Organophosphate esters in UK diet;

Gbadamosi, Muideen Remilekun; Abdallah, Mohamed Abou Elwafa; Harrad, Stuart

DOI:
10.1016/j.scitotenv.2022.158368

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (Harvard):
Gbadamosi, MR, Abdallah, MAE & Harrad, S 2022, 'Organophosphate esters in UK diet; exposure and risk assessment', *Science of the Total Environment*, vol. 849, 158368.
https://doi.org/10.1016/j.scitotenv.2022.158368

Science of the Total Environment 849 (2022) 158368

Contents lists available at ScienceDirect

Science of the Total Environment

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

Organophosphate esters in UK diet; exposure and risk assessment

Muideen Remilekun Gbadamosi [a,b,*], Mohamed Abou-Elwafa Abdallah [a], Stuart Harrad [a]

[a] School of Geography, Earth, and Environmental Sciences, University of Birmingham, Birmingham B15 2TT, UK
[b] Department of Chemical Sciences, Tai Solarin University of Education, Ijebu-Ode, Ogun State, Nigeria

HIGHLIGHTS

- Food ingestion is a substantial pathway of human exposure to OPEs in the UK.
- OPE concentrations in UK foods of similar magnitude to those elsewhere.
- TBOEP was the major contributor to dietary exposure to Σ_8OPEs but other OPEs contributed.
- Dietary exposure to OPEs not restricted to animal-derived foods.

GRAPHICAL ABSTRACT

ARTICLE INFO

Editor: Adrian Covaci

Keywords:
Food
Ingestion
Organophosphate esters
Dietary exposure

ABSTRACT

Food ingestion has been established as an important human exposure route to many environmental contaminants (brominated flame retardants, dioxins, organochlorine pesticides etc). However, information regarding dietary exposure to organophosphate esters (OPEs) in the UK remains limited. This study provides the first comprehensive dataset on OPEs in the UK diet by measuring concentrations of eight OPEs in 393 food samples, divided into 15 food groups, collected from Birmingham, UK. All target OPEs were measured above the limit of quantification in at least one of the food groups analysed. Concentrations were highest (mean Σ_8OPEs = 18.4 ng/g wet weight (ww)) in milk and milk products, followed by those in cereal and cereal products (mean Σ_8OPEs = 15.9 ng/g ww), with concentrations lowest in chickens' eggs (mean Σ_8OPEs = 1.61 ng/g ww). Interestingly, concentrations in animal-derived foods (mean Σ_8OPEs = 44.2 ng/g ww) were statistically indistinguishable ($p^{>}0.05$) from plant-derived foods (mean Σ_8OPEs = 36.8 ng/g ww). Estimated daily dietary intakes (EDIs) of Σ_8OPEs under mean and high-end exposure scenarios for the four age groups considered were: toddlers (420 and 1547 ng/kg bw/day) $^{>}$ children (155 and 836) $^{>}$ elderly (74.3 and 377) $^{>}$ adults (62.3 and 278) ng/kg bw/day, respectively. Baby food contributed 39 % of Σ_8OPEs exposure for toddlers, with non-alcoholic beverages contributing 27 % of exposure for children, while cereal and cereal products (25 %) and fruits (22 %) were the main contributors for adults and the elderly. The concentrations of OPEs in UK foodstuffs were generally of the same order of magnitude as those reported for other countries and our estimates of dietary exposure were well below the corresponding health-based limit values.

1. Introduction

Organophosphate esters (OPEs) are tri-esters of phosphoric acid with varying alkyl or aryl side chains and may also contain halogens such as chlorine (Fu et al., 2021; Bastiaensen et al., 2021). They are widely applied as flame retardants (FRs) and plasticisers in a wide range of consumer

* Corresponding author at: School of Geography, Earth, and Environmental Sciences, University of Birmingham, Birmingham B15 2TT, UK.
E-mail address: m.r.gbadamosi@bham.ac.uk (M.R. Gbadamosi).

http://dx.doi.org/10.1016/j.scitotenv.2022.158368
Received 13 June 2022; Received in revised form 22 August 2022; Accepted 24 August 2022
Available online 15 September 2022

products such as polyurethane and polystyrene foam, textiles, furniture, building and decorating materials, paints, insulating materials, resins, and polyvinyl chloride (PVC) etc. (Wei et al., 2015). While there is some uncertainty about the exact extent of OPE production and usage, the available data are consistent in suggesting that they are high production chemicals. Specifically, as of 2017, the global market demand of OPEs was estimated at about 797,234 tons, accounting for >30 % of the global consumption of FRs (McWilliams, 2018; Wang et al., 2021). Another study estimated the total usage of OPEs in the EU, US, and Asia was about 200,000 tons in 2007, accounting for about 12 % of the global FRs market at that time (Xu et al., 2019). Furthermore, in Europe alone, the total usage of phosphorus flame retardants was an estimated 89,640 tons (PINFA, 2017). Such extensive use of OPEs has raised concerns however, in light of several toxicological studies that have linked exposure to OPEs with many adverse health effects including: neurotoxicity, endocrine disruption, cardiotoxicity, thyroid cancer, asthma, and allergies as well as reproductive and developmental toxicity (Yao et al., 2021). Moreover, human epidemiological studies suggest that exposure to tris(2-chloroisopropyl) phosphate (TCIPP), tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), and tris(2-butoxyethyl) phosphate (TBOEP) adversely impacts human hormone levels and semen quality parameters (Meeker and Stapleton, 2010; Egloff et al., 2014; Zhang et al., 2016a).

The physicochemical properties which determine the fate and environmental behaviour of OPEs vary greatly with the side chains (alkyl or aryl functionality) (see Table S1; Fu et al., 2021). However, due to the use of OPEs in everyday products as additives FRs that are only physically incorporated rather than chemically bonded to products; they migrate or evaporate from such products before depositing into various environmental matrices, resulting in their detection in: indoor dust (Abdallah and Covaci, 2014; Brommer and Harrad, 2015; Stubbings et al., 2018), biota, water, and air (He et al., 2019; Xu et al., 2021), sediment (Liang et al., 2021; Zhong et al., 2018), human milk (Chen et al., 2021a), human placenta (Ding et al., 2016) blood, serum, and urine (Hou et al., 2020). Such environmental contamination has led to demonstrable human exposure via a variety of pathways including the diet (Gbadamosi et al., 2021; Zhao et al., 2019). Moreover, the level of contamination of various environmental compartments with OPEs and thus human exposure is likely to rise in line with increases in their production and usage (Ding et al., 2018). With respect to dietary exposure to OPEs, reports that this occurs via consumption of foods such as pastries, savoury snacks, sweet, sugar and chocolate confectioneries, means that the extent to which dietary contamination occurs via bioaccumulation or during food processing and storage is unclear (Poma et al., 2018; Li et al., 2019a).

Recently, a small number of studies have reported the presence of OPEs in foodstuffs at median concentrations of 0.08–70 ng ΣOPEs/g in fish, meat, cereals, dairy products, vegetables, and egg and other foodstuffs from the USA, Sweden, Belgium, China, and Australia (Wang and Kannan, 2018; Poma et al., 2017, 2018; Zhao et al., 2019; Chen et al., 2021b; He et al., 2018). Consequently, a previous review conducted by the authors established that dietary intake is an important human exposure pathway to OPEs (Gbadamosi et al., 2021).

Therefore, in this present study, we measured concentrations of eight OPEs in a wide variety of foodstuffs collected from major stores in Birmingham, UK, with the objective of investigating the occurrence, distribution, and magnitude of UK dietary exposure to OPEs. To the best of our knowledge, this is the first comprehensive study to determine the concentrations of OPEs in UK foodstuffs.

2. Materials and methods

2.1. Chemicals and materials

Individual standards of tris(2-chloroethyl) phosphate (TCEP), tris(2-chloroisopropyl) phosphate (TCIPP), tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), tris(2-butoxyethyl) phosphate (TBOEP), tri-n-butyl phosphate (TnBP), triphenyl phosphate (TPHP), 2-ethylhexyl-diphenyl phosphate (EHDPP), and tri-m-tolyl phosphate (TMTP), isotopically-labelled internal (or surrogate) standards of d_{27}-TBP and d_{15}-TPHP (50 μg/mL toluene) as well as 2,3,4,6-tetrachlorobiphenyl (PCB-62) used as a recovery determination (or syringe) standard were purchased from Wellington laboratories, (Guelph, ON, Canada). Organic solvents and reagents used were HPLC grade: with acetonitrile (ACN, 99.8 %), n-hexane (HEX, 95 %), toluene (TOL, 99.8 %), isooctane (ISOC, 99.5 %), dichloromethane (DCM, 99.8 %), ethyl acetate (ETAC), sodium sulfate, and formic acid (FA) (98–100 %) were purchased from Fisher scientific (Loughborough, UK) and Sigma-Aldrich (St Louis, MO, USA). Dispersive solid phase extraction (d-SPE) sorbent primary secondary amine (PSA) and octadecyl-silanised (C18 bulk sorbent) were purchased from Agilent Technologies (Folsom, CA, USA), while Hypersep Florisil® SPE cartridges were purchased from Thermo Scientific (Rockwood, USA), and the nitrogen gas used for solvent evaporation was purchased from BOC Gases, UK. All glassware, metal scissors, knife, and weighing spoon were baked at 450 °C overnight and rinsed before each use with DCM (three times), toluene, and acetonitrile; while Na_2SO_4 was baked at 600 °C for 4 h in a muffle furnace prior to use, to minimize residual organic contamination.

2.2. Sample collection and preparation

A total of 393 fresh food samples were collected from five major grocery stores in Birmingham, UK between September 2020, and April 2021 (Table S2). Samples of individual food items falling within the 14 food groups most frequently consumed by UK adults, along with baby food (BBF) (for toddlers only) were collected (Defra, 2017, 2019). The samples collected were classified broadly as: plant-derived (n = 98) (comprising fats and oils (FAT-O) (n = 11), vegetables (VEG) (n = 29), fruits (FRT) (n = 18), nuts (NUT) (n = 8), potatoes (POT) (n = 14), and non-alcoholic beverages (NAB) (n = 18)) (Zhao et al., 2020); animal-derived (n = 161) (covering milk and milk products (MLK) (n = 75), baby food (BBF) (n = 9), egg and egg products (EGG) (n = 5), fish (FSH) (n = 42), meat and meat products (MPT) (n = 30)) (Chen et al., 2021b; Zhang et al., 2022); other foods were pastries (PAST) (n = 42), savoury snacks (SAVS) (n = 28), and sweets, sugar and chocolate confectioneries (SCC) (n = 18)). Following collection, samples were transported to the laboratory, and stored at −18 °C frozen until removed for analysis.

The edible portion of each food sample was chopped into small pieces using scissors/knife, pooled, blended, and homogenized thoroughly to form a composite. The liquid samples were directly aliquoted and analysed as fresh. The composited samples were either freeze dried (after weighing the fresh material to facilitate determination of moisture content) and stored at −20 °C prior to analysis, some were analysed fresh (samples with high fat contents) or directly aliquoted (grain, milk, non-alcoholic beverages, potatoes, baby food, and vegetables) and analysed as fresh. From these food group composites; samples were taken for analysis.

2.3. Sample extraction

The extraction method used was adapted from the method of Xu et al. (2015) with slight modifications. An accurately weighed aliquot of between ~1 g of dry sample and ~ 1.5–2 g of wet weight sample (depending on the food group) was added into a 15 mL Greiner centrifuge tube. For fatty foods, a smaller (0.5–0.8 g) of the sample was taken to minimize the matrix effect. For liquid samples, ~1 g of the homogenized fresh liquid samples was weighed into the centrifuge tube containing the extracting solvents. Each sample was spiked with 50 ng of internal standards (IS; d_{15}-TPHP and d_{27}-TBP). Samples were extracted using 5 mL of ACN and 5 mL of 5 % formic acid (FA) in acetonitrile by a combination of vortexing and ultrasonication (3 × 1 min vortexing, followed by 15 min ultrasonication) and then centrifuged at 3500 rpm for 5 mins. This process was repeated three times before the pooled supernatants were carefully transferred to a precleaned glass tube and concentrated to 2 mL under a gentle nitrogen stream. Dispersive SPE (d-SPE) was performed on the concentrated extracts by adding 100 mg of C18 and 50 mg of primary-secondary amine (PSA)

sorbent powder to remove interferences such as fats, sugar, and pigments, vortexed for 1 min and centrifuged at 3500 rpm for 5 mins. The supernatant was collected into a clean glass tube and evaporated carefully to incipient dryness before reconstitution in 0.5 mL n-hexane: ETAC (1:1 *v*/v). The sample was further cleaned by loading onto a Florisil® cartridge preconditioned with 6 mL of ETAC and 6 mL of n-hexane. Fractionation was achieved using 12 mL of n-Hex (F1, discarded) and 10 mL ETAC (F2, containing the target OPEs). F2 containing the target analytes was concentrated to near dryness and reconstituted in 200 μL isooctane: ETAC (8:2 *v*/v) containing 100 pg/μL PCB-62 as recovery determination (or syringe) standard (RDS). The purified extract was stood for 30 min to allow precipitation of residual lipid if any at −20 °C, after which the clear top layer was transferred into a glass vial and stored at −20 °C prior to GC-EIMS analysis.

2.4. Instrumental analysis

Target OPEs were analysed using an Agilent GC coupled to an Agilent 5975C MSD operated in electron ionisation mode (EI) fitted with a 30 m DB-5 MS column (0.25 mm ID, 0.25 μm film thickness) (Restek, USA). Helium was used as carrier gas with constant flow rate of 1.0 mL/min. The injector temperature was set at 290 °C in split-less mode and the MS operated with a solvent delay of 5 mins. Ion source, quadrupole and interface temperatures were: 230 °C, 150 °C and 300 °C respectively. The GC temperature programme was 65 °C, hold for 0.75 min, ramp 20 °C/min to 250 °C, hold for 1 min, ramp 5 °C/min to 260 °C, hold for 0 min, ramp 30 °C/min to 305 °C, and hold for 1 min. The MS was operated in EI selected ion monitoring (SIM) mode with two characteristic ions monitored for each analyte and IS (further details are provided in Table S3).

2.5. Quality assurance and quality control

Five-point calibration plots were constructed with excellent linearity of response observed for all target OPEs (R^2 > 0.997; Table S4). The relative standard deviation (RSD) of the relative response factor (RRF) for the five-point calibration standards (50–750 pg/μL) for all the target OPEs were < 6. Due to the lack of certified reference materials for food, aliquots of prebaked Na_2SO_4 (450 °C for 6 h) were used as a surrogate matrix for assessment of blank contamination and method accuracy via analysis of matrix spike samples. The Na_2SO_4 went through the same extraction and clean-up process as samples. To evaluate recoveries of internal standards (ISs) and target OPEs; five samples each of vegetable oil and egg samples (from one grocery store) were spiked with IS (spiked at 50 ng each) and the target OPEs standards (spiked at 50 ng each), analysed and good recoveries obtained. Specifically, average recoveries of the internal standards were 62.3 ± 16.9 % for d_{15}-TPHP and 79.4 ± 7.3 % for d_{12}-TBP (Table S4), while the average recoveries for the target OPEs spiked were in the range of 73.1 ± 9.1–95.5 ± 18.8 for vegetable oil and 71.4 ± 13.6–99.6 ± 8.8 for egg respectively (Table S5). Average recoveries of the ISs spiked into Na_2SO_4 ranged between 63 and 114 % (Table S4). Two procedural blanks comprising 1 g Na_2SO_4 treated as a sample were analysed per each batch of 20 samples (n = 40). This revealed some low-level contamination (ranging between 0.016 and 0.059 ng/g dw) for TCEP only (Table S4). Concentrations of TCEP in real samples were thus calculated by subtracting the average concentration detected in the two procedural blanks conducted with samples from that batch. Instrumental contamination was assessed by injecting pure solvent (nonane and later toluene) between real samples, with no analyte detected in any such tests. For the chlorinated OPEs, peak identification was confirmed only when the isotope ratio of the two monitored ions was within 15 % of the average values for the two calibration standards run before and after that batch of samples. For all target OPEs, a further criterion for peak confirmation in samples was that the relative retention time (RRT) of the peak fell within 0.2 % of the average values obtained for the calibration standard run before and after each batch. The limit of detection (LOD) and the limit of quantification (LOQ) were calculated as the amounts of an analyte that yielded signal to noise ratio of 3 and 10 respectively (Table S6). However, for TCEP with procedural blank contamination the LOD and LOQ was calculated as 3 and 10 times the standard deviation of the blanks (Table S6).

2.6. Data analysis

Statistical analyses were performed using IBM SPSS statistics 28 and Microsoft 365 Excel. Summary statistics are presented as arithmetic mean, median, standard deviation, minimum, maximum, and 97.5th percentile values. The normality of the data distribution was tested using the Shapiro-Wilk test and found to be not normally distributed. Consequently, data were log10 transformed prior to analysis to permit use of parametric tests. Bivariate correlations (Spearman's rank correlation analysis) were used to investigate associations between analytes. Following satisfactory outcomes from a Kaiser-Meyer Olkin (KMO) measurement of sampling adequacy and Bartlett's Test of sphericity (Table S7); principal component analysis (PCA) was employed. Combined with the Spearman's correlation analysis, PCA helped identify whether common sources exist of our target OPEs in foods, and if so, for which OPEs. A one-way analysis of variance (ANOVA) was used to assess the differences in concentrations of analytes detected in animal-derived foods andplant-derived foods. All data on OPE concentrations in food are presented on a wet weight (ww) basis (i.e., uncooked). For non-quantifiable OPEs, concentration values were assigned as half of the quantification limits for such OPEs (< LOQ = 0.5 x LOQ).

2.7. Dietary exposure assessment

The estimated human dietary intakes (EDIs) of OPEs were estimated by multiplying the arithmetic mean of the OPE concentration (Ci) in each food group by the food consumption rate (DC_i) for both average ("typical" – i.e. assuming average consumption of each food group of foods containing the average concentration) and high-end consumption scenarios (the latter assumed to be those consuming foods contaminated at the 97.5th percentile concentration for each food group at the average consumption rate plus 2 x standard deviation) for the four age groups of the UK population considered in this study (see Table S8b) (Tao et al., 2017). Note that for food groups where concentrations of a given OPE were < LOQ, dietary exposure to that OPE for that food group, was calculated using lower bound (LB) and upper bound (UB) concentrations where LB = 0 and UB = LOQ.

Estimated dietary intakes (EDIs) normalised to body weight (ng/kg bw/day) were calculated for the following age groups: toddlers (1–3 yrs), children (4–18 yrs), adults (19–64 yrs), and elderly (65+ yrs) using Eq. (1) (Zhao et al., 2019)

$$EDI = \frac{\sum_{i=1}^{n} C_i x\, DC_1}{BW} \quad (1)$$

BW is the average body weight (kg) of the UK population assumed to be 12 kg for toddlers, 20 kg for children, 70 kg for adults, and 50 kg for elderly respectively (Brommer and Harrad, 2015; Harrad et al., 2008; Wu et al., 2016). DC_i values used were obtained from the UK's National Diet and Nutrition Survey (NDNS) report published by Public Health England and the Food Standards Agency (2014) and updated in 2017 (Tables S8a-b).

3. Results and discussion

3.1. Concentrations of OPEs in UK foodstuffs

A statistical summary of concentrations of eight OPEs (TCEP, TCIPP, TDCIPP, TPHP, EHDPP, TnBP, TBOEP, and TMTP) in UK food samples is presented in Table S9. Detection frequencies (DFs) for chlorinated OPEs were generally higher than those of other target OPEs in all the food samples analysed except for eggs and egg products and meat and meat products, for which DFs were low for TCIPP and TDCIPP (Table S9). DFs

for the aryl and alkyl-OPEs: TPHP, EHDPP, TnBP, TBOEP, and TMTP were generally very low except for TPHP and EHDPP which displayed higher DFs for cereal and cereal products (CRL), baby food (BBF), fish (FSH), fats and oils (FAT—O), sweet, sugar and chocolate confectioneries (SCC) and potatoes (POT), as well as meat and meat products (MPT) (Table S9). TnBP was only detected in vegetable samples (DF = 21 %), TMTP was detected in milk and milk products (DF = 8 %), vegetables (DF = 10 %), meat, and meat products (DF = 25 %), while TBOEP was detected at higher concentrations ($^{<}$LOQ – 9.32 ng/g ww) in a few of the food groups (cereals and cereal products, milk and milk products, vegetables, non-alcoholic beverages, fruits and sweets, sugar and chocolate confectioneries) (Fig. 2). The non-detection of the two alkyl-OPEs (TBOEP and TnBP) (DF = 0) in fish, meat and meat products, and egg and egg products may be attributed to their low bioaccumulation potential and their ability to be metabolised easily in biota and fatty tissue (Greaves et al., 2016; Van der Veen and de Boer, 2012; Poma et al., 2017). Among the fifteen food groups analysed, milk and milk products (MLK) were the most contaminated (average Σ_8OPEs = 18.4 ng/g ww), followed by cereals and cereal products (CRL) (average Σ_8OPEs = 15.9 ng/g ww) and the least contaminated food was egg and egg products (1.61 ng/g, ww), and potato (2.52 ng/g ww) respectively (Table S9, Fig. 2 and Fig. S1). While in this study, the highest concentrations of Σ_8OPEs (average = 18.4, range = $^{<}$LOQ - 49.6 ng/g ww) were found in milk and milk products; other studies in the USA, China, Australia, Sweden, and Belgium, reported the highest concentrations to be present in fish, meat, rice, vegetables, cereals, fats, and oils (Wang and Kannan, 2018; Chen et al., 2021b; Zhang et al., 2016b; He et al., 2018; Poma et al., 2017, 2018). Comparison of concentrations in this study between the broader categories of plant-derived and animal-derived foods, reveals animal-derived foods (mean Σ_8OPEs = 44.2 ng/g ww) display concentrations that are statistically indistinguishable ($p > 0.05$) from those detected in plant-derived foods (mean Σ_8OPEs = 36.8 ng/g ww). The higher concentrations of OPEs in animal-derived food samples (milk and milk products, fish and meat and meat products), might be due to contamination of animal-derived food due to heavy industrial processing or via transfer from contaminated feed to animals (He et al., 2019; Zhang et al., 2022). Any variations in OPEs distribution between food groups, may be attributable to differences in food processing, variations in their rate of migration from food packaging materials, and/or metabolic processes in the plants and animals from which the foods were derived. The chlorinated OPEs: TCEP, TCIPP, and TDCIPP are relatively more abundant in animal derived foods representing 28 %, 16 % and 22 % of the total mean concentrations of Σ_8OPEs for egg and egg products, meat and meat products, and fish respectively (Fig. 2). This relatively higher concentration of Cl-OPEs in animal-derived foods may be a result of the transfer of the contaminants from feeds to the animals in question (Zhang et al., 2022; Rigby et al., 2021). With respect to ruminant species like cattle, sheep etc., it was found that the translocation of TCIPP into leaves of meadow fescue, a livestock forage species, indicates a potential accumulation of OPEs by herbivorous animals (Eggen et al., 2013; Zhang et al., 2022). Moreover, with respect to fish and seafood, Zhang et al. (2022) report that Cl-OPEs contributed the greatest proportion (97.8 %) of the OPEs in aquaculture feed which this constitutes an important source of OPEs in mariculture (Zhang et al., 2020).

However, in plant-derived foods such as vegetables (11.2 ng/g ww), fruits (5.61 ng/g ww) and non-alcoholic beverages (5.54 ng/g ww), TBOEP was the main OPE representing between 58 and 65 % of the total mean concentrations of Σ_8OPEs in such foodstuffs. Higher concentrations of TBOEP were also detected in milk and milk products (6.81 ng/g ww) (animal-derived food) and cereal and cereal products (9.32 ng/g ww), representing 37 and 59 % of the total mean concentrations of Σ_8OPEs (Fig. 2). The higher concentration of TBOEP found in these foods was responsible for the overall higher concentration observed in Fig. 1 with greater concentration spread as shown by the error bar. However, the actual distribution of OPEs in various food groups are shown in Fig. 2. The high presence of TBOEP in animal-derived and industrial-processed foods can result from food processing and storage and can also occur due to higher biota-air accumulation factors

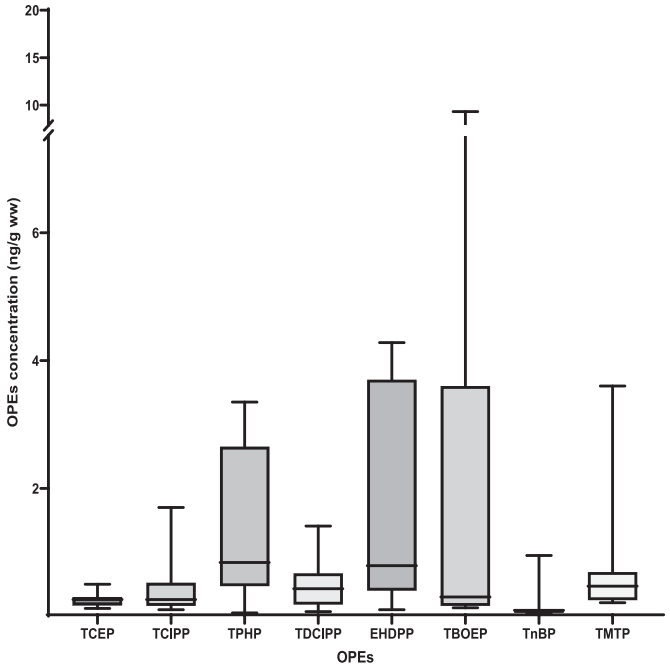

Fig. 1. Box plots of OPE concentrations (ng/g, ww) in UK foodstuffs [NB: the middle line of the box is the median OPE concentrations, the top and bottom lines of the box represent the 75th percentile and 25th percentile OPE concentrations, while the top and bottom lines of the y-error bars represent the maximum and minimum OPE concentrations].

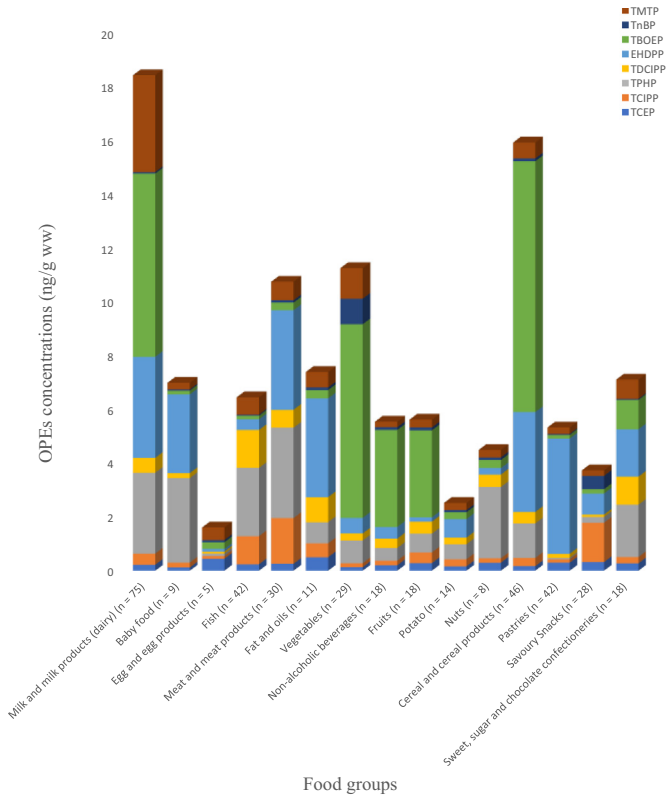

Fig. 2. Mean distribution of individual OPEs (ng/g ww) in different UK Food Groups.

(BAAFs) and lower biota-water accumulation factors (BWAFs) for TBOEP (Zhang et al., 2022).

The most common OPEs in sweets, sugars and chocolate confectioneries were TPHP (average = 1.95 ng/g ww, 27 % Σ_8OPEs) and EHDPP (1.76 ng/g ww, 25 %) (Table S9; Fig. 2). More so, the aryl-OPEs: TPHP (3.14–3.35 ng/g, ww) and EHDPP (2.93–3.70 ng/g ww) representing between 31 and 45 % and 34–42 %, were the dominant OPEs in baby food and meat and meat products (Table S9; Fig. 2). EHDPP and TPHP also made substantial contributions to Σ_8OPEs in other foods such as pastries (81 and 1 %) as well as cereal and cereal (23 and 8.1 %) products and in some plant-derived foods such as fat and oils (50 and 11 %), nuts (5.4 and 59 %), and potatoes (28 and 22 %) (Table S9; Fig. 2; Fig. S4). Coupled with reports that migration of these chemicals from food packaging constitute possible sources in foods (He et al., 2018; Poma et al., 2018); this suggests that industrial food processing and packaging materials for cereal and cereal products, pastries and sweets, sugars and chocolate confectioneries are likely sources of TPHP and EHDPP (Poma et al., 2017). TnBP was not detected in food samples except in vegetables (average = 0.95, $^{<}$LOQ - 6.05 ng/g ww) and savoury snacks (average = 0.50, $^{<}$LOQ – 0.86 ng/g ww).

3.1.1. Comparison of concentrations of OPEs in UK foods with those reported in other countries

Overall, concentrations of OPEs observed in UK food samples in this study were generally within the range of those reported in food samples from Sweden (Poma et al., 2017) and China (Chen et al., 2021b); exceeded slightly those reported by Wang and Kannan (2018) for the USA, by He et al. (2018) in Australia, and by Ding et al. (2018) in China; but were below those reported in food from China, Belgium, and Norway (Zhang et al., 2016b; Poma et al., 2018; Xu et al., 2017). Our arithmetic mean Σ_8OPEs concentration for meat and meat products (10.7 ng/g ww) was comparable to that reported in China (16.3 ng/g ww) (Chen et al., 2021b), while the median values obtained for milk and milk products (17.6 ng/g ww), cereal and cereal products (13.8 ng/g ww) and fat and oils (7.49 ng/g ww) exceeded the median values of: 1.22 ng/g ww, 1.94 ng/g ww, and 1.16 ng/g ww reported in the same food groups by Wang and Kannan (2018) in Albany, USA as well as that reported in milk in China (6.47 ng/g ww; Chen et al., 2021b) (Table S9). This observed variation in OPE concentrations in the UK may be attributed to the fact that these food groups (milk and milk products, cereal and cereal products as well as fats and oils) can undergo considerable industrial processing which may introduce variable degrees of OPE contamination. The mean concentration of TCEP (0.44 ng/g ww) in eggs and egg products was comparable to that reported in Australia (0.50 ng/g) (He et al., 2018), exceeded that reported for Sweden (0.08 ng/g ww; Poma et al., 2017), Belgium (0.03 ng/g ww; Poma et al., 2018) and China (0.015 ng/g ww; Zhao et al., 2019), but was lower than that reported for eggs collected from 24 provinces in China (1.41 ng/g ww; Chen et al., 2021b). TBOEP accounted for between 58 and 65 % of Σ_8OPEs concentrations in non-alcoholic beverages, fruits, vegetables, and cereals and cereal products (Fig. 2, Fig. S4). This was in contrast with what was reported in the USA by Wang and Kannan (2018), who identified the highest contributions to ΣOPEs of TBOEP to occur in meat (55–90 %) and fish (26–44 %). Our mean Σ_8OPEs concentrations measured in meat and meat products (10.7 ng/g ww) and fish (6.44 ng/g ww) were comparable to those reported for meat and fish from China (4.13–11.9 ng/g ww), (1.1–9.0 ng/g ww) and (1.82–2.20 ng/g ww) (Zhang et al., 2016b; Ding et al., 2018; Zhao et al., 2019), Sweden (1.46–3.56 ng/g ww), Belgium (3.14–4.11 ng/g ww) (Poma et al., 2017; Poma et al., 2018) and (0.71–1.37 ng/g ww) (Xu et al., 2015), Canada (0.26–3.20 ng/g ww) (McGoldrick et al., 2014), the USA (6.2–8.7 ng/g ww) and (6.76–7.11 ng/g ww) (Han et al., 2019; Wang and Kannan, 2018), and the Philippines (1.10–9.00 ng/g ww) (Kim et al., 2011) (Table S10). In contrast, our mean Σ_8OPEs concentrations in fish (mean: 6.44, range: $^{<}$LOQ - 21.2 ng/g ww) were exceeded by those reported by Chen et al. (2021b) in China (12.1 ng/g ww) (Tables S9 and S10). The variation in the distribution of OPEs in foodstuffs from different countries likely result from international differences in production and use patterns. However, our results corroborate previous findings that food packaging materials can be an important source of OPEs in foodstuffs (Poma et al., 2017, 2018; Zhao et al., 2019; Wang et al., 2022). Hence serious attention should be paid to the occurrence of OPEs in the food-packaging materials as well their migration to the foodstuffs they contain.

3.1.2. Correlations between concentrations of individual OPEs in UK foods

The degree of association and the direction of any linear relationship between concentrations of individual target OPEs in food were assessed using Spearman's correlation. Combined with principal component analysis (PCA), the outcomes helped identify whether there exist common sources of our target OPEs in foods, and if so, for which OPEs. Concentrations of the three chlorinated OPEs in the fourteen UK food groups analysed were significantly positively correlated with each other (r = 0.595–0.609, $p < 0.05$) (Table S11). TCEP also correlated significantly with TnBP and TMTP at (r = 0.748, $p < 0.01$) (Table S11). In line with what was reported in US food samples by Wang and Kannan (2018), concentrations of TnBP showed significant positive correlation with TCIPP (r = 0.583, $p < 0.05$), TDCIPP (r = 0.560, $p < 0.05$) and TBOEP (r = 0.562, $p < 0.05$) but not significant weak correlation with TPHP (r = 0.327, $p > 0.05$), EHDPP (r = 0.310, $p > 0.05$) (Table S11). These strong correlations revealed a common contamination sources or similar environmental fates of the OPEs in the foodstuffs. Significant correlation also existed between the concentrations of TMTP and TBOEP (r = 0.595, $p<0.05$) and TnBP (r = 0.964, $p < 0.01$). This also suggests similar contamination sources of these compounds and combined use of multiple OPEs in the same industrial/consumer products might be the main reason for these correlations. Concentrations of TCEP in all foodstuffs showed a significant positive correlation with all other OPEs except TPHP (Table S11). This finding was broadly corroborated by principal component analysis (PCA). In PCA, three components were extracted (Table S12) that explained 78.9 % of the total variation. The first component (PC-1) explained 33.4 % of the total variation and was driven strongly by high concentrations of TMTP (0.938), TCIPP (0.919), TnBP (0.643), and TCEP (0.645) (Table S12). The second component (PC-2) accounted for 26.2 % of the total variation explained and was essentially driven with high loadings by TPHP (0.767), EHDPP (0.713), and TDCIPP (0.700) (Table S12) while the third component (PC-3) which explained 19.2 % of the total variation and loaded highly by TBOEP (0.953). This implies that TBOEP in our samples is derived from different sources to the other OPEs targeted, which may likely be from it single used as floor finish.

3.2. Estimation of UK human dietary intake of OPEs, comparison with other countries and other exposure pathways

The mean and high-end exposure scenario values for the EDI of Σ_8OPEs for the four age groups were: toddlers (420 and 1547 ng/kg bw/day) $^{>}$ children (155 and 836 ng/kg bw/day) $^{>}$ elderly (74.3 and 377 ng/kg bw/day) $^{>}$ adults (62.3 and 278 ng/kg bw/day) respectively (Table 1, Table S13 (a-d); Fig. 3; Fig. S6). The estimated mean EDI values for the Σ_8OPEs in this present study for adults (62.3 ng/kg bw/day) and children (155 ng/kg bw/day) were similar to those reported in China (adults: 44.3 ng/kg bw/day) (Zhao et al., 2019), (adults: 55.0 ng/kg bw/day; children: 97.7 ng/kg bw/day) (Ding et al., 2018), Sweden (adults: 84.7 ng/kg bw/day) (Poma et al., 2017), Belgium (adults: 103 ± 21 ng/kg bw/day) (Poma et al., 2018). The EDIs of the Σ_8OPEs obtained in this study do however, exceed those reported in USA (adults: 25.1 ng/kg bw/day, children: 56.6 ng/kg bw/day) (Wang and Kannan, 2018), and are lower than those reported in China for males (539 ng/kg bw/day) and females (601 ng/kg bw/day) (Zhang et al., 2016b). However, we compared the ΣEDIs for six OPEs (TCEP, TCIPP, TDCIPP, TPHP, EHDPP and TnBP) for adults in our study with the values obtained from previous studies (Fig. 5). This is to allow direct comparison of our data with previous studies that measured the same six OPEs. This showed that our values were comparable to those reported in China (Ding et al., 2018; Zhao et al., 2019; Chen et al., 2021b) and Australia

Table 1
Average UK daily dietary intakes (ng/kg bw/day) (high end exposure scenario in parentheses) for individual OPEs and corresponding reference doses (RfDs).

Age group	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TBOEP	TnBP	TMTP	ΣOPEs
Toddlers (1.5–3 yrs)	12.5 (41.6)	19.4 (71.5)	20.5 (74.2)	117 (284)	116 (296)	102 (641)	4.97 (19.5)	27.6 (119)	420 (1547)
Children (4–18 yrs)	6.70 (25.0)	11.0 (42.8)	10.4 (42.5)	27.0 (108)	29.8 (107)	56.0 (446)	2.33 (12.3)	12.0 (52.3)	155 (836)
Adults (19–64 yrs)	2.34 (9.07)	4.16 (16.1)	3.73 (15.0)	10.3 (38.4)	14.2 (41.3)	22.0 (134)	1.05 (4.39)	4.59 (19.3)	62.3 (278)
Elderly (>65 yrs)	3.07 (12.7)	5.20 (22.1)	4.84 (20.4)	12.5 (52.5)	14.2 (55.3)	27.5 (181)	1.31 (6.01)	5.60 (26.9)	74.3 (377)
RfD (ng/kg bw/day) [a]	7000	10,000	20,000	NA	NA	NA	10,000	NA	
RfD (ng/kg bw/day) [b]	2200	8000	1500	7000	600 [d]	1500	2400	NA	
RfD (ng/kg bw/day) [c]	22,000	80,000	15,000	70,000	NA	15,000	24,000	NA	
RfD (ng/kg bw/day) [e]	NA	3600	NA	NA	NA	NA	NA	NA	

RfD = Reference dose.
NA = not available.
[a] Reference dose (RfD) values of USEPA (2017).
[b] Van den Eede et al. (2011).
[c] Ali et al. (2012).
[d] Zhao et al. (2019).
[e] Saito et al. (2007).

(He et al., 2018), slightly above those reported in USA (Wang and Kannan, 2018) and below those from other studies with which ΣEDIs is compared (Fig. 5).

Interestingly, the mean ΣEDI values of Σ_6OPEs (TCEP, TCIPP, TDCIPP, TPHP, EHDPP, and TnBP) for UK children (87.2 ng/kg bw/day) via their diet in our study were comparable to those reported for indoor dust ingestion for children (69.8 ng/kg bw/day) in the UK (Brommer and Harrad, 2015). However, the mean EDI for UK via dietary intake for these Σ_6OPEs for: toddlers (290 ng/kg bw/day), adults (34.7 ng/kg bw/day) and elderly (41.1 ng/kg bw/day) exceeded the values reported via indoor dust ingestion in Egypt (adults: 10.7, toddlers: 26.6 ng/kg bw/day) (Abdallah and Covaci, 2014), Beijing, China (adults: 3.0; toddler: 15.9 ng/kg bw/day) (Cao et al., 2019), in Southern China (adults: 1.54 ng/kg bw/day; toddlers: 19.0 ng/kg bw/day) (He et al., 2015), Nepal (adults: 0.12 and 0.04; children: 1.07 and 0.42 ng/kg bw/day) (Yadav et al., 2017; Yadav et al., 2019), Iraq (adults: 0.78; toddler: 15.4 ng/kg bw/day) (Al-Omran et al., 2021), Oslo, Norway (adults: 13.1 ng/kg bw/day) (Xu et al., 2016) and in USA (adults: 1.64; toddlers:19.2 ng/kg bw/day) (Stubbings et al., 2018) (Table S14). In contrast, our mean ΣEDI values for Σ_6OPEs obtained for children (87.2 ng/kg bw/day) and adults (34.7 ng/kg bw/day) were about two times lower than the reported values based on dust samples from an airport in New York, USA (children: 187; adults: 48.0 ng/kg bw/day) (Li et al., 2019b) (Table S14). In addition, our estimated ΣEDIs for diet for the Σ_6OPEs for the age groups considered in this study exceeded those reported via household air inhalation and dermal uptake in China (air inhalation - adults: 1.02; toddler: 1.82 ng/kg bw/day) (dermal uptake – adults: 1.17; toddler: 7.16 ng/kg bw/day) (Cao et al., 2019), Nepal (air – inhalation - adults:0.35; children: 1.34 ng/kg bw/day) (dermal uptake – adults: 5.58; children: 15.0 ng/kg bw/day) (Yadav et al., 2017) and in Germany (air inhalation - adults: 4.44; toddler: 1.60 ng/kg bw/day) (dermal uptake – adults: 0.98; toddler: 10.1 ng/kg bw/day) (Zhou et al., 2017) (Table S14). It also exceeded estimated exposure via drinking water ingestion for TCEP and TCIPP in Korea (adult: 1.07; children: 1.24; toddler: 1.50 ng/kg bw/day) (Lee et al., 2016), China (male: 4.36; female: 3.75 ng/kg bw/day) (Liu et al., 2019). Our data for the mean EDI for TCIPP for toddlers (19.4 ng/kg bw/day) was comparable to the value reported via dermal absorption for toddlers (14.3 ng/kg bw/day) from UK fabrics (Abdallah and Harrad, 2022). However, for adults, our mean EDI for TCIPP (4.16 ng/kg bw/day) was about 5 times lower than the value reported via dermal absorption (20.4 ng/kg bw/day) from UK fabrics (Abdallah and Harrad, 2022) (Table S14). Overall, our data on UK dietary exposure corroborate the conclusion of our critical review that human exposure to ΣOPEs through food ingestion is of comparable importance to that received via other exposure pathways (Gbadamosi et al., 2021).

3.2.1. Contributions of different food types to overall UK dietary exposure to OPEs

Baby food is a major source of Σ_8OPEs exposure for toddlers (mean: 163 ng/kg bw/day, 39 %; high-end exposure: 230 ng/kg bw/day, 15 %) (Fig. 3 and Fig. S6); similar to the results reported in US food by Wang and Kannan (2018), who also observed that dairy products accounted for largest percentage (40.4–50.1 %) of the ΣOPE exposure for toddlers and infants (Wang and Kannan, 2018). However, for children in our study, non-alcoholic beverages (mean: 42.1 ng/kg bw/day, 27 %; high-end scenario: 364 ng/kg bw/day, 44 %) is the main source of Σ_8OPEs (Table S13b, Fig. 3 and Fig. S6). Interestingly, cereal and cereal products were the main dietary source of Σ_8OPEs for adults (mean: 15.6 ng/kg bw/day, 25 %), while fruits were the main dietary source of the Σ_8OPEs for elderly (mean: 16.1 ng/kg bw/day, 22 %), followed by non-alcoholic beverages for adults (mean:10.5 ng/kg bw/day, 17 %) and elderly (mean: 14.7 ng/kg bw/day, 20 %) (Fig. 3 and Fig. S6). For toddlers, the mean and high exposure ΣEDI values for Σ_8OPEs in our three broad food categories are in the following order: animal-derived food (275 and 759 ng/kg bw/day) > plant-derived food (119 and 714 ng/kg bw/day) > industrial processed food (25.3 and 73.5 ng/kg bw/day). In contrast, the order was: plant-derived food > animal-derived food for children, adults, and the elderly (Fig. 4). However, there are statistically significant differences ($p<0.05$) between EDIs of Σ_8OPEs for animal-derived foods (299 ng/kg bw/day) and plant-derived foods (112 ng/kg bw/day) for toddlers. In contrast, for children, adults and elderly, there are no statistically significant differences ($p>0.05$) between the EDIs for the Σ_8OPEs considered in this study. In a study carried by Zhao et al. (2019), the EDI of Σ_9OPEs for Chinese adults was 44.3 ng/kg bw/day, to which TCEP (14.3 ng/kg bw/day), triethyl phosphate (TEP) (12.7 ng/kg bw/day), and EHDPP (8.4 ng/kg bw/day) were the main contributors. Moreover, in the same study, the EDI of Σ_9OPEs assigned to foods of animal origin (9 ng/kg bw/day) was comparable to our adult EDI (17.2 ng/kg bw/day) of Σ_8OPEs obtained for animal-derived food. This was also comparable to the results reported by Wang and Kannan (2018) in New York, USA in which meat contributed about 47 % to the total adult EDI of Σ_{15}OPEs (25.1 ng/kg bw/day). Past studies in Sweden and Belgium have emphasised that "industrially processed foods" were the main sources of some OPEs such as EHDPP and TPHP, and that contamination by OPEs occurs during food production, processing, and storage (Poma et al., 2017, 2018). However, our results were not entirely consistent with this, with industrially processed foods making the lowest contribution to ΣEDIs for all 15 food groups. Instead, our results were more consistent with those reported in the USA (Wang and Kannan, 2018) for toddlers and in Sweden and China (Poma et al., 2017; Zhao et al., 2019; Ding et al., 2018) for adults, but not in agreement with studies on dietary exposure in Belgium and 24 provinces in China where grains and meat were the major contributors to dietary ΣOPEs exposure for adults (Poma et al., 2018; Chen et al., 2021b). Our mean adult EDI of ΣOPEs for fish (1.05 ng/kg bw/day) was comparable to that attributed to fish consumption in the USA (1.17 ng/kg bw/day) (Wang and Kannan, 2018), China (1.8 ng/kg bw/day) (Zhao et al., 2019), and the Philippines (5.9 ng/kg bw/day) (Sundkvist et al., 2010) but markedly lower than that

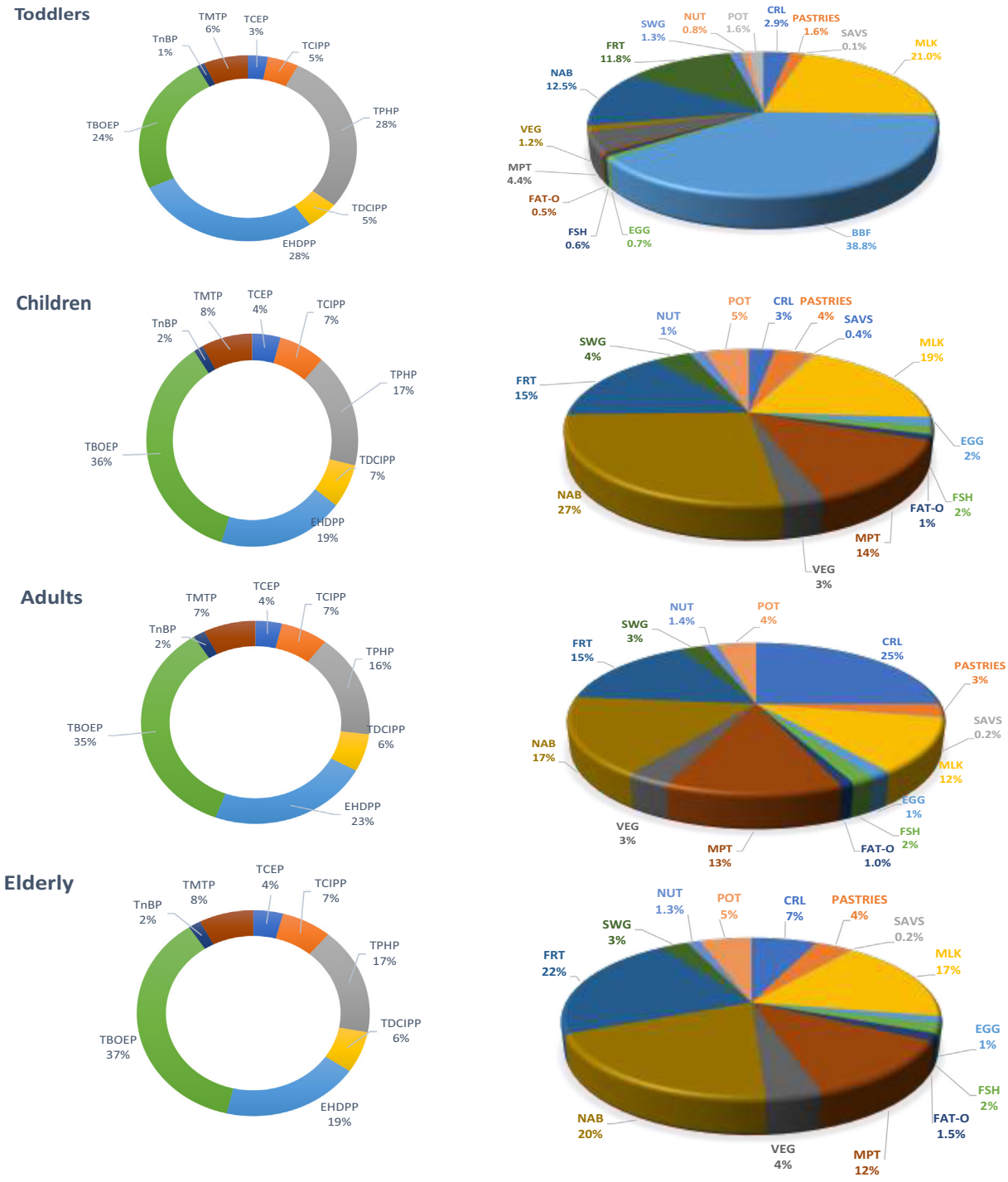

Fig. 3. The contribution of individual OPEs and food groups to estimated daily intakes (EDI) of Σ_8OPEs for various age groups in the UK [MPT = meat and meat products, FAT-O = Fat and oils, FSH = Fish, FRT = Fruits, NAB = Non-alcoholic beverages, EGG = egg and egg products, BBF = Babby food, MLK = Milk and milk products, SAVS = Savoury snacks, CRL = cereal and cereal products, Nut = Nuts, VEG = Vegetables, Pastries, POT = Potatoes, SWG = Sweet, sugar and chocolate confectioneries].

attributed to fish and seafood (300 ± 54 ng/kg bw/day) in Belgium (Poma et al., 2018). Surprisingly, UK dietary exposure to ΣOPEs via eggs and egg products for adults (0.96 ng/kg bw/day, 1.5 % overall dietary exposure), children (2.83 ng/kg bw/day, 2 %), and the elderly (1.07 ng/kg bw/day, 1.4 %) (Table 1); were comparable to the value reported for eggs from an e-waste recycling region in China (adults: 0.32–0.52 ng/kg bw/day, children: 1.89–3.02 ng/kg bw/day) (Zheng et al., 2015), but lower than the value reported in another study in China (3.0 ng/kg bw/day) (Zhao et al., 2019) and in Belgium (7 ± 3 ng/kg bw/day) (Poma et al., 2018). In all the food analysed in our study, savoury snacks (SAVS) displayed the lowest EDIs of Σ_8OPEs (0.14–0.66 ng/kg bw/day) for all age groups followed by fats and oils for toddlers, children, and adults (0.61–1.91 ng/kg bw/day) and nuts for elderly (0.99 ng/kg bw/day) respectively (Fig. 3, Table S13a-d).

3.2.2. Relative contribution of individual OPEs to Σ_8OPE dietary exposure

TBOEP is the major contributor to EDIs for Σ_8OPEs (24–37 %) for all foods and age groups (Table 1, Fig. 3, and Fig. S6). The overall

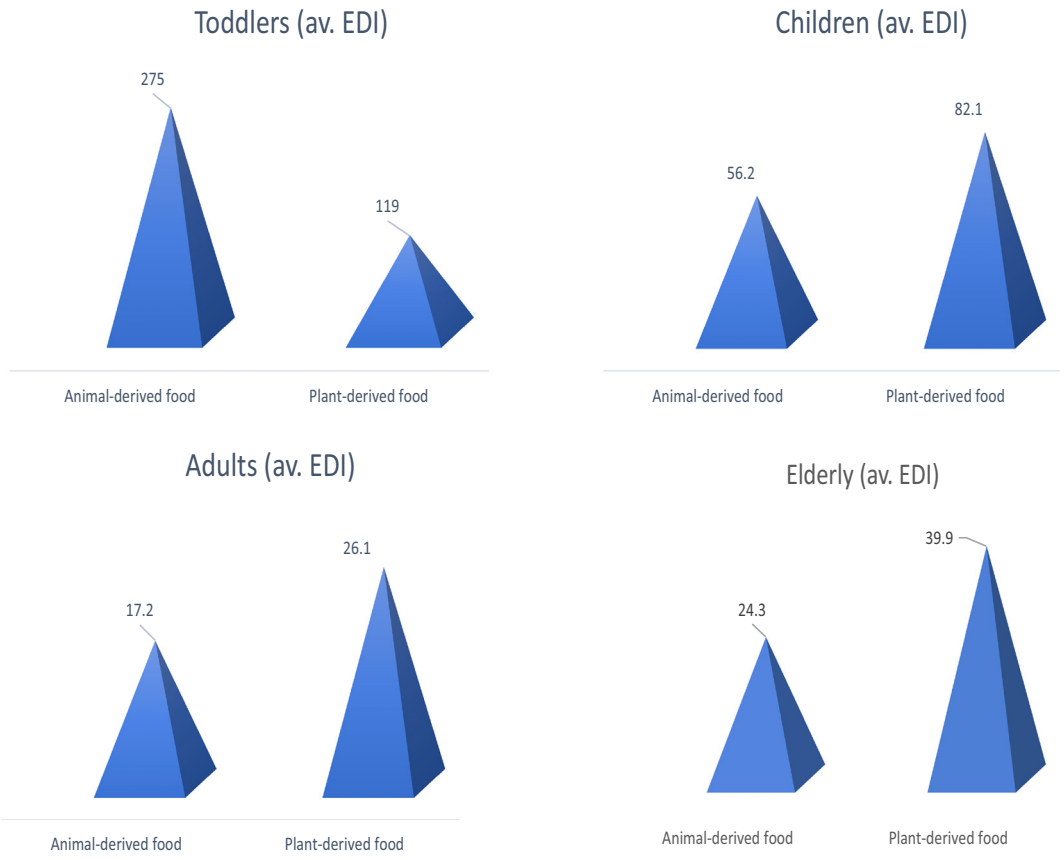

Fig. 4. Contributions of the three broad food categories (animal-derived and plant-derived food) to the total average dietary EDIs for four age groups in the UK.

predominance of TBOEP in UK foodstuffs was consistent with those found in US food (Wang and Kannan, 2018) and in edible fish in China (Ma et al., 2013). However, it is important to note that this elevated contribution to overall dietary exposure stems largely from consumption of vegetables, non-alcoholic beverages, and fruits (plant-derived food) milk and milk products (animal-derived food) and cereal and cereal

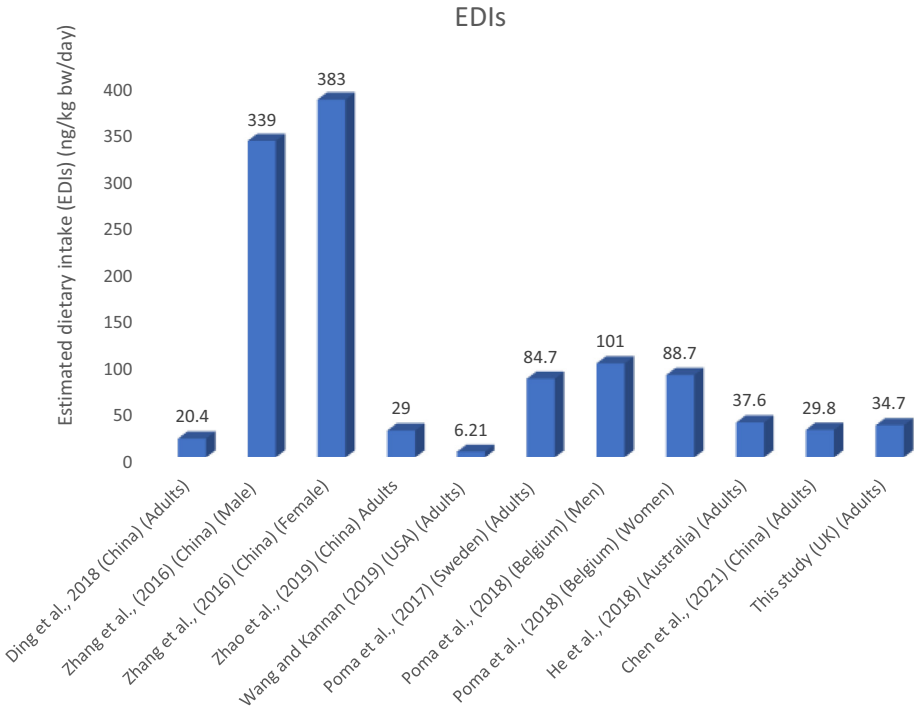

Fig. 5. Comparison of the mean dietary intake of Σ_6OPEs (TCEP, TCIPP, TDCIPP, TPHP, EHDPP, and TnBP) for UK adults with previous studies from other countries.

products, rather than uniformly from all the 15 food groups studies. Instead, for animal-derived foods such as: fish, egg and egg products, and meat and meat products; the Cl-OPEs (TCEP, TCIPP, TDCIPP) and aryl-OPEs (TPHP and EHDPP) were the dominant OPEs contributing to Σ_8OPEs EDI values for all four age groups (Fig. 3).

3.3. Assessment of human health risk arising from UK exposure to OPEs

The EDI values for individual OPEs obtained in this study were compared with the corresponding oral reference dose (RfD) values from five different sources. These comprise: the USEPA (2017) RfD values for TCEP (7000 ng/kg bw/day), TCIPP (10,000 ng/kg bw/day), TDCIPP (20,000 ng/kg bw/day), and TnBP (10,000 ng/kg bw/day), along with those calculated by Van den Eede et al. (2011) for TCEP (2200 ng/kg bw/day), TCIPP (8000 ng/kg bw/day), TDCIPP (1500 ng/kg bw/day), TPHP (7000 ng/kg bw/day), TBOEP (1500 ng/kg bw/day), and TnBP (2400 ng/kg bw/day), as well as those calculated by Ali et al. (2012) for TCEP (22,000 ng/kg bw/day), TCIPP (80,000 ng/kg bw/day), TDCIPP (15,000 ng/kg bw/day), TPHP (70,000 ng/kg bw/day), TBOEP (15,000 ng/kg bw/day) and TnBP (24,000 ng/kg bw/day). The RfD (600 ng/kg bw/day) for EHDPP was obtained from Zhao et al. (2019) while an alternative RfD (3600 ng/kg bw/day) for TCIPP was obtained from Saito et al. (2007) (Table 1). The differences between the RfD values of Van den Eede et al. (2011) and Ali et al. (2012) lies with the uncertainty factors (UFs); with the former using a UF of 10,000 and the latter 1000. It is also important to note that the RfDs reported by Ali et al. (2012) were acknowledged by the authors as likely overestimated. The RfDs provided by the USEPA (2017) were used to calculate hazard quotients (HQs) in this study. HQs (i.e., EDI/RfD) express how close the EDI is to the RfD; higher HQs denoting higher risk, with HQs > 1 indicating the RfD value is exceeded (Table S15a-c). Reassuringly, the mean and high-end values for EDIs via the diet for each OPE were several orders of magnitude lower than the corresponding RfD values from all three sources. Among our target OPEs, TBOEP, EHDPP, and TPHP posed the highest risk and TCIPP and TDCIPP the least using the RfD values of both Van den Eede et al. (2011), Ali et al. (2012) and Saito et al. (2007) (Table 1).

As the diet is not the only pathway of human exposure to OPEs, our estimated UK dietary intakes were combined with previously reported EDIs via indoor dust ingestion for adults and children (Brommer and Harrad, 2015) and toddlers (Kademoglou et al., 2017), the recent mean EDI for dermal uptake for TCEP, TCIPP, and TDCIPP for adults and toddlers were obtained from Abdallah and Harrad (2022), while – as this more recent study did not provide a high-end exposure estimate - the high-end exposure scenario estimate of dermal uptake for adults and toddlers used was taken from Abdallah et al. (2016). To evaluate the combined exposure risks, the mean and high exposure EDI value for TCEP, TCIPP and TDCIPP via UK dust ingestion, food ingestion, and dermal uptake were used for toddlers and adults. For all other target OPEs, there are no dermal uptake EDI data, so the combined EDI were calculated for dust and food ingestion only. A further caveat is that there are no UK data for exposure to OPEs via air inhalation for all age groups and no data for dermal uptake for all OPEs for children and the elderly. Mean and high-end scenario EDIs for the three Cl-OPEs for adults via dust ingestion, food ingestion, and dermal uptake combined were: TCIPP (25.5 and 51.7 ng/kg bw/day) > TDCIPP (6.80 and 22.4 ng/kg bw/day) > TCEP (4.07 and 20.4 ng/kg bw/day) (Table S15a). For toddlers, the mean and high-end exposure scenario EDIs for the Cl-OPEs were: TCIPP (296 and 1339 ng/kg bw/day) > TDCIPP (23.6 and 123 ng/kg bw/day) > TCEP (17.2 and 94.4 ng/kg bw/day) (Table S15c). Interestingly, for toddlers the HQ for TCIPP is 0.37 using the lowest TCIPP RfD value of 3600 ng/kg bw/day obtained from Saito et al. (2007).

For the other OPEs: aryl-OPEs (TPHP, EHDPP and TMTP) and alkyl-OPEs (TBOEP and TnBP), the combined exposure risks were calculated for dust and food ingestion only, as dermal and inhalation exposure data are not available. For aryl OPEs, the mean and high-end EDI values for adults were: EHDPP (14.3 and 46.4 ng/kg bw/day) > TPHP (10.4 and 44.0 ng/kg bw/day) > TMTP (4.59 and 19.3 ng/kg bw/day) (Table S15a). The combined EDI values for children were: EHDPP (43.8 and 527 ng/kg bw/day) > TPHP (34.0 and 468 ng/kg bw/day) > TMTP (12.0 and 52.3 ng/kg bw/day) (Table S15b), and those for toddlers were: EHDPP (126 and 335 ng/kg bw/day) > TPHP (123 and 309 ng/kg bw/day) > (27.6 and 119 ng/kg bw/day) respectively (Table S15c). This shows that for adults, children, and toddlers, exposure to EHDPP was greater than for the other two aryl-OPEs, with the caveat that only the dietary intake exposure data for TMTP was used for this calculation as there are no EDI data via UK dust ingestion for TMTP currently. For the two alkyl-OPEs (TBOEP and TnBP), mean and high-exposure estimates for diet and dust ingestion combined were: (toddler - TBOEP: 135 and 772 ng/kg bw/day; TnBP: 6.04 and 23.8 ng/kg bw/day) > (children – TBOEP: 56.0 and 446 ng/kg bw/day; TnBP: 2.41 and 13.6 ng/kg bw/day) > (adults – TBOEP: 24.3 and 140 ng/kg bw/day; TnBP: 1.06 and 4.41 ng/kg bw/day) respectively (Table S15a-c). Our dietary EDIs for elderly were: TBOEP (27.5 and 181 ng/kg bw/day) > EHDPP (14.2 and 55.3 ng/kg bw/day) > TPHP (12.5 and 52.5 ng/kg bw/day) > TMTP (5.60 and 26.9 ng/kg bw/day) > TCIPP (5.20 and 22.1 ng/kg bw/day) > TDCIPP (4.84 and 20.4 ng/kg bw/day) > TCEP (3.07 and 12.7 ng/kg bw/day) > TnBP (1.31 and 6.01 ng/kg bw/day) respectively (Table 1). To our knowledge, no data exist on exposure of this sector of the UK population via other pathways, so comparison of exposure of the elderly with RfD values is based on dietary intake alone.

Overall, our calculations suggest exposure to OPEs (even via several pathways combined under high-end scenarios) is in most instances several orders of magnitude below the RfD values (ΣEDIs <<< RfDs) (Table S15 a-c, Table 1). However, a significant cautionary note is that HQ values under high-end exposure scenarios for some OPEs when compared to some RfD values are within an order of magnitude of 1.0 (i.e., a level where exposure matches the RfD). Specifically, Table S15 b-c show HQ values of: EHDPP (0.88 and 0.56) using the RfD value of 600 ng/kg bw/day obtained from (Zhao et al., 2019), TBOEP (0.30 and 0.52) using the RfD value of 1500 ng/kg bw/day) (Van den Eede et al., 2011), TCIPP (0.22 and 0.37) using the RfD value of 3600 ng/kg bw/day obtained from (Saito et al., 2007), and TDCIPP (0.14 and 0.10) using the RfD value of 1500 ng/kg bw/day (Van den Eede et al., 2011) for children and toddlers respectively.

4. Conclusion

In this study, concentrations of eight OPEs were measured in 393 fresh food samples representing 15 different food groups collected between September 2020 to April 2021 from major grocery stores in Birmingham, UK. Milk and milk products (average concentration of Σ_8OPEs = 18.4 ng/g ww, range = <LOQ – 49.6 ng/kg ww) was the most contaminated food group, while eggs and egg products (average = 1.61 ng/g ww, range = <LOQ – 2.97 ng/g ww) was the least contaminated food group. Vegetables (average = 11.2 ng/g ww, range = <LOQ – 31.4 ng/g ww) and cereals and cereal products (average = 15.9 ng/g ww, range = <LOQ – 38.3 ng/g ww) were the most contaminated plant-derived. Our data revealed that the Cl-OPEs: TCEP, TCIPP, and TDCIPP were the OPEs present at the highest concentrations in animal-derived foods (egg and egg products, meat and meat products, and fish) representing between 16 and 28 % of the total mean concentration of Σ_8OPEs in such foodstuffs. By comparison, in plant-derived foods such as: vegetables, non-alcoholic beverages, and fruits; TBOEP was predominant, representing between 58 and 65 % Σ_8OPEs. The aryl-OPEs: TPHP (3.14 ng/g ww, 45 %) and EHDPP (2.93 ng/g ww, 42 %) were the main OPEs in baby food, meat and meat products, potatoes, as well as in sweets, sugars, and chocolate confectionery. Our data also reveal that EHDPP and TPHP were present in all food samples except egg and egg products. The ubiquity of dietary contamination with these two OPEs may likely result from their widespread use in food packaging materials. Among the four age groups considered, exposure to Σ_8OPEs via the diet followed the order: toddlers > children > elderly > adults. Our data shows that UK dietary exposure to OPEs is well below health-based limit values (RfDs). This reassuring

conclusion remains even for adults when combined exposure via UK dust ingestion, dermal uptake (Cl-OPEs only) as well as dietary exposure (this study) were considered. However, for children and toddlers, our dietary intake data was combined with UK dust ingestion data, and with dermal uptake of Cl-OPEs for toddlers. The HQ values obtained from dividing these combined exposure estimates under high-end exposure scenarios by available RfD values were between 0.1 and 0.88 for EHDPP, TBOEP, TCIPP, and TDCIPP. The rather narrow margin of safety implied by these figures, means that studies to elucidate the exposure of UK toddlers and children via air inhalation are urgently needed to complete the exposure and risk assessment of OPEs. In conclusion, this study confirms that – in line with other industrialised countries - food ingestion is a substantial pathway of human exposure to OPEs in the UK. Further investigation of human exposure to OPEs via the diet and other pathways in countries where there are no data on human dietary exposure is thus highly recommended.

CRediT authorship contribution statement

Muideen Remilekun Gbadamosi: Investigation, Software, Validation, Funding acquisition, Visualization, Writing – original draft, Writing – review & editing. **Mohamed Abou-Elwafa Abdallah:** Methodology, Conceptualization, Supervision, Resources, Validation, Writing – review & editing. **Stuart Harrad:** Conceptualization, Supervision, Resources, Validation, Writing – review & editing.

Data availability

Data will be made available on request.

Declaration of competing interest

All the authors declare that they have no known competing interest that could appear to influence the work/data reported in this paper.

Acknowledgements

The authors would like to appreciate the Petroleum Technology Development Fund (PTDF) for the award of a scholarship to Muideen Gbadamosi (PTDF ID: PTDF/ED/PHD/GMR/1382/18).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.158368.

References

Abdallah, M.A.E., 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.

Abdallah, M.A.E., Harrad, S., 2022. Dermal uptake of chlorinated organophosphate flame retardants via contact with furniture fabrics; implications for human exposure. Environ. Res. 209, 112847. https://doi.org/10.1016/j.envres.2022.112847.

Abdallah, M.A., Pawar, G., Harrad, S., 2016. Human dermal absorption of chlorinated organophosphate flame retardants; implications for human exposure. Toxicol. Appl. Pharmacol. 291, 28–37.

Ali, N., Dirtu, A.C., Van den Eede, N., Goosey, E., Harrad, S., Neels, H., Mannetje, A.T., 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.

Al-Omran, L.S., Gbadamosi, M.R., Stubbings, W.A., Drage, D.S., Abdallah, M.A, Harrad, S., 2021. Organophosphate esters in indoor and outdoor dust from Iraq: implications for human exposure. Emerg. Contam. 7, 204–212.

Bastiaensen, M., Gys, C., Colles, A., Verheyen, V., Koppen, G., Govarts, E., Bruckers, L., Morrens, B., Loots, I., De Decker, A., Nelen, V., Nawrot, T., De Henauw, S., Van Larebeke, N., Schoeters, G., Covaci, A., 2021. Exposure levels, determinants and risk assessment of organophosphate flame retardants and plasticizers in adolescents (14–15 years) from the Flemish environment and health study. Environ. Int. 147, 106368. https://doi.org/10.1016/j.envint.2020.106368.

Brommer, S., Harrad, S., 2015. Sources and human exposure implications of concentrations of organophosphate flame retardants in dust from UK cars, classrooms, living rooms, and offices. Environ. Int. 83, 202–207. https://doi.org/10.1016/j.envint.2015.07.002.

Cao, D., Lv, K., Gao, W., Fu, J., Wu, J., Fu, J., Wang, Y., Jiang, G., 2019. Presence and human exposure assessment of organophosphate flame retardants (OPEs) in indoor dust and air Beijing, China. Ecotoxicol. Environ. Saf. 169, 383–391. https://doi.org/10.1016/j.ecoenv.2018.11.038.

Chen, X., Zhao, X., Shi, Z., 2021a. Organophosphorus flame retardants in breast milk from Beijing, China: occurrence, nursing infant's exposure and risk assessment. Sci. Total Environ. 771, 145404. https://doi.org/10.1016/j.scitotenv.2021.145404.

Chen, X., Fan, S., Lyu, B., Zhang, L., Yao, S., Liu, J., Shi, Z., Wu, Y., 2021b. Occurrence and dietary intake of organophosphate esters via animal-origin food consumption in China: results of a Chinese Total diet study. J. Agric. Food Chem. 69 (46), 13964–13973. https://doi.org/10.1021/acs.jafc.1c05697.

Defra, 2017. Family Food 2015. As of 11 May 2020. https://www.gov.uk/government/statistics/family-food-2015. (Accessed 23 December 2021).

Defra, 2019. Food Statistics Pocketbook. As of 30 November 2020. https://www.gov.uk/government/collections/food-statistics-pocketbook. (Accessed 23 December 2021).

Ding, J., Xu, Z., Huang, W., Feng, L., Yang, F., 2016. Organophosphate ester flame retardants and plasticizers in human placenta in Eastern China. Sci. Total Environ. 554–555 (July 2020), 211–217. https://doi.org/10.1016/j.scitotenv.2016.02.171.

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.

Eggen, T., Heimstad, E.S., Stuanes, A.O., Norli, H.R., 2013. Uptake and translocation of organophosphates and other emerging contaminants in food and forage crops. Environ. Sci. Pollut. Res. 20, 4520–4531. https://doi.org/10.1007/s11356-012-1363-5.

Egloff, C., Crump, D., Porter, E., Williams, K.L., Letcher, R.J., Gauthier, L.T., Kennedy, S.W., 2014. Tris(2-butoxyethyl) phosphate and triethyl phosphate alter embryonic development, hepatic mRNA expression, thyroid hormone levels, and circulating bile acid concentrations in chicken embryos. Toxicol. Appl. Pharmacol. 279, 303–310.

England, Public Health, Agency, Food Standards, 2014. National Diet and Nutrition Survey: Results From Years 1 to 4 (Combined) of the Rolling Programme for 2008 and 2009 to 2011 and 2012 - Publications - gov.uk. https://www.gov.uk/government/ statistics/national-diet-and-nutrition-survey-results-from-years-1-to-4-combined-of the- rolling-programme-for-2008-and-2009-to-2011-and-2012. (Accessed 15 August 2021).

Fu, J., Fu, K., Chen, Y., Li, X., Ye, T., Gao, K., Pan, W., Zhang, A., Fu, J., 2021. Long-range transport, trophic transfer, and ecological risks of organophosphate esters in remote areas. Environ. Sci. Technol. 55 (15), 10192–10209. https://doi.org/10.1021/acs.est.0c08822.

Gbadamosi, M.R., Abdallah, M.A.E., Harrad, S., 2021. A critical review of human exposure to organophosphate esters with a focus on dietary intake. Sci. Total Environ. 771, 144752. https://doi.org/10.1016/j.scitotenv.2020.144752.

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.

Han, L., Sapozhnikova, Y., Nuñez, A., 2019. Analysis and occurrence of organophosphate esters in meats and fish consumed in the United States. J. Agric. Food Chem. 67, 12652–12662.

Harrad, S., Ibarra, C., Abdallah, M.A., Boon, R., Neels, H., Covaci, A., 2008. Concentrations of brominated flame retardants in dust from United Kingdom cars, homes, and offices: causes of variability and implications for human exposure. Environ. Int. 34 (8), 1170–1175. https://doi.org/10.1016/j.envint.2008.05.001.

He, C.T., Zheng, J., Qiao, L., Chen, S.J., Yang, J.Z., Yuan, J.G., Mai, B.X., 2015. Occurrence of organophosphorus flame retardants in indoor dust in multiple microenvironments of southern China and implications for human exposure. Chemosphere 133, 47–52.

He, C., Wang, X., Tang, S., Thai, P., Li, Z., Baduel, 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. https://doi.org/10.1021/acs.est.8b03043.

He, M.J., Lu, J.F., Wei, S.Q., 2019. Organophosphate esters in biota, water, and air from an agricultural area of Chongqing, western China: concentrations, composition profiles, partition and human exposure. Environ. Pollut. 244, 388–397. https://doi.org/10.1016/j.envpol.2018.10.085.

Hou, M., Shi, Y., Jin, Q., Cai, Y., 2020. Organophosphate esters and their metabolites in paired human whole blood, serum, and urine as biomarkers of exposure. Environ. Int. 139 (February), 105698. https://doi.org/10.1016/j.envint.2020.105698.

Kademoglou, K., Xu, F., Padilla-Sanchez, J.A., Haug, L.S., Covaci, A., Collins, C.D., 2017. Legacy and alternative flame retardants in norwegian and UK indoor environment: implications of human exposure via dust ingestion. Environ. Int. 102, 48–56.

Kim, J.W., Isobe, T., Chang, K.H., Amano, A., Maneja, R.H., Zamora, P.B., Siringan, F.P., Tanabe, S., 2011. Levels and distribution of organophosphorus flame retardants and plasticizers in fishes from Manila Bay, the Philippines. Environ. Pollut. 159 (12), 3653–3659.

Lee, S., Jeong, W., Kannan, K., Moon, H.B., 2016. Occurrence and exposure assessment of organophosphate flame retardants (OPFRs) through the consumption of drinking water in Korea. Water Res. 103, 182–188.

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, W., Wang, Y., Kannan, K., 2019b. Occurrence, distribution and human exposure to 20 organophosphate esters in air, soil, pine needles, river water, and dust samples collected around an airport in New York state, United States. Environ. Int. 131, 105054. https://doi.org/10.1016/j.envint.2019.105054.

Liang, C., Peng, B., Wei, G.-L., Gong, Y., Liu, G., Zeng, L., Liu, L.-Y., Zeng, E.Y., 2021. Organophosphate diesters in urban river sediment from South China: call for more research on their occurrence and fate in field environment. ACS ES & T Water 1 (4), 871–880. https://doi.org/10.1021/acsestwater.0c00217.

Liu, X., Xiong, L., Li, D., Chen, C., Cao, Q., 2019. Monitoring and exposure assessment of organophosphorus flame retardants in source and drinking water, Nanjing, China. Environ. Monit. Assess. 191 (2), 119. https://doi.org/10.1007/s10661-019-7239-0.

Ma, Y., Cui, K., Zeng, F., Wen, J., Liu, H., Zhu, F., Ouyang, G., Luan, T., Zeng, Z., 2013. Microwave-assisted extraction combined with gel permeation chromatography and silica gel cleanup followed by gas chromatography-mass spectrometry for the determination of organophosphorus flame retardants and plasticizers in biological samples. Anal. Chim. Acta 786, 47–53. https://doi.org/10.1016/j.aca.2013.04.062.

McGoldrick, D.J., Letcher, R.J., Barresi, E., Keir, M.J., Small, J., Clark, M.G., Sverko, E., Backus, S.M., 2014. Organophosphate flame retardants and organosiloxanes in predatory freshwater fish from locations across Canada. Environ. Pollut. 193, 254–261.

McWilliams, A., 2018. Flame retardant chemicals: technologies and global markets. BCC Res. Rep. Overv. https://www.bccresearch.com/market-research/chemicals/flame-retardant-chemicals-markets-report.html.

Meeker, J.D., Stapleton, H.M., 2010. House dust concentrations of organophosphate flame retardants in relation to hormone levels and semen quality parameters. Environ. Health Perspect. 118 (3), 318–323.

PINFA, 2017. Non-halogenated Phosphorus, Inorganic and Nitrogen Flame Retardants. Available online. https://www.pinfa.eu/wp-content/uploads/2018/05/pinfa_BC_edit-2017-web.pdf. (Accessed 21 August 2021).

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.

Rigby, H., Dowding, A., Fernandes, A., Humphries, D., Jones, N.R., Lake, I., Petch, R.G., Reynolds, C.K., Rose, M., Smith, S.R., 2021. Concentrations of organic contaminants in industrial and municipal bioresources recycled in agriculture in the UK. Sci. Total Environ. 765, 142787. https://doi.org/10.1016/j.scitotenv.2020.142787.

Saito, I., Onuki, A., Seto, H., 2007. Indoor organophosphate and polybrominated flame retardants in Tokyo. Indoor Air 1, 28–36. https://doi.org/10.1111/j.1600-0668.2006.00442.x.

Stubbings, W.A., Schreder, E.D., Thomas, M.B., Romanak, K., Venier, M., Salamova, A., 2018. Exposure to brominated and organophosphate ester flame retardants in U.S. Childcare environments: effect of removal of flame-retarded nap mats on indoor levels. Environ. Pollut. 238, 1056–1068. https://doi.org/10.1016/j.envpol.2018.03.083.

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.

Tao, F., Abdallah, M.A., Ashworth, D.C., Douglas, P., Toledano, M.B., Harrad, S., 2017. Emerging and legacy flame retardants in UK human milk and food suggest slow response to restrictions on use of PBDEs and HBCDD. Environ. Int. 105, 95–104. https://doi.org/10.1016/j.envint.2017.05.010.

USEPA, 2017. Mid Atlantic risk assessment, regional screening levels (RSLs) - generic tables. accessed January, 2022. http://www.epa.gov/region9/superfund/prg.

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 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, Y., Kannan, K., 2018. Concentrations and dietary exposure to organophosphate esters in foodstuffs from Albany, New York, United States. J. Agric. Food Chem. 66, 13525–13532.

Wang, X., Zhu, Q., Liao, C., Jiang, G., 2021. Human internal exposure to organophosphate esters: a short review of urinary monitoring on the basis of biological metabolism research. J. Hazard. Mater. 15 (418), 126279. https://doi.org/10.1016/j.jhazmat.2021.126279.

Wang, X., Wang, W., Zhu, Q., Wang, Y., Liao, C., Jiang, G., 2022. Organophosphate esters in foodstuffs from multiple provinces in China: possible sources during food processing and implications for human exposure. J. Agric. Food Chem. https://doi.org/10.1021/acs.jafc.2c03603.

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

Wu, M., Yu, G., Cao, Z., Wu, D., Liu, K., Deng, S., Huang, J., Wang, B., Wang, Y., 2016. Characterization and human exposure assessment of organophosphate flame retardants in indoor dust from several microenvironments of Beijing, China. Chemosphere 150, 465–471. https://doi.org/10.1016/j.chemosphere.2015.12.111.

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

Xu, F., Giovanoulis, G., van Waes, S., Padilla-Sanchez, J.A., Papadopoulou, E., Magnér, J., Haug, L.S., Neels, H., Covaci, A., 2016. Comprehensive study of human external exposureto organophosphate flame retardants via air, dust, and hand wipes: the importance of sampling and assessment strategy. Environ. Sci. Technol. 50 (14), 7752–7760. https://doi.org/10.1021/acs.est.6b00246.

Xu, F., Tay, J., Covaci, A., Padilla-Sánchez, J.A., Papadopoulou, E., Haug, L., Neels, H., Sellström, U., de Wit, C., 2017. Assessment of dietary exposure to organohalogen contaminants, legacy and emerging flame retardants in a Norwegian cohort. Environ. Int. 102, 236–243.

Xu, F., Eulaers, I., Alves, A., Papadopoulou, E., Padilla-Sanchez, J.A., Lai, F.Y., Haug, L.S., Voorspoels, S., Neels, H., Covaci, A., 2019. Human exposure pathways to organophosphate flame retardants: associations between human biomonitoring and external exposure. Environ. Int. 127, 462–472.

Xu, L., Zhang, B., Hu, Q., Liu, Y., Shang, T., Zeng, X., Yu, Z., 2021. Occurrence and spatio-seasonal distribution of organophosphate tri- and di-esters in surface water from Dongting Lake and their potential biological risk. Environ. Pollut. 282, 117031. https://doi.org/10.1016/j.envpol.2021.117031.

Yadav, I.C., Devi, N.L., Zhong, G., Li, J., Zhang, G., Covaci, A., 2017. Occurrence and fate of organophosphate ester flame retardants and plasticizers in indoor air and dust of Nepal: implication for human exposure. Environ. Pollut. 229, 668–678.

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.

Yao, C., Yang, H., Li, Y., 2021. A review on organophosphate flame retardants in the environment: occurrence, accumulation, metabolism, and toxicity. Sci. Total Environ. 795, 148837. https://doi.org/10.1016/j.scitotenv.2021.14883.

Zhang, Q., Ji, C., Yin, X., Yan, L., Lu, M., Zhao, M., 2016a. Thyroid hormone-disrupting activity and ecological risk assessment of phosphorus-containing flame retardants by in vitro, in vivo and in silico approaches. Environ. Pollut. 210, 27–33. https://doi.org/10.1016/j.envpol.2015.11.051.

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

Zhang, R., Yu, K., Li, A., Zeng, W., Lin, T., Wang, Y., 2020. Occurrence, phase distribution, and bioaccumulation of organophosphate esters (OPEs) in mariculture farms of the Beibu gulf, China: a health risk assessment through seafood consumption. Environ. Pollut. 263, 114426. https://doi.org/10.1016/j.envpol.2020.114426.

Zhang, W., Giesy, J.P., Wang, P., 2022. Organophosphate esters in agro-foods: occurrence, sources and emerging challenges. Sci. Total Environ. 827, 154271. https://doi.org/10.1016/j.scitotenv.2022.154271.

Zhao, L., Jian, K., Su, H., Zhang, Y., Li, J., Letcher, R.J., Su, G., 2019. Organophosphate esters (OPEs) in Chinese foodstuffs: dietary intake estimation via a market basket method, and suspect screening using high-resolution mass spectrometry. Environ. Int. 128, 343–352.

Zhao, N., Fu, J., Liu, Y., Wang, P., Su, X., Li, X., 2020. Animal-derived and plant-derived protein supplement feeds are important sources of organophosphate esters in the food supply. J. Agric. Food Chem. 68 (42), 11694–11701. https://doi.org/10.1021/acs.jafc.0c04235.

Zheng, X., Xu, F., Chen, K., Zeng, Y., Luo, X., Chen, S., Mai, B., Covaci, A., 2015. Flame retardants and organochlorines in indoor dust from several e-waste recycling sites in South China: composition variations and implications for human exposure. Environ. Int. 78, 1–7.

Zhong, M., Wu, H., Mi, W., Li, F., Ji, C., Ebinghaus, R., Tang, J., Xie, Z., 2018. Occurrences and distribution characteristics of organophosphate ester flame retardants and plasticizers in the sediments of the Bohai and Yellow Seas, China. Sci. Total Environ. 615, 1305–1311.

Zhou, L., Hiltscher, M., Püttmann, W., 2017. Occurrence and human exposure assessment of organophosphate flame retardants in indoor dust from various microenvironments of the Rhine/Main region, Germany. Indoor Air 27, 1113–1127.