentile | 247 | 112 | 112 | 126 | – | – | – | – | 67 | 290 | – | – | – | 880 |
| Norway      | 6.0 | 8.5 | 11.9 | 9.7 | – | – | – | – | 48.6 | – | – | – | – | – |
| 95th percentile | 236 | 105 | 103 | 114 | – | – | – | – | 60 | 282 | – | – | – | 818 |
| A city in Eastern China |      |      |        |      |      |     |      |       |     |     |     |     |     |      | Ding et al. (2018)           |
| Median      | 6.0 | 8.5 | 11.9 | 9.7 | – | – | – | – | 48.6 | – | – | – | – | – |
| 95th percentile | 236 | 105 | 103 | 114 | – | – | – | – | 60 | 282 | – | – | – | 818 |
| Belgium     | 6.0 | 8.5 | 11.9 | 9.7 | – | – | – | – | 48.6 | – | – | – | – | – |
| 95th percentile | 236 | 105 | 103 | 114 | – | – | – | – | 60 | 282 | – | – | – | 818 |
| Southeast Queensland (Australian) |      |      |        |      |      |     |      |       |     |     |     |     |     |      | He et al. (2018)             |
| Mean        | 4.1 | 25 | < 1.1 | < 0.15 | 6.7 | < 0.15 | < 5.0 | 1.8 | < 0.088 | – | – | – | – | – |
| Albany (the United States) |      |      |        |      |      |     |      |       |     |     |     |     |     |      | Wang et al. (2018)           |
| Median      | 6.0 | 8.5 | 11.9 | 9.7 | – | – | – | – | 48.6 | – | – | – | – | – |
| 95th percentile | 236 | 105 | 103 | 114 | – | – | – | – | 60 | 282 | – | – | – | 818 |

a RfD value is not available for this OPE congener.
1340 ng/kg/bw/day (Wang et al., 2018). In the city of Tianjin (North China), the total mean EDI (95th percentile) values of ΣOPE for men and women were estimated to be 818 and 880 ng/kg bw/day, respectively (Zhang et al., 2016), higher than those reported for people from other regions. The differences among the estimated EDI exposures reported in these studies could also be attributed to the different sampling strategies that were employed. No significant differences were found between the EDI values of ΣOPE at different sampling sites, including in the United States (adults: 25.1, children: 56.6 ng/kg/bw/day), China (adults: 55.0, children: 97.7 ng/kg/bw/day), Sweden (adults: 84.7 ng/kg/bw/day), and Belgium (adults: 102.8 ng/kg/bw/day) (Ding et al., 2018; Poma et al., 2017, 2018; Wang et al., 2018). The EDI values of ΣOPE in adult (male and female) from China (male: 539 ng/kg/bw/day, female: 601 ng/kg/bw/day) were higher than those in adults (men and women) from Belgium (men: 106.1 ng/kg/bw/day; women: 93.2 ng/kg/bw/day) (Poma et al., 2018; Zhang et al., 2016). Children had a higher exposure risk than adults as indicated by the higher OPE EDI values. TEHP was the primary contributor to the total OPE exposure via dietary intake and accounted for about 30% to 58% of the overall OPE intake for adults, including both men and women and children in China, followed by TCEP and TCIPP (Zhang et al., 2016). EHDPP, TPHP, and TCIPP overwhelmingly contributed 57%, 45% and 66% of the total EDI values of OPEs for the general adult population in Sweden, Belgium and Australia, respectively (Poma et al., 2017, 2018). TBOP accounted for 32%, 48%, 44%, 52% and 54% of OPE exposure in infants, toddlers, children, teenagers and adults from the United States, respectively (Wang et al., 2018) (Fig. 8 and Table 2).

Although there is insufficient evidence related to the toxicological effects of all the targeted OPEs, certain findings have indicated the adverse effects of OPEs in both animals and humans. For example, TPHP and TDCIPP have been found to induce neurotoxicity in Chinese rare minnow (Gobio cypris rar us) (Hong et al., 2018; Yuan et al., 2015), developmental and reproductive toxicity in zebrafish and/or cardiotoxicity (Du et al., 2015; McGee et al., 2012; Zhu et al., 2015). These two chemicals, with concentrations of up to 1.8 mg/g detected in the house dust from 50 samples, were found to be associated with hormone levels and decrease semen quality in men (Meeker and Stapleton, 2010). EHDPP, TPHP, TNBP, TBOEP, TEP, and TCIPP levels at several to ten ng/mL in human blood samples were able to disrupt sphingolipid homeostasis (Zhao et al., 2016). As such, assessing whether the measured concentrations of OPEs in food pose a risk via the diet to human health is urgent matter. The EDI values of OPEs were either compared with the oral reference dose (RfD) proposed by the U.S. EPA or calculated by dividing the chronic no observed adverse effect level (NOAEL) by 1000 (safety factor) (Xu et al., 2017; Zhang et al., 2016). Apart from the ΣOPEs and OPEs, except for TRP, which has no established available RfD value, the EDI values were far lower than their corresponding RfD values (Table S2). Nevertheless, other factors could affect the EDI values of OPEs in food products, including dilution effects arising from composite foods and the effects of cooking processes, which may reduce the levels of OPE contamination in food (Ding et al., 2015, 2018). Other OPEs, such as TiBP, dBPhP, BdPhP, and TPeP, have been detected in food products for human consumption, as reported in the published literature (Kim et al., 2011a, 2011b; Sundkvist et al., 2010; Zhao et al., 2018), but were not considered here because of their low detection rate or few studies.

Apart from dietary exposure, humans can be exposed to OPEs via other pathways, such as dust ingestion, air inhalation, and dermal absorption. The median ΣOPE exposure concentrations via dust ingestion and air inhalation for a Norwegian cohort was 8.8 and 9.3 ng/kg bw/
day, and EDI values of EHDPP via the same routes were 0.19 and 0.13 ng/kg bw/day, respectively (Xu et al., 2015, 2017). The EDI values of OPEs via suspended particulate inhalation during a typical 8 h work day and ingestion via drinking water (tap water) were 0.6 and 7.1 ng/kg bw/day for an adult male, respectively (Ding et al., 2015). These reported OPE EDI data were lower than those reported via dietary intake summarized in this review, which strongly suggests the equal or greater importance of human OPE exposure via the diet. However, the relative human exposure to OPEs on the basis of bioavailability via ingestion, inhalation, and dermal contact has not yet been fully elucidated.

5. Research gaps and future directions

The contamination levels of OPEs in various food products and in the dietary intake of human populations around the world up to 2018 have been summarized in this review. Four major research gaps or future directions are presently identified and summarized.

There dearth of monitoring studies on OPEs in foodstuffs consumed by humans is currently mainly limited to several countries, i.e., China, Sweden, Belgium and Australia. Reports on the contamination levels of OPEs in foodstuffs for other regions are rare to non-existent. Western Europe, North America, and China are three major consumers of flame retardants, accounting for approximately 60% of its global consumption (European Commission, 2011). (Abiotic) environmental matrices collected from these regions have frequently reported high concentrations of OPEs with μg/L levels in water and μg/kg levels in sediment samples (Aznar-Alemany et al., 2018; Cristale et al., 2013; Kim et al., 2017; Kim and Kannan, 2018). India has been forecasted to become the first rapidly expanding national markets for flame retardants, followed by Thailand (Liu, 2018). Thus, the systematic global monitoring of OPE contamination in foodstuffs, especially in the countries where they have already been reported e.g., Western Europe, North America, and China, is urgently warranted. This would provide an insight into different patterns of occurrence and intake, as well as a better assessment of human exposure.

Studies have shown that the mean dietary exposure to OPEs mainly originates from industrially processed food groups, such as grains, oils, and dairy products (Poma et al., 2018). For this reason, it is plausible to suggest that processed foodstuff samples should have higher priority compared to raw foodstuffs in future studies on OPEs, especially regarding EHDPP, which was found to contaminate foodstuff via its migration from food packaging materials (Poma et al., 2018). In fact, EHDPP and its metabolites also showed an increasing detection frequency in human samples (Zhao et al., 2016; Araki et al., 2018; Shen et al., 2019). More importantly, EHDPP was proven to be a potent disruptor of metabolic pathways in humans. Zhao et al. determined the concentrations of sphingolipid levels and EHDPP in human blood and observed a significant correlation between In-transformed sphingolipid levels and EHDPP concentrations (Zhao et al., 2016).

The literature currently reporting on OPE concentrations in foodstuffs varied greatly in terms of the selected OPE congeners, sampling protocols, and analytical methods, making it extremely difficult for comparison between foodstuff categories and geographical regions (He et al., 2018; Poma et al., 2017, 2018; Zhang et al., 2016). As such, the development of an appropriate multi-residue methodology to amend the extraction, isolation, and separation processes, and the establishment of universal analytical criteria for the measurement of the above priority OPEs and even additional OPEs in foodstuffs could lead to a more reliable comparison of OPEs levels among various food categories as well as from different sampling regions. For future OPEs in food matrices studies, it would be the best to employ a consistent sample collection approach (i.e., whole or partial sample, in ww, dw, lw, or total weight) at least in the same food category, and the method detection limit, range, geometric mean and/or median of individual and total OPE concentrations should be provided. In terms of the concentration units, we strongly suggest that wet weight should be consistently used in future reports.

The large amounts of OPEs produced and used worldwide have resulted in their widespread occurrence in various environmental matrices (e.g., biota, soil, sediment, water, and air), including in highly remote regions, such as the Arctic (AMAP, 2016; Greaves and Letcher, 2017; Hou et al., 2016; van der Veen and de Boer, 2012; Salamova et al., 2014). OPEs can be transformed/degraded into unknown by-products under environmental conditions, particularly in biota. For instance, it has been frequently reported that OPE derivatives, especially OP diesters, can be potentially generated by the rapid enzyme-catalyzed metabolism of OPEs in humans and animals, including wildlife that is consumed by humans, as well as through other degradation pathways, such as microbial metabolism/biotransformation, base-catalyzed hydrolysis, and photodegradation (Cequier et al., 2015; Greaves et al., 2016; Hou et al., 2016; Ou et al., 2017; Strobel et al., 2018a, 2018b; Su et al., 2014, 2016). These processes suggest that OPE derivatives could potentially co-exist with parent OPEs in environmental samples or foodstuffs (Fu et al., 2017). More importantly, some studies have stated that these derivatives/by-products, as compared to parent OPE triesters, are more biologically active with respect to several toxicological endpoints (Elliott et al., 1982; Kojima et al., 2016; Su et al., 2014). However, to the best of our knowledge, there has been no published report on OPE derivatives/by-products in foodstuffs apart from a very recent study that reported the presence of 11 OPE metabolites in foodstuff samples collected in Queensland, Australia (He et al., 2018). Thus, further studies are needed to elucidate future trends of food contamination by both OPEs and their by-products, such as OP diesters and hydroxylated metabolites, and also to improve the risk assessment for these chemicals.

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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.2019.03.009.

References

AMAP, 2016. Chemicals of Emerging Arctic Concern. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. https://www.amap.no/documents/doc/amap-assessment-2016-chemicals-of-emerging-arctic-concern/1624. Araki, A., Bastiensen, M., Ramat, Y.A., Van den Eede, N., Kawai, T., Tsuboi, T., Ketema, R.M., Covaci, A., Kishi, R., 2018. Associations between allergic symptoms and phosphate flame retardants in dust and their urinary metabolites among school children. Environ. Int. 119, 438–446.

Aznar-Alemany, O., Aminot, V., Vilà-Can, J., Kock-Schulmeier, M., Readman, J.W., Marques, A., Godinho, L., Botteon, E., Ferrari, F., Boti, V., Albani, T., 2018. Halogenated and organophosphorus flame retardants in European aquatic samples. Sci. Total Environ. 612, 492–500.

Cencic, I., Pietrini, A.L., Ostman, G., Rastrelli, L., 2010. Determination of organophosphorus flame retardants in fish tissues by matrix solid-phase dispersion and gas chromatography. Anal. Bioanal. Chem. 397 (2), 799–806.

Cequier, E., Sakhi, A.K., Marce, R.M., Becher, G., Thomsen, C., 2015. Human exposure pathways to organophosphate triesters-A biomonitoring study of mother-child pairs. Environ. Int. 59, 155–165.

Cristale, J., Vázquez, A.G., Barala, C., Lacorte, S., 2013. Priority and emerging flame retardants in rivers: occurrence in water and sediment. DNPb magna toxicity and risk assessment. Environ. Int. 59, 232–243.

Ding, J., Shen, X., Liu, W., Covaci, A., Yang, F., 2015. Occurrence and risk assessment of organophosphate esters in drinking water from Eastern China. Sci. Total Environ.
538, 959–965.
Ding, J., Deng, T., Xu, M., Wang, S., Yang, F., 2018. Residuals of organophosphate esters in foods and implication for human exposure. Environ. Pollut. 233, 986–991.
Dui, Z.K., Wang, G.W., Gao, S.X., Wang, Z.Y., 2015. Aryl organophosphate flame retardants induced neurotoxicity in Daphnia magna by disrupting expression of the transcriptional regulators. Aquat. Toxicol. 161, 25–32.
Elliott, W.C., Lynn, R.K., Houghton, D.C., Kennish, J.M., Bennett, W.M., 1982. Neophytotoxicity of the fish flame retardant, Tris (2,3-dibromopropyl) phosphate, and its metabolites. Toxicol. Ind. Health. 8, 179–182.
European Commission, 2011. Identification and evaluation of data on flame retardants in consumer products. Contract 17.020020/09/549040.
Fu, L.F., Du, R.B., Wang, F., Lamm, J.C.W., Zeng, L.X., Zeng, E.Y., 2017. Organophosphate transformers and diesters degradation products in municipal sludge from wastewater treatment plants in China: spatial patterns and ecological implications. Environ. Sci. Technol. 51, 13614–13623.
Gao, Z.Q., Den, Y.H., Yuan, W., He, H., Yang, S.G., Sun, C., 2014. Determination of organophosphate flame retardants in fish by pressurized liquid extraction using aqueous solutions and solid-phase microextraction coupled with gas chromatography-flame photometric detector. J. Chromatogr. A. 1356, 31–37.
Greaves, A.K., Letcher, R.J., 2017. Organophosphate esters: a review on wildlife distribution, fate and ecotoxicology. Bull. Environ. Contam. Toxicol. 98, 2–7.
Guo, A.K., Su, G., Letcher, R.J., 2016. Environmentally relevant organophosphate triesters in herring gills: in vitro biotransformation and kinetics and diester metabolism using a hepatic microsomal assay. Toxicol. Appl. Pharmacol. 308, 59–65.
Guo, X.D., Mu, T.N., Xian, Y.P., Luo, D.H., Wang, C., 2016. Ultra-performance liquid chromatography tandem mass spectrometry for the rapid simultaneous analysis of nine organophosphate esters in milk powder. Food Chem. 196, 673–681.
He, C., Wang, X.Y., Tang, S.Y., Thai, P., Li, Z.R., Buduel, C., Mueller, J.F., 2018. 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.
Hong, X.S., Chen, R., Hou, R., Yuan, L.L., Zha, J.M., 2018. Triphenyl phosphate (TPHP)-induced neurotoxicity in adult male Chinese rare minnows (Gobiocypris rarus). Environ. Sci. Technol. 52, 11950–11959.
Hou, R., Xu, X., Wang, Z., 2016. Review of OPPFs in animals and humans: absorption, bioaccumulation, metabolism, and internal exposure research. Chemosphere 153, 75–89.
Hyland, R.C., Blaine, A.C., Higgins, C.P., 2015. Accumulation of contaminations of emerging concern in food crops part 2: plant distribution. Environ. Toxicol. Chem. 2015 (34), 2222–2230.
Jones-Otano, H.A., Clarke, J.P., Diamond, M.L., Archbold, J.A., Ferguson, G., Harner, T., Richardson, G.M., Ryan, J.J., Wilford, R., 2005. Is house dust the missing exposure pathway for PBDEs? An analysis of the urban fate and human exposure to PBDEs. Environ. Sci. Technol. 39 (14), 5121–5130.
Kanazawa, A., Saito, I., Araki, A., Takeda, M., Ma, S., Saito, Y., Kishi, R., 2010. Association between indoor exposure to semi-volatile organic compounds and building-related symptoms among the occupants of residential dwellings. Indoor Air 20 (1), 72–84.
Keml, P. 2018. The Products Register. National Chemical Inspectorate of Sweden, Personal communication.
Kim, U.J., Kannan, K., 2018. Occurrence and distribution of organophosphate flame retardants/plasticizers in indoor air and dust from various microenvironments in the United States. Environ. Int. 127, 342–349.
Kojima, H., Takesuki, Y., Kondo, T., 2016. Determination of primary metabolites of organophosphate flame retardants on transcriptional activity via human nuclear receptors. Toxicol. Lett. 245, 31–39.
Lee, S., Jeong, W., Kannan, K., Moon, H., 2015. Occurrence of organophosphate flame retardants/plasticizers in wastewater treatment plant in New York State. Environ. Sci. Technol. 51, 7872–7880.
Lim, U.J., Kannan, K., 2019. Occurrence of and human exposure to organophosphate flame retardants/plasticizers in indoor air and dust from various microenvironments in the United States. Environ. Int. 125, 342–349.
Pomar, G., Sales, C., Bruyland, B., Christia, C., Goscinny, S., Van Loco, J., Covaci, A., 2018. Concentrations of organophosphate flame retardants/plasticizers in indoor air and dust from various indoor environments. Chemosphere. 53 (9), 78–90.
Richardson, G.M., Ryan, J.J., Wilford, B., 2005. Is house dust the missing exposure pathway for PBDEs? An analysis of the urban fate and human exposure to PBDEs. Environ. Sci. Technol. 39 (14), 5121–5130.
Sundkvist, A.M., Olofsson, U., Haglund, P., 2010. Organophosphorus flame retardants and plasticizers in marine biota: a review of environmental distribution, fate and ecotoxicology. Bull. Environ. Contam. Toxicol. 98, 2–7.
Su, G., Letcher, R.J., Kennedy, S.W., 2014. Rapid in vitro metabolism of the organophosphate flame retardant triphenyl phosphate and effects on cytoxicity and mRNA expression in human embryonic hepatocytes. Environ. Sci. Technol. 48 (12), 13511–13519.
Su, G., Letcher, R.J., Yu, H., 2016. Organophosphate flame retardants and plasticizers in aqueous solution: pH-dependency hydrolysis, kinetics, and pathways. Environ. Sci. Technol. 50 (15), 8103–8112.
Su, G., Letcher, R.J., Yu, H., 2016. Organophosphate flame retardants and plasticizers in aqueous solution: pH-dependency hydrolysis, kinetics, and pathways. Environ. Sci. Technol. 50 (15), 8103–8112.
Su, G., Letcher, R.J., Yu, H., 2016. Organophosphate flame retardants and plasticizers in aqueous solution: pH-dependency hydrolysis, kinetics, and pathways. Environ. Sci. Technol. 50 (15), 8103–8112.
Strobel, A., Letcher, R.J., Willmore, W.G., Sonne, C., Dietz, R., 2018a. Organophosphate esters in East Greenland polar bears and ringed seals: adipose tissue concentrations and in vivo depletion and metabolism formation. Chemosphere 196, 240–250.
Strobel, A., Letcher, R.J., Willmore, W.G., Sonne, C., Dietz, R., 2018b. Structure-dependen
tent in vivo metabolism of alkyl-substituted analogues of the organophosphate ester, triphenyl phosphate, in East Greenland polar bears and ringed seals. Environ. Sci. Technol. Lett. 5, 214–219.
Su, G., Grump, D., Letcher, R.J., Kennedy, S.W., 2014. Rapid in vitro metabolism of the organophosphate flame retardant triphenyl phosphate and effects on cytotoxicity and mRNA expression in human embryonic hepatocytes. Environ. Sci. Technol. 48 (12), 13511–13519.
Su, G., Letcher, R.J., Yu, H., 2016. Organophosphate flame retardants and plasticizers in aqueous solution: pH-dependency hydrolysis, kinetics, and pathways. Environ. Sci. Technol. 50 (15), 8103–8112.
Sundkvist, A.M., Olofson, U., Haglund, P., 2010. Organophosphorus flame retardants and plasticizers in marine biota: a review of environmental distribution, fate and ecotoxicology. Bull. Environ. Contam. Toxicol. 98, 2–7.
van der Veen, I., de Boer, J., 2012. Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis. Chemosphere 88 (10), 1119–1153.
van Oort, I., de Boer, J., 2012. Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis. Chemosphere 88 (10), 1119–1153.
Wu, Z.J., Liu, J.P., Peng, Y., 2017. QuEChERS purification prior to stable isotope dilution-mass spectrometry matrix-matched calibration method for simultaneous quantification of organophosphate flame retardants in atmospheric particles from a European Arctic site. Environ. Sci. Technol. 48 (11), 6133–6140.
Yadav, I.C., Devi, N.L., Li, J., Zhang, G., Covaci, A., 2018. Concentration and spatial distribution of organophosphate esters in the soil-sediment profile of Kathmandu Valley. Nepal: implication of risk assessment. Sci. Total Environ. 613–614, 502–512.
Yuan, L.L., Li, J.S., Zha, J.M., Wang, Z.J., 2015. Targeting neurotoxic factors and their impacts on the occurrence and exposure assessment of organophosphate flame retardants in food and related consumer products. J. Anal. Chem. 1406, 251–257.
receptors, but not cholinesterase or neurotransmitter, in the neurotoxicity of TDCPP in Chinese rare minnow adults (Gobiocypris rarus). Environ. Pollut. 208, 670–677.
Yuan, S.L., Li, H., Dang, Y., Liu, C.S., 2018. Effects of triphenyl phosphate on growth, reproduction and transcription of genes of daphnia magna. Aquat. Toxicol. 195, 58–66.
Zhang, Y., 2014. Global market analysis of flame retardant (in Chinese). Fine and Specialty Chem. 22 (8), 20–24.
Zhang, X.L., Zou, W., Mu, L., Chen, Y.M., Ren, C.X., Hu, X.G., Zhou, Q.X., 2016. Rice ingestion is a major pathway for human exposure to organophosphate flame retardants (OPFRs) in China. J. Hazard Mater. 318, 686-693.
Zhao, F.R., Wan, Y., Zhao, H.Q., Hu, W.X., Mu, D., Webster, T.F., Hu, J.Y., 2016. Levels of blood organophosphorus flame retardants and association with changes in human sphingolipid homeostasis. Environ Sci Technol 50 (16), 8896–8903.
Zhao, H.Q., Zhao, F.R., Liu, J.X., Zhang, S.Y., Mu, D., An, L.H., Wan, Y., Hu, J.Y., 2018. Trophic transfer of organophosphorus flame retardants in a lake food web. Environ. Pollut. 242, 1887–1893.
Zheng, X.B., Xu, P.C., Luo, X.J., Mai, B.X., Covaci, A., 2016. Phosphate flame retardants and novel brominated flame retardants in home-produced eggs from an e-waste recycling region in China. Chemosphere. 150, 545–550.
Zhu, Y., Ma, X.F., Su, G.Y., Yu, L.Q., Letcher, R.L., Hou, J., Yu, H.X., Giesy, J.P., Liu, C.S., 2015. Environmentally relevant concentrations of the flame retardant Tris (1,3-dichloro-2-propyl) phosphate inhibit growth of female zebrafish and decrease fecundity. Environ. Sci. Technol. 49, 14579–14587.