

UNIVERSITY OF BIRMINGHAM

TOWARD UNDERSTANDING OF THE MAGNITUDE AND PATHWAYS OF HUMAN DIETARY EXPOSURE TO ORGANOPHOSPHATE ESTERS (OPEs)

By

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ABSTRACT

Organophosphate esters (OPEs) are flame retardant and plasticizer used as a substitute for brominated flame retardants (BFRs) and are added to electronics, furniture, textiles, and other consumer products. The ubiquitous presence of OPEs in various environmental matrices and their suspected adverse effects worldwide has become a major concern. Numerous studies have indicated that components of OPEs have several significant biological effects including, neurotoxicity, kidney toxicity carcinogenicity and reproductive toxicity. Findings from our previous review has established that food is an important and the main human exposure pathway to OPEs and evaluated the relative significant of dietary exposure in comparison with other human exposure pathways such as air inhalation, dust ingestion, water ingestion and infant exposure through breast milk. While inhalation exposure and especially exposure via indoor dust ingestion are relatively well-characterised, exposure via the diet and drinking water were highlighted as potentially important omissions. Furthermore, a dearth of data for Africa was highlighted. Therefore, the purpose of this thesis is to evaluate the occurrence, fate, and magnitude of dietary exposure to eight (8) OPEs in UK foodstuffs and UK drinking water and foodstuffs from African origin, estimate the magnitude of human exposure risk in indoor dust from Nigeria and sediment samples from major Rivers in Southwest Nigeria.

The chapter one and two of this thesis entails a detailed introduction and published critical review on human exposure to OPEs with a focus on dietary intake. Chapter three contained the description of analytical method and first comprehensive study to determine the concentrations of eight OPEs in UK foodstuffs and evaluate the exposure risk for all age groups using GC-MS. In UK foodstuffs, the concentrations of the$\sum_8$OPEs were highest (mean $\sum_8$OPEs = 18.4 ng/g wet weight (ww)) in milk and milk products, followed by those in cereal and cereal products (mean $\sum_8$OPEs = 15.9 ng/g ww), with concentrations lowest in chickens' eggs (mean $\sum_8$OPEs = 1.61 ng/g ww). Chapter four of this thesis determined the significance of water

ingestion as a pathway of human exposure to OPEs in UK population. Our results showed that water ingestion (most especially tap water) was a significant source of chlorinated OPEs (TCEP and TCIPP) and alkyl-OPEs (TBOEP) and aryl-OPEs (TPHP and EHDPP). Based on the developed method, in Chapter five we investigated the concentrations of the 8 OPEs in indoor dust from homes, car/bus, office and medical centres from Nigeria to investigate the concentrations and profiles of target OPEs in indoor dust from Nigeria, (ii) compare the concentrations profiles of OPEs in the different microenvironment (cars, offices, medical centres, and residential homes) (iii) to identify and apportion the possible sources of the OPEs in the indoor dust from the selected microenvironment in Nigeria (iv) to estimates the magnitude of human exposure risks to OPEs via indoor dust ingestion in Nigeria. Our results showed that OPEs concentrations from the indoor dust were among the lowest reported from other countries. This may be ascribed to less strict fire safety standard and lack of regulatory actions against brominated flame retardants. There are no significant differences ($p > 0.05$) between the $\sum_8$OPEs mean concentrations found in dust samples from car/bus (295 ng/g), offices (231 ng/g), residential homes (277 ng/g) and medical centres (127 ng/g). Then finally, in Chapter six, determined the level, distribution and dietary exposure assessment of the OPEs in a wide range of foodstuffs of Nigeria origin. Our findings in chapter three and six further established that food processing and packaging materials is an important potential food contamination source. To the best of our knowledge, findings from all the chapters represents the first comprehensive studies for the target OPEs in UK and Nigeria and first survey of OPEs presence in foodstuffs from African origin.

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LIST OF PUBLICATIONS

Academic Journal Papers

Published

1. **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. Science of the Total Environment, 771:144752.
2. Al-Omran, L.S., **Gbadamosi, M.R.,** Stubbings, W.A., Drage, D.S., Abdallah, M. A. E, Harrad, S. 2021. Organophosphate esters in indoor and outdoor dust from Iraq: Implications for human exposure. Emerging Contaminants, 7, 204-212
3. **Gbadamosi, M. R.,** Abdallah, M. A. E, Harrad, S. 2022. Organophosphate esters in UK diet; exposure and risk assessment. Science of the Total Environment, 849: 158368
4. **Gbadamosi, M.R.,** Al-Omran, L.S., Abdallah, M.A., Harrad, S. 2023a. Concentrations of organophosphate esters in drinking water from the United Kingdom: implications for human exposure, Emerging contaminants 9 (1), 100203. https://doi.org/10.1016/j.emcon.2023.100203
5. **Gbadamosi, M. R.,** Ogunneye, A. L., Al-Omran, L.S., Abdallah, M. A., Harrad, S. 2023b. Presence, source attribution, and human exposure to organophosphate esters in indoor dust from various microenvironments in Nigeria. Emerging Contaminants, 9(2), 100208

Submitted Manuscripts

(a) **Food Control (FOODCONT) (Under review)**

1. **Gbadamosi, M. R.,** Moberuagba, K.H., Abdallah, M. A. E, Harrad, S. Occurrence and Dietary Exposure to Organophosphorus Esters in foodstuffs of Nigerian origin

(b) Environmental Pollution (ENPO) (Under review)

2. **Gbadamosi, M. R.,** Ogunneye, A. L., Jegede, D. O., Al-Omran, L.S., Abdallah, M. A. E., Harrad, S. Occurrence, source apportionment and ecological risk assessment of organophosphate esters in surface sediment from Ogun and Osun River, Southwest Nigeria

(c) Journal of Environmental Exposure Assessment (JEEA) (Under review)

3. **Gbadamosi, M. R.,** Abdallah, M. A. E, Harrad, S. A critical review of human internal exposure and health risks estimate of urinary OPEs metabolites for all age group.

CONFERENCE PRESENTATIONS

OP = oral presentation and PP = Poster presentation

1. **Gbadamosi, M. R.,** Abdallah, M. A. E, Harrad, S. 2019. Investigating human dietary exposure to organophosphate esters (OPEs). School of Geography, Earth and Environmental Sciences (GEES) DR Conference, 2019. University of Birmingham, UK. PP
2. **Gbadamosi, M. R.,** Abdallah, M. A. E, Harrad, S. 2022. Occurrence, distribution, and dietary exposure to Organophosphate esters in UK foodstuffs. 10th International Symposium on Flame retardants (BFR 2022), Athens, Greece.
3. **Gbadamosi, M. R.,** Abdallah, M. A. E, Harrad, S. 2023. Organophosphate esters in UK diet; exposure and risk assessment. ACS Spring Conference, Indianapolis, March 26-30, 2023.

ABBREVIATIONS

OPEs = Organophosphate esters

BFRs = Brominated flame retardants

FRs = Flame retardants

POPs = Persistent organic pollutants

TCEP = Tris(2-chloroethyl) phosphate

TCIPP = Tris(2-chloroisopropyl) phosphate

TDCIPP = Tris(1,3-dichloropropyl) phosphate

TPHP = Triphenyl phosphate

TBOEP = Tris(butoxyethyl) phosphate

EHDPP = 2-ethylhexyldiphenylphsophate

TnBP = Tri-n-butylphosphate

TMTP = Tri-m-tolyl phosphate

TBP = Tributyl phosphate

Cl-OPEs = Chlorinated OPEs

BAF: Bio-accumulation factor

MW = Molecular weight

K_{ow} = n-octanol: water partition coefficient

BP = Boiling point

P = Vapor pressure

S = solubility

PUFs = Polyurethane foams

ABS = Acrylonitrile-butadiene-styrene

EPDM = Ethylene propylene diene monomer (M-class) rubber

HIPS = High impact polystyrene

EPS = Expanded polystyrene

HIPS/PPO = Copolymer of HIPS and PPO

PC = Polycarbonate

PC/ABS = Copolymer of PC and ABS

PE = Polyethylene

PP = Polypropylene

PPO = Polyphenylene oxide

PUR = Polyurethane

PVC = Polyvinyl chloride

TPU = Thermoplastic polyurethane

EDIs = Estimated daily intakes

DF = Degree of freedom

RfD = Reference dose

HQ = Hazard quotient

USEPA = United State Environmental Protection Agency

3D-HSE = 3-D human skin equivalent

SFO = Oral cancer slope factor

UK = United Kingdom

USA = United States of America

EFRA = European Flame Retardants Association

DEPA = Danish Environmental Protection Agency

ATSDR = Agency for Toxic Substances and Disease Registry

EU = European Union

US FDA = US Food and Drug Administration

NICNAS = National Industry Chemicals Notification and Assessment Scheme

WHO = World Health Organization

d-SPE = Dispersive solid phase extraction

PSA = Primary secondary amine

RDS = Recovery determination standard

ISs = Internal standards

CAN = Acetonitrile

GC-EIMS = Gas Chromatography – electron ionisation mass spectrometry

RSD = Relative standard deviation

RRF = Relative response factor

LOD = Limit of detection

LOQ = Limit of quantification

RRT = Relative retention time

SRs = Standard recoveries

PCA = Principal component analysis

KMO = Kaiser-Meyer Olkin

ANOVA = Analysis of variance

LB = Lower bound

UB = Upper bound

NDNS = National Diet and Nutrition Survey

PHE = Public Health England

FSA = Food Standards Agency

BW = Body weight

ND = Not detected

NIST = National Institute of Standards and Technology

HPLC = High Performance Liquid Chromatography

SRM = Standard reference material

HCA = Hierarchical cluster analysis

CA = Correlational analysis

PBDEs = Polybrominated diphenyl ethers

PMEs = Public microenvironments

RQ = Risk quotient

PNEC = Predicted no-effect concentration

MEC = Measured environmental concentrations

ROS = Reactive oxygen species

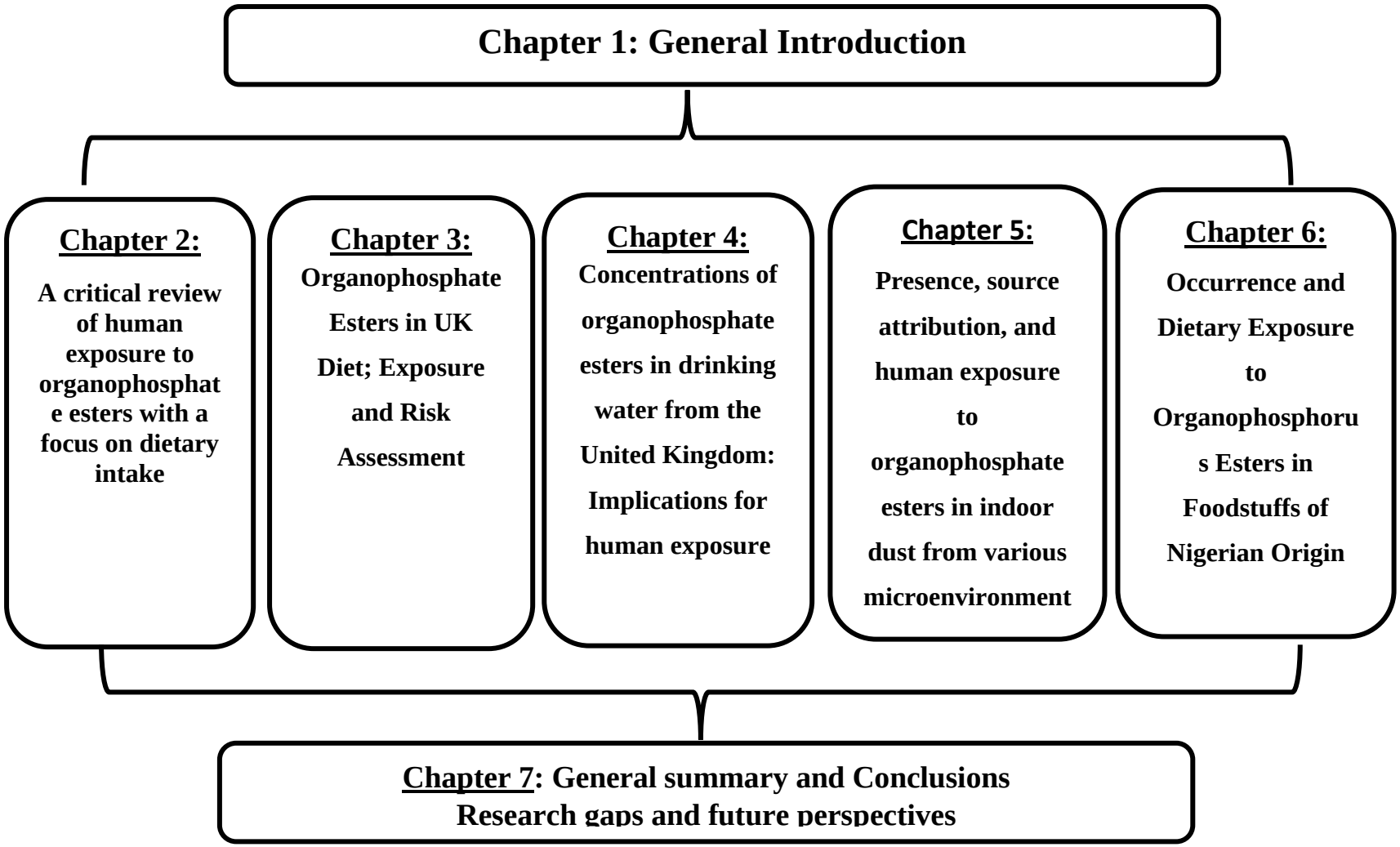


Fig. 1.2: A graphical overview of the chapters of the current thesis

CHAPTER I

General Introduction

1.1 Rationale of the thesis

It has been established that food is not only a source of nutrients but also contains various classes of chemical contaminants, that potentially include organophosphate esters (OPEs). OPEs are used as additives in various consumer and industrial products, which leads to their widespread release into the environment via volatilisation, leaching, and abrasion (Gbadamosi et al., 2021). This leads to contamination of various environmental compartments such as: air, dust, water, as well as body fluids such as: urine, blood, breast milk etc. Several toxicological studies have implicated OPEs as potentially toxic chemicals which human prolonged exposure to may induce several adverse effects including: carcinogenicity, neurotoxicity, reproductive toxicity, and endocrine disruption etc (Wei et al., 2015; Gbadamosi et al., 2021;2022; Yao et al., 2021). Although reports of contamination of food samples with OPEs are to date few, such studies suggest that diet may be an important pathway of human exposure to these contaminants. Hence, there is an urgent need for comprehensive monitoring of OPEs in foodstuffs to examine the significance of diet as a human exposure pathway and facilitate estimation of the potential health risk of OPEs arising from such exposure. In similar fashion, while recent reports from around the world suggest that OPEs are present in drinking water (Hou et al., 2021; Li et al., 2019a; Lee et al., 2016; Zhang et al., 2022; Kim and Kannan, 2018), there are no data to the author's knowledge on their presence in UK drinking water and its

potential contribution to human exposure. Despite the increasing number of publications on the presence of OPEs in indoor microenvironments in developing countries, it is worth noting that only three studies have investigated the presence of OPEs in indoor dust in Africa: specifically in Egypt (Abdallah and Covaci, 2014, Shoeib et al., 2019) and South Africa (Abafe and Martincigh, 2019). Therefore, our data on the presence of OPEs in indoor dust from various microenvironments (car/bus, offices, medical centres, and homes) constitutes the first report in Nigeria. In addition, given the dearth of information on dietary exposure to OPEs in Africa, in this thesis selected foodstuffs of Nigerian origin were analysed for OPEs and the data used to evaluate human exposure risk to the compounds under different exposure scenarios. These identified research gaps concerning the presence of OPEs in food, drinking water, and indoor dust from UK and Nigeria are addressed in different chapters of this thesis in the form of papers either published or submitted for publication in high-impact peer reviewed journals.

1.2 Introduction to flame retardants

There is nothing in this world with advantage without disadvantage, what is more important is that the advantage should be more beneficial than the disadvantages for it to serve a real purpose. Fire has numerous functions such as for cooking, heat and light generation in the house, incineration, smelting, and for transportation etc. As useful as this may be, fire can pose great risks to life and property, and thus new ways are continuously being developed to prevent and reduce their impacts (Labuschagne, 2003). In recent times, there has been a global decline in the rate of fire accidents (Center of fire Statistics, 2019). While in some societies this may be a result of reduced levels of smoking, it may also be partly attributed to the increased use of chemicals called flame retardants (FRs) in many consumer and industrial products including plastics and other polymeric materials, textiles, building materials, electrical and electronic appliances (Wei et al., 2015).

FRs are chemicals used in various consumer products to inhibit, suppress, or slow ignition rate to limit the spread of fire (Aschberger et al., 2017). They can act in different ways, from interfering with fire's ability to consume oxidisers, to forming a barrier, or acting as a chemical coolant (Morgan and Wilkie, 2006).

FRs are added to products as either additive or reactive flame retardants. Reactive flame retardants are those that are chemically bonded to the materials, while additive flame retardants are those that are incorporated into the materials by physical mixing only (Beard, 2013; Ortiz, 2017). FRs are usually grouped based on their "main" chemical element – such as: halogens (mostly bromine, but also chlorine), phosphorus, nitrogen, metals such as aluminium, magnesium, and zinc (Aschberger et al., 2017). Among the four major groups of FRs currently in use are the phosphate-based flame retardants (OPFRs) also referred to as organophosphate esters (OPEs). OPEs are used as non-reactive (additive) FRs (Greaves and Letcher, 2016). In fire, OPEs decompose in the presence of heat in one of two ways. Non-halogenated OPEs react mainly in the solid phase of burning materials. The phosphorous compounds, when heated, react to generate a polymeric form of phosphorous acid. This acid causes a char layer, shielding the burning material from oxygen, and thus slowing the reaction (van der Veen and de Boer, 2012). Chlorinated OPEs (Cl-OPEs) also cause a char layer on the burning materials but also decompose to react in the gas phase (Greaves and Letcher, 2016). Liberated chlorine atoms react with hydrogen ($H^{\cdot}$) and hydroxide ($OH^{\cdot}$) radicals to further slow the burning process and reduced the spread of the fire (Greaves and Letcher, 2016). The effectiveness of the OPE increases with increasing numbers of halogen atoms in the molecule (Greaves and Letcher, 2016).

1.3 Classification of flame retardants and OPEs

OPEs may be classified into five groups, namely: organophosphates, organoposphine oxide, organophosphonates, organophosphites, and organophosphinates (Figure 1.2b).

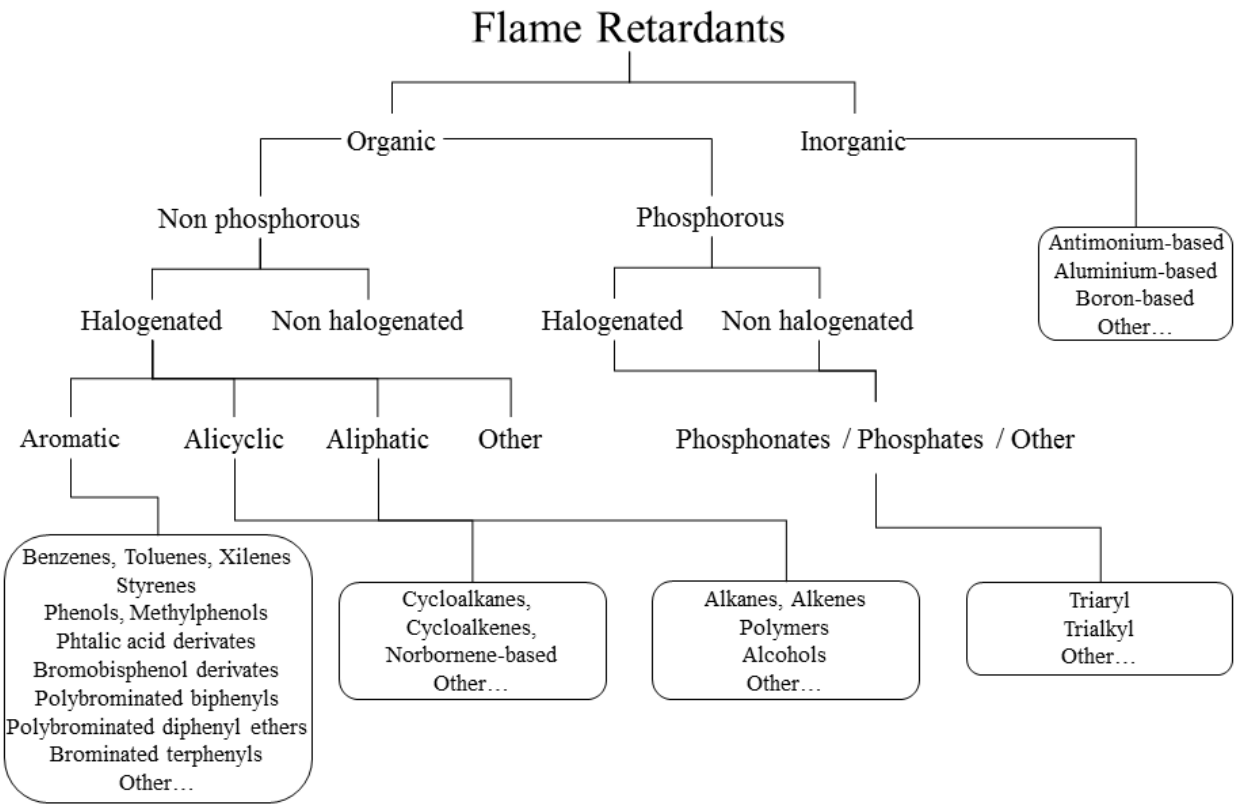


Figure 1.1a: Classification of Flame Retardants (Fisk et al., 2014)

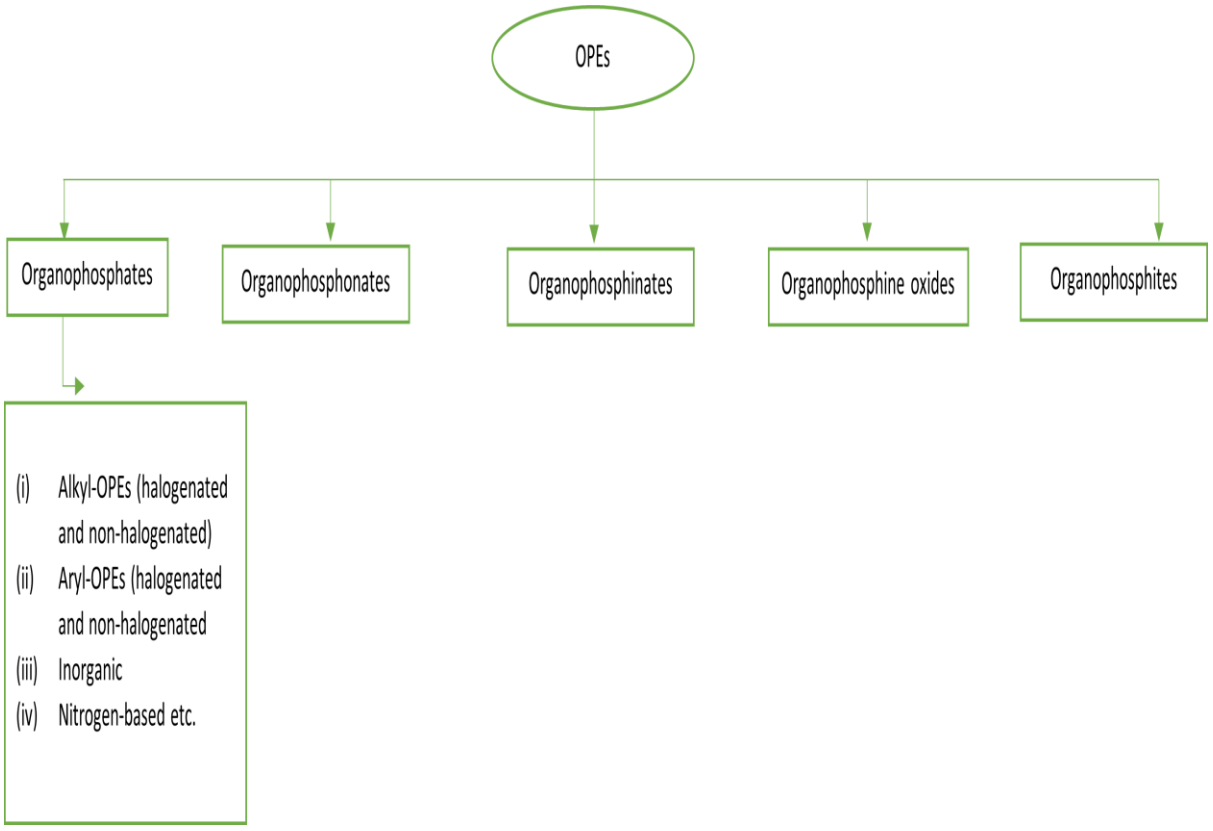


Figure 1.1b: Classification of OPEs

1.4 Production and Uses of OPEs

Because of the bans and restrictions placed on the use of some brominated flame retardants (BFRs), production volumes and use of OPEs are expected to increase. In 1992, the worldwide usage of FRs was estimated at 600,000 tons, of which about one-fifth was OPEs (OECD, 1995; World Health Organization, 1997). In Germany, the annual production volumes of tributyl phosphate (TBP) (the sum of tri-n-butyl phosphate (TNBP) and tri-isobutyl phosphate (TIBP)) and tris (2-chloroethyl) phosphate (TCEP) in 1991 were estimated at approximately 500 and 4,000-5,000 t/yr, respectively (Fries and Püttmann, 2001). By 2001 and 2004, the global consumption volume of OPEs totalled 186,000 tons (Marklund et al., 2005) and 300,000 tons (of which 70 % was consumed as FRs) (Makinen et al., 2009; Moller et al., 2012), respectively. In Western Europe, the usage of OPEs sharply increased from 58,000 tons in 1998 to 83,000 tons in 2001 and to 85,000 tons in 2005, and up to 91,000 tons in 2006. OPEs were responsible for 20 % of the total consumption of FRs in 2006 (European Flame Retardant Association, 2007, 2010; Reemtsma et al., 2008). In Japan, approximately 22,000 and 30,000 tons of OPEs were consumed in 2001 and 2005, respectively (Japan Chemical Daily, 2002; Moller et al., 2012). In addition, the production and shipment quantity of OPE plasticisers in Japan were estimated at 45,400 and 85,700 tons in 2005 and 2010, respectively (Research and Statistics Department, 2010). In 2007, 70,000 tonnes of OPEs were produced in China, and 40,000 tonnes of these OPEs were exported (Li et al., 2015). In 2011, 500,000 tonnes of OPEs were consumed globally, and annual consumption was expected to reach 680,000 t in 2015 (Wang et al., 2015a). In 2016, organophosphate compounds represented the second most produced flame-retardant group reaching 18% of the total market worldwide after aluminium hydroxide (38%) (Al-Omran et al., 2021). Global consumption of OPEs increased from 186,000 t in 2001 to 680,000 t in 2015 (Van der Veen and de Boer, 2012; Wang et al., 2015a). According to a US EPA survey, tris (butoxyethyl) phosphate (TBOEP), TNBP, and TCEP were listed as high

production volume chemicals with individual production volumes from 454 to 4535 tonnes annually (US EPA, 2010). In addition to their use as FRs and plasticisers, OPEs are also used as stabilisers for anti-foaming agents, and as additives to floor polishes, lubricants, lacquers, and hydraulic fluids. For example, the most common chlorinated OPEs (i.e., TCEP, tris(2-chloroisopropyl) phosphate (TCIPP) and tris (1, 3-dichloro-2-propyl) phosphate (TDCIPP)) are generally applied in flexible and rigid PUFs, whereas TBOEP is widely used in floor wax and as a plasticiser in vinyl plastics and rubber stoppers (Marklund et al., 2003) (Table 1.1). triphenyl phosphate (TPHP) is primarily used in unsaturated polyester resins and in PVC for its plasticising properties. Additionally, TBOEP, TPHP, and TBP are utilised as extreme pressure additives and anti-wear agents in hydraulic fluids, lubricants, transmission fluids, and motor oils (Regnery et al., 2011). In addition to being the primary ingredient in hydraulic fluids, TBP is used as an antifoaming agent in concrete, as a wetting agent in casein glue and as a pasting agent in pigment paste (Marklund et al., 2005), while 2-ethylhexyl diphenyl phosphate (EHDPP) is approved for use in food packaging (United States Food and Drug Administration, 2006).

1.5 Physicochemical properties of OPEs

Due to the varying nature of the substituents, OPEs have a wide range of physicochemical properties such as solubility in water (S_w), vapour pressure, octanol–water (K_{OW}) and octanol–air (K_{OA}) partition coefficients, and bioconcentration factors (BCFs) which define their environmental behaviour; in particular, their availability for uptake by biota and routes of human exposure. The bioaccumulation factor (BAF) used as a metric of the bioaccumulation potential of hydrophobic chemicals, is defined as the ratio of the concentration of an environmental chemical in an organism (from food and direct exposure) to the concentration in the immediate environment (Ivanciuc et al., 2006). BAF relates to all exposure pathways,

and more importantly to dietary exposure pathways of a hydrophobic chemical (Constanza et al., 2012; Arnot and Gobas, 2006) (Table 1.1). The emissions and release of OPEs via volatilisation or migration will depend on their vapour pressure and concentrations in the treated products (Gbadamosi et al., 2021; Carlsson et al., 1997; Ni et al., 2007). Meanwhile, the extent of OPE bioaccumulation is dependent on their K_{OW} and the rate at which they metabolise in biota (Regnery and Püttmann, 2010). For example, halogenated OPEs were reported to be more persistent in the environment and more resistant to degradation than alkyl and aryl OPEs (Marklund et al., 2005). K_{OW} is defined as a measure for a chemical's preference for water. Chemicals with low K_{OW} are regarded as hydrophilic chemicals, whereas a high K_{OW} favours the chemical partitioning into octanol over water, with such chemicals referred to as hydrophobic (Zhang et al., 2021). Degradation rates (often expressed as overall degradation half-lives for each environmental medium of interest) determine environmental persistence and are thus also fundamental input to chemical fate models.

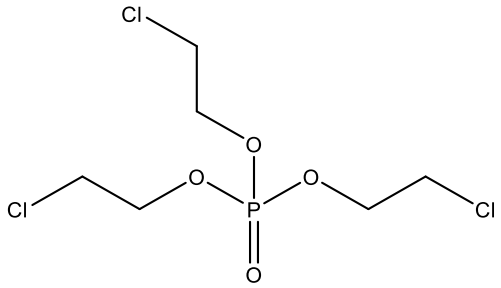
Table 1.1: Physicochemical properties of common OPEs

OPE (chemical formula)	MW	Log K_{ow}	P (mmHg at 25°C)	S (mg/L at 25°C)	BP (°C)	BAF
Halogenated phosphates						
TCEP ($C_6H_{12}Cl_3O_4P$)	285.49	1.63	0.0613	7000	351	0.425
TCIPP ($C_9H_{18}Cl_3O_4P$)	327.57	2.89	$5.64x10^{-5}$	1200	>270	3.27
T2CPP ($C_9H_{18}Cl_3O_4P$)	327.57	2.58	-	740	358.5	-
TDCIPP ($C_9H_{15}Cl_6O_4P$)	430.89	3.65	$2.98x10^{-7}$	7	237	21.4
TDBPP ($C_9H_{15}Br_6O_4P$)	697.61	3.71	-	8	390	
V6 ($C_{13}H_{24}Cl_6O_8P_2$)	582.99	1.9	$1.2x10^{14}$	2.1	620	17.07
Aryl phosphates						
TPHP ($C_{18}H_{15}O_4P$)	326.28	4.59	$1.12x10^{-5}$	1.9	370	113.3
TCP ($C_{21}H_{21}O_4P$)	368.36	5.11	$4.9x10^{-7}$	0.36	439	-
EHDPP ($C_{20}H_{27}O_4P$)	362.41	6.30	$5x10^{-5}$	1.9	421	855.3
DCP ($C_{19}H_{17}O_4P$)	340.31	4.51	$4.7x10^{-6}$	0.24	235	1711
BADP ($C_{39}H_{34}O_8P_2$)	692.64	4.5	-	0.4151	680	3.16
RDP	574.46	7.41	$2.1x1^{-8}$	$1.11x10^{-4}$	587	$2.05x10^{4}$

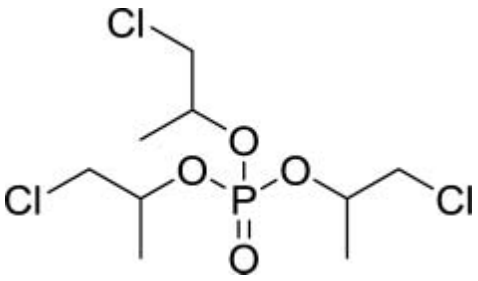
OPE (chemical formula)	**MW**	**Log K_{ow}**	**P (mmHg at 25°C)**	**S (mg/L at 25°C)**	**BP (°C)**	**BAF**
($C_{30}H_{24}O_8P_2$)						
TIPPP ($C_{27}H_{33}O_4P$)	452.53	8.0-10.8	-	-	494	
TPCP ($C_{21}H_{21}O_4P$)	368.36	5.48	-	$7.4x10^{-2}$	439	$8.56x10^{3}$
IDPP ($C_{22}H_{31}O_4P$)	390.45	5.44	1.08	0.75	448	$4.17x10^{5}$
DIPPP $C_{21}H_{21}O_4P$)	368.36	5.31	1.196	2.2	424	$7.97x10^{3}$
DPOP ($C_{20}H_{27}O_4P$)	286.30	6.82	1.105	0.14	426	$8.96x10^{4}$
DPP ($C_{12}H_{11}O_4P$)	250.19	2.88	-	82	378	5.44
TXP ($C_{24}H_{27}O_4P$)	202.14	5.63	$8.76x10^{-8}$	$1.86x10^{-2}$	491	$9.59x10^{4}$
Alkyl phosphates						
TNBP ($C_{12}H_{27}O_4P$)	266.31	4.00	$1.13x10^{-3}$	280	289	39.81
TMP ($C_3H_9O_4P$)	140.07	-0.65	$2.5x10^{-7}$	$3.00x10^{5}$	197	3.16
TEP ($C_6H_{15}O_4P$)	182.15	0.87	0.29	1115	216	3.162
TIBP ($C_{12}H_{27}O_4P$)	266.31	3.60	$1.29x10^{-2}$	3.72	264	391
TBOEP ($C_{18}H_{39}O_7P$)	398.48	3.65	$1.23x10^{-6}$	$1.20x10^{3}$	414	$1.08x10^{3}$
TEHP ($C_{24}H_{51}O_4P$)	434.64	9.49	$8.25x10^{-8}$	0.6	220	$1x10^{6}$

OPE (chemical formula)	**MW**	**Log K_{ow}**	**P (mmHg at 25°C)**	**S (mg/L at 25°C)**	**BP (°C)**	**BAF**
TIPP ($C_9H_{21}O_4P$)	224.23	-	1.108	1.4	490	-
Trioctyl phosphate($C_{24}H_{51}O_4P$)	434.64	10.6	0.928	$9.47x10^{-6}$	415	$1.00x10^{6}$
DMMP $(CH_3)P(O)(OCH_3)_2$	124.08	-0.61	1.08	$3.22x10^{5}$	181	3.16
TPrP ($C_9H_{21}O_4P$)	224.23	1.87	-	6450	284.2	-

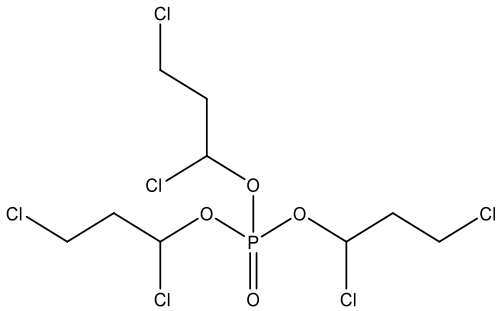
Where: S = solubility (mg/L) in water at 25°C; P = vapor pressure (mmHg) at 25°C; log K_{ow} = n-octanol: water partition coefficient; BAF: bio-accumulation factor which defined as the ratio of the chemical concentrations in the organism (C_s) and the water (C_w) and, MW = molecular weight and TDBPP is tris(2,3-dibromopropyl) phosphate. The data are compiled from databases (Chemspider, 2015), Gbadamosi et al. (2021) and Pantelaki and Voutsa (2019).



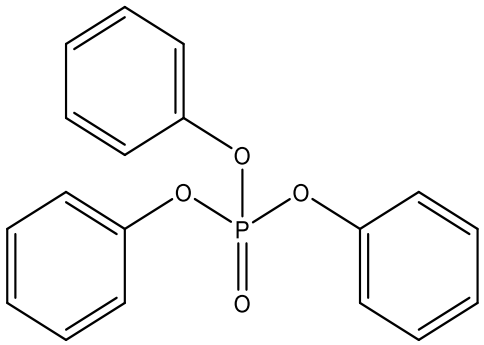
Tris(2-chloroethyl) phosphate (TCEP)



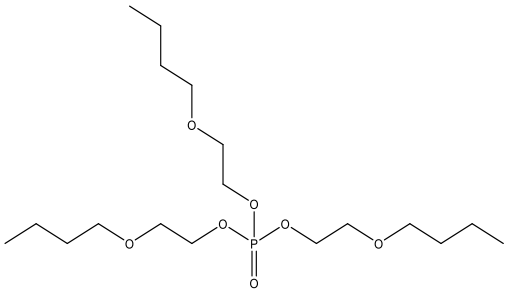
Tris(2-chloroisopropyl) phosphate (TCIPP)



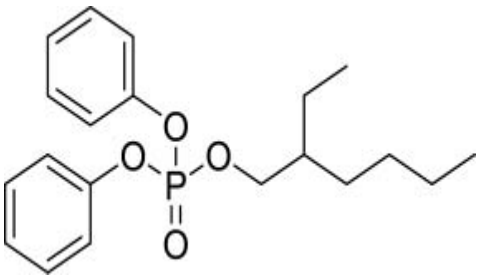
Tris(1,3-dichloropropyl) phosphate (TDCIPP)



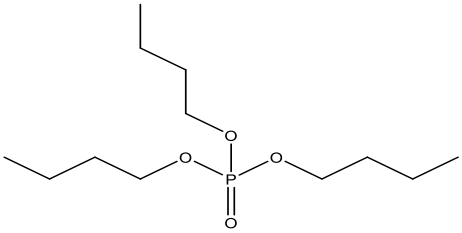
Triphenyl phosphate (TPHP)



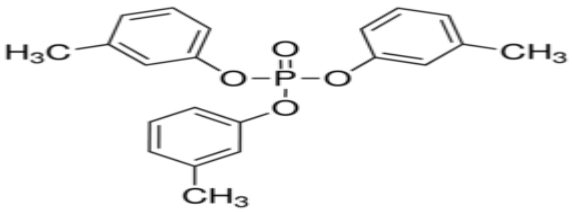
Tris(butoxyethyl) phosphate (TBOEP)



2-ethylhexyldiphenylphsophate (EHDPP)



Tri-n-butylphosphate (TnBP)



Tri-m-tolyl phosphate

Fig. 1.2: Chemical structures of some frequently studied OPEs

1.6 OPE emissions from consumer products

Because of the extremely high concentrations of OPEs (typically low percent) in a wide variety of consumer products and building materials, such articles represent putative sources of OPEs to the environment (Wei et al., 2015). The investigated OPEs are frequently present as additives rather than chemically bonded to the final products, resulting in relatively widespread release via volatilisation, abrasion and/or leaching during their lifetime, including production, usage, disposal, and recycling processes. Due to their moderate vapour pressures (Table 1.2), the release of OPEs from products is likely to occur. A previous study has verified that TPHP could be continuously emitted into indoor air during the normal operation of a computer (Carlsson et al., 1997).

The release of TMPP from plastic films into water occurred at a rate of 7.7 µg/g of film over a period of two years (Wei et al., 2015; Cho et al., 1996). Area-specific emission rates of TCIPP from selected consumer products made of assembly foams, upholstery/mattresses, insulation boards and electronic equipment were determined in test chambers, which varied from 20 to 140 µg/m^2/h, depending on the sample type (Wei et al., 2015; Kemmlein et al., 2003). The emission flux of TCIPP was significantly positively correlated with its concentration in PVC wallpaper samples, with emission rates ranging from 262 to 2167 µg/m^2/h for wallpaper samples containing 1-20% w/w TCIPP (Wei et al., 2015; Ni et al., 2007).

With respect to temperature, a linear relationship was established between the inverse of the temperature and the logarithm of the TCIPP emission (Wei et al., 2015; Ni et al., 2007). Furthermore, the emission rates of TCIPP decreased from 645 to 73.2 µg/m^2/h with an elapsed time increase to 280 days (Wei et al., 2015; Ni et al., 2007). Based on the EU risk assessment report on TCIPP, approximately 40 % of TCIPP in a finished product was available for release, whereas the total continental European discharges of TCIPP to the air were estimated at 89.6 and 135 kg/d, respectively (European Union, 2007). According to migration tests performed

on interior surfaces consisting of floors, walls and ceilings, and the outer casings of computer monitors and TV sets; among the seven OPEs studied (TBP, TCIPP, TCEP, TBEP, TDCIPP, TPHP, and TCP), TBEP gave the highest migration rate of up to 339 μg/m^2/h emitted from building materials and electrical appliances (Wei et al., 2015; Saito et al., 2007).

1.7 Toxicity of OPEs

Toxicological studies have revealed that elevated and prolonged exposure to OPEs can induce several adverse effects including: carcinogenicity, neurotoxicity, kidney toxicity, reproductive toxicity, liver toxicity, and endocrine disruption (Liu et al., 2016; Ding et al., 2016). The existence and concentrations of OPEs in various biotic and abiotic environmental matrices has been reviewed (Wei et al., 2015; Sugeng et al., 2017; Hou et al., 2016; Ding et al., 2016; Greaves and Letcher, 2017). TCEP has been reported to be carcinogenic to small animals such as rats and mice, and toxicological data suggests it to be a neurotoxin (Dishaw et al., 2011; Van der Veen and de Boer, 2012). In experimental studies, TCIPP, TPhP, and TBP have been observed to disrupt normal endocrine and reproductive function, nervous system development and are suspected carcinogens (van de Veen and Boer, 2012; WHO, 1998, 1991). Although data are scarce, human epidemiological studies suggest that exposure to TCIPP, TDCIPP, and TBOEP is associated adversely with human thyroid hormone levels and semen quality parameters (Meeker, 2010; Egloff et al., 2014), while EHDPP is considered highly toxic to fish and aquatic plants and has potential to bio-accumulate (Malarvannan et al., 2015; Bolgar et al., 2008).

Chlorinated organophosphates (Cl-OPEs) were suspected carcinogens with observed tumour growth in rats not only in the kidney, liver and thyroid for TCEP and TCIPP but also in the brain and testes for TDCIPP (World Health Organization, 1998). The LC_{50} values of TCEP documented for fish (96 h) ranged from 6.3 to 250 mg/L (Fisk et al., 2003). The additional

association of acute deaths in dogs with the ingestion of car seat cushions strongly suggested that TCEP was linked to death through its known seizure-inducing activity (Lehner et al., 2010). It had been reported that TDCIPP could increase reactive oxygen species (ROS) production and induce oxidative stress (Chen et al., 2018). TPP, TCEP, TNBP, TBEP, and TCIPP caused oxidative stress in ICR mice (Mus musculus), hepatocellular carcinoma cells (HepG2), hypotriploid alveolar basal epithelial cells (A549), and human Cancer coli-2 (Caco-2) colon cancer cell lines (An et al., 2016; Chen et al., 2015; Chen et al., 2018). TDCIPP could induce DNA damage, block DNA repair and arrest cell cycle along with ROS level increased in zebrafish and Chinese rare minnow (Hong et al., 2018; Wang et al., 2015b). Researchers reported that TPHP is possibly associated with delayed neurotoxicity in cats and monkeys (Smith et al., 1930; 1932; Andresen et al., 2004; Ni et al., 2007). On the contrary, Pakalin et al. (2007) mentioned a low neurotoxicity for TPHP. Several adverse behavioral outcomes (e.g., suppression of axonal growth, interference with neurotransmitter release, and abnormal neuron differentiation) were documented for TNBP/TBEP/TCEP/TPP (Li et al., 2019b; Shi et al., 2018; Sun et al., 2016b) and further affected the cognitive abnormality of offspring (Wang et al., 2015b, c). Sun et al. (2016a, b) also reported that TNBP/TBEP/TPP/TCEP could inhibit AChE activity and interfere with neural regulation, causing locomotor activity inhibition in Japanese medaka fish (d-rR strain, in-vivo).

Therefore, understanding human exposure to OPEs and evaluating the risk through the multiple exposure pathways is important for developing strategies to manage their potential risks.

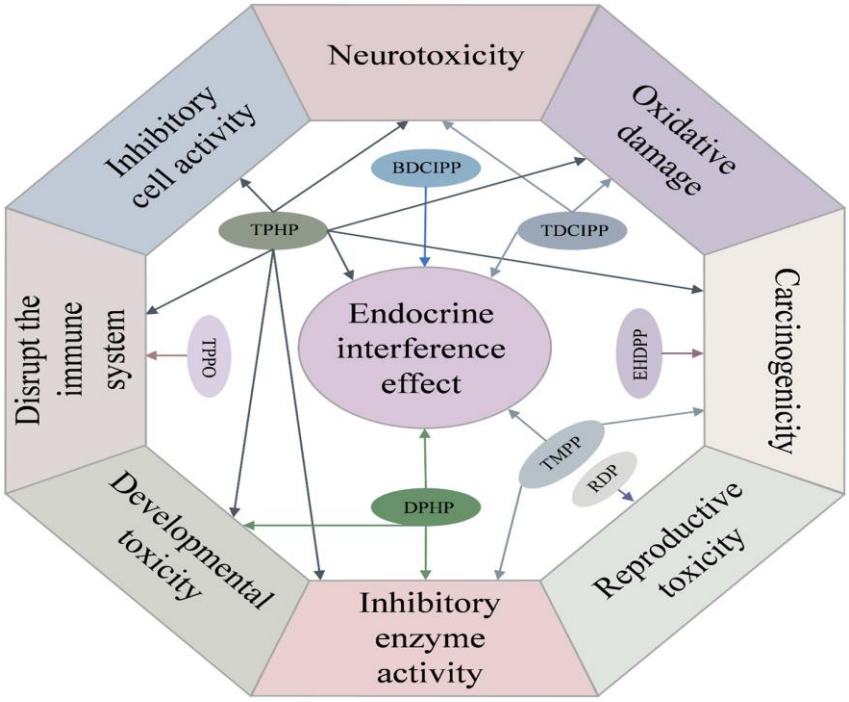


Figure 1.3a: Toxicity of OPEs and their metabolites in organisms (Yao et al., 2021)

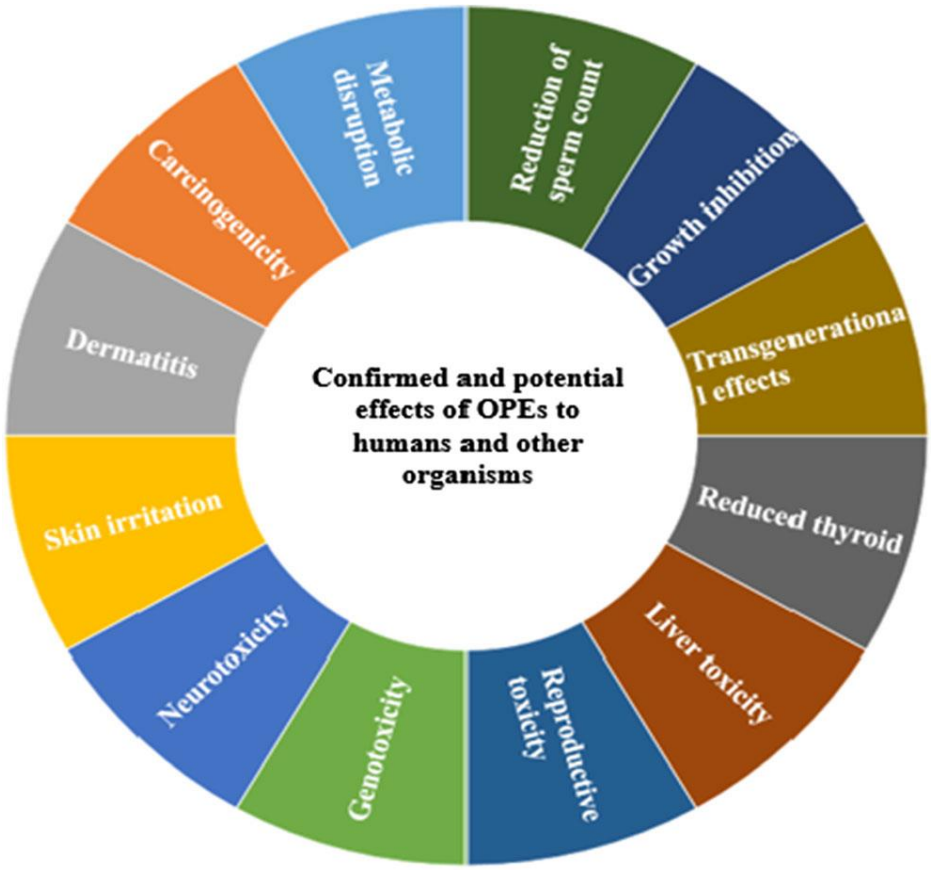


Fig. 1.3b: Toxicity of OPEs to humans and other organisms (Bekele et al., 2021)

1.8 Pathways of human exposure to OPEs.

Physicochemical properties govern the distribution of OPEs between various environmental compartments such as food, water, air, dust etc and thus influence pathways of human exposure (Zhang et al., 2021). Humans are exposed to environmental chemicals through a variety of pathways, including: oral ingestion of the chemicals, inhalation, and dermal contact and absorption. Exposure to environmental chemicals such as OPEs via oral ingestion may be further described to include ingestion of contaminated food, contaminated drinking water and non-food items such as settled dust, air, and soil particles. OPEs appear in food either because of their bioaccumulation through food webs, leaching and migration from food containers, or contamination during the processes involved in food production, preparation, and delivery (Poma et al., 2017; Gbadamosi et al., 2021; 2022; Zhang et al., 2021). Dermal uptake can result from contact with dust and with products containing environmental chemicals. The relative contribution that each pathway makes to overall exposure depends *inter alia* on the physicochemical properties and commercial applications of the chemicals, as well as lifestyle and demographic factors related to the exposed individual. Evidence to date has demonstrated that human exposure to OPEs can occur via dermal contact (Abdallah et al., 2016; Abdallah and Harrad, 2022), ingestion of contaminated dust (Abdallah and Covaci, 2014; Brommer and Harrad, 2015), inhalation of air (Schreder et al., 2016), and more recently diet (Poma et al. 2018; Zhao et al., 2019; Chen et al., 2021) (Fig.1.3). However, despite this mounting evidence, there exist no data on the presence of these compounds in the UK diet, drinking water, and air as well as in foodstuffs of Nigerian origin and indoor dust from Nigeria. It is on this premise that this study was designed to investigate the magnitude of human exposure to OPEs in UK foodstuffs, UK drinking water, and foodstuffs of Nigerian origin, collected from major African stores in Birmingham, UK and from major markets in Lagos, Nigeria, and indoor dust from four indoor microenvironment categories in Nigeria.

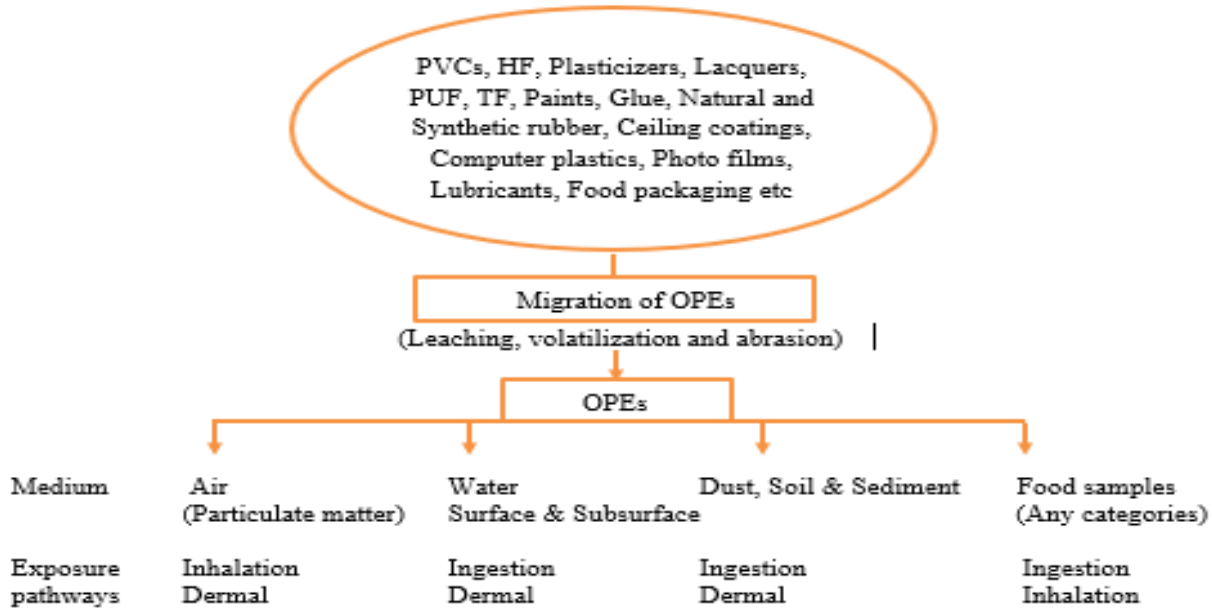


Figure 1.4: Schematic representation of the pathways of transmission of OPEs from treated products to humans (Gbadamosi et al., 2021)

1.9 Risk assessment of OPEs via dietary intake.

According to the definition given by the USEPA, the RfD (ng/kg bw/day) value represents the reference dose of oral toxicity of a chemical compound via daily oral exposure to human body and is regarded as an important indicator of risk assessment of human exposure to non-carcinogenic toxic substances (USEPA, 2017). This was calculated by dividing the chronic no-observed adverse effect levels by a safety factor (SF) (1000) or provided by USEPA's Integrated Risk Information System (Ding et al., 2018; He et al., 2018b; Zhang et al., 2016) (Equation 1). The SF has been replaced by the uncertainty factor (UF) since it contains more parameters for deriving RfD from experimental data than the SF since 2002 (USEPA, 2002). Another critical indicator for estimating the risk of OPEs to human health are hazard quotient (HQ) and hazard index (HI) (Equation 2 and 3). These indices can be calculated using the estimated daily intake (EDI) and RfD of OPEs by the following equation (Ding et al., 2018).

$$RfD = \frac{NOAEL}{1000} \quad (1)$$

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

$$HI = \sum HQ \quad (3)$$

The RfD and oral cancer slope factor (SFO) are key parameters in health risk assessment on human exposure to toxic substances. RfD is used to characterize the non-carcinogenic risk (non-CR) of a toxic substance via environmental exposure. SFO is used to estimate the carcinogenic risk (CR) associated with exposure to a carcinogenic or potentially carcinogenic substance (Li et al., 2018). As of 2011 and 2012, when research on OPEs and its human health implications was at the early stage, data on the synergistic or additive toxicity of the compound were not available (Van den Eede et al., 2011). This prompted the calculation of the RfD values by Van den Eede et al., (2011) and Ali et al., (2012) from the few available data using no observed adverse effect levels (NOAELs) in order to have an understanding of the health risk of OPEs to humans (Li et al., 2018). These RfDs values were used by several researchers (Poma et al., 2017; Brommer and Harrad, 2015; Abdallah and Covaci, 2014; Ding et al., 2016; He et al., 2015) to assess human exposure risk to OPEs until in 2017 when the USEPA updated the values after several toxicological studies (Li et al., 2018) (Table 1). This provided the scientific community with a set of revised RfD values. Prior to that, Saito et al. (2007) also reported an RfD value for TCIPP and recently a calculated RfD value for EHDPP was given by Zhao et al., 2019 (Table 1). From table 1, the differences between the RfD values from Van den Eede et al., 2011) and Ali et al., (2012) is one order of magnitude and this is mainly due to the different uncertainty factors (UFs) used by the authors (UF = 10000 used by Van den Eede et al. (2011) and UF = 1000 used by Ali et al. (2012) respectively. However, the difference between the RfDs of Ali et al., (2012) and the revised USEPA (2017) RfDs for most OPEs is limited (≤3 fold) (Li et al., 2018). This difference could be due to one or all of the following reasons. (i) hazard evaluations of OPEs and (ii) the data of laboratory animal exposure data for

calculating the organ/system-specific RfDs were available in 2015, including developmental (neurodevelopmental impairments), reproductive (decreased ovary weight and ovarian follicles), and immunological (decreased thymus weight and serum IgM) (USEPA, 2015; Li et al., 2018). In addition, to this, another factor could be that the calculation equations to derive RfD used by USEPA (2017) is different than that of Ali et al. (2012). Due to advances in toxicological research over the years, the calculation equation of RfD has been upgraded (Bhat et al., 2014; USEPA, 2014).

Table 1.2: Oral reference dose (RfD) (ng/kg bw/day) and oral cancer slope factor ((ng/kg bw/day)$^{-1}$) values for individual OPEs from different sources.

OPEs	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TBOEP**	**TnBP**	**TMTP**
RfD (ng/kg bw/day) [a]	7,000	10,000	20,000	NA	NA	NA	10,000	NA
RfD (ng/kg bw/day) [b]	2,200	8,000	1,500	7,000	600 [d]	1,500	2,400	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	3,600	NA	NA	NA	NA	NA	NA
Oral cancer slope factor (SFO) ((ng/kg bw/day)$^{-1}$) [a, f]	$2x10^{-8}$	-	-	-	-	-	$9x10^{-9}$	-

[a] Reference dose (RfD) and SFO 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)

[f] Li et al., (2018)

RfD = Reference dose

NA = not available

1.10 Regulatory framework for PBDEs and OPEs

Brominated flame retardants such as tetra-, penta-, hexa-, hepta-, and octa BDEs were added to Annex A in the Stockholm Convention in 2009 (UNEP, 2009) with over 150 countries signatories to legislate their phasing out and banned by the persistent organic pollutants (POPs) regulations (Blum et al., 2019) (see Fig 1 and Table 2 for detailed on the regulatory timeline). Consequently, in 2013 and 2017, HBCDD and deca-BDE were listed as POPs were listed and identified as POPs, marking them as chemicals whose usage and production should be phased out (UNEP, 2013, 2017; Misbah et al., 2022; Blum et al., 2019; Gbadamosi et al., 2023c). Furthermore, according to the European Unions "Registration, Evaluation, Authorization and Restriction of Chemicals" (REACH), some flame retardants should not be found in commercial products at levels greater than 0.1% (Blum et al., 2019) (Table 1). Based on the potential exposure health risks of OPEs in various products, the European Union (EU) in 2008 set regulations and criteria 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 pose major health and/or environmental hazards (Chen et al., 2021; Gbadamosi et al., 2023c). Consequently, while over 100 countries regulate the use of certain OPEs (Blum et al., 2019; Chen et al., 2021; Gbadamosi et al., 2023c), there is to our knowledge no regulation on the production and use of OPEs in Africa. In 2014, within the European Commission's Toy Directive, the maximum permissible concentration of TCEP, TDCIPP, and TCIPP in toys allowed onto the EU market was restricted to 5000 ng/g (ECHA, 2018)

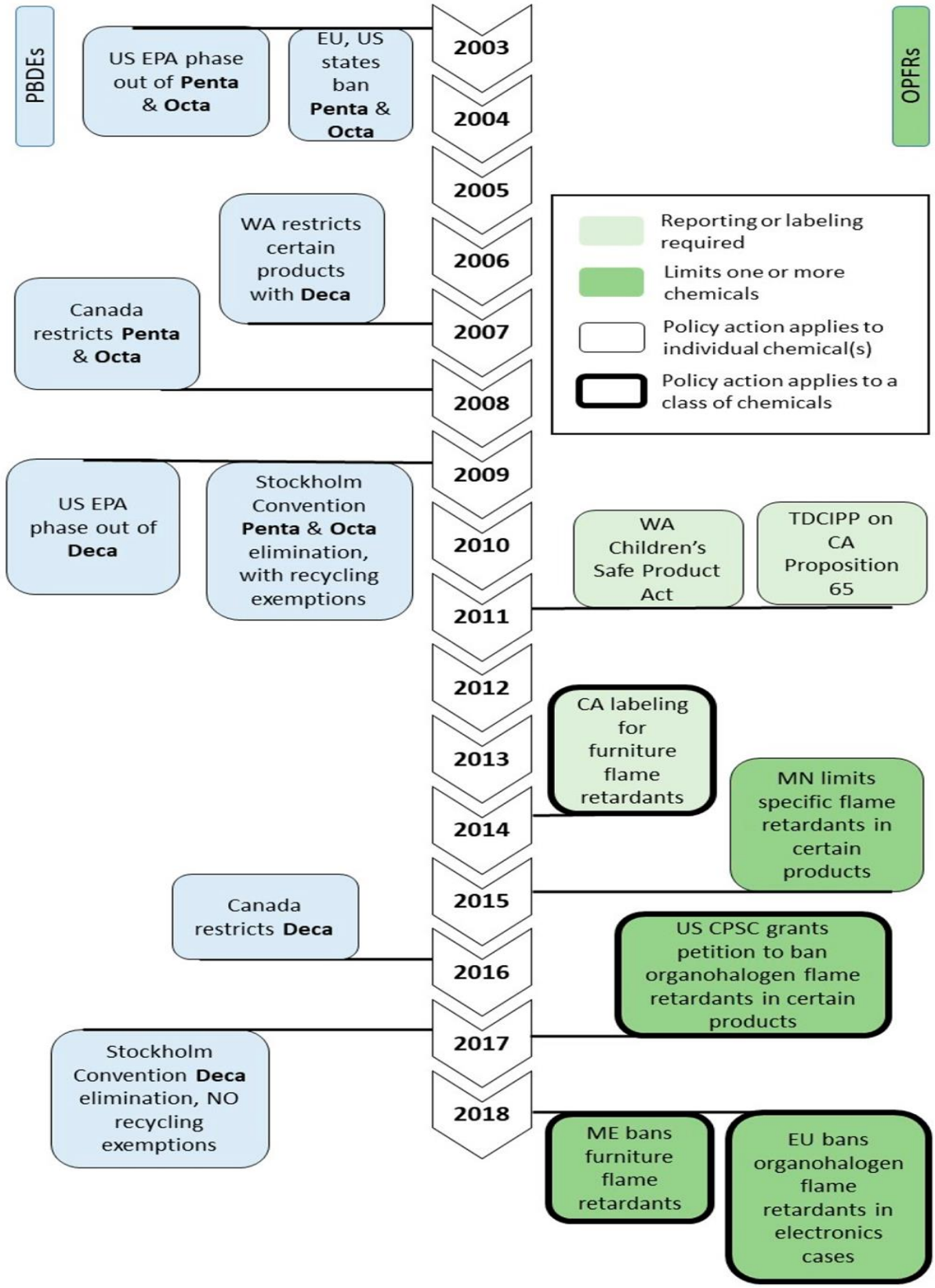


Figure 1.5. Timeline of major regulatory milestones for PBDEs and OPEs (Blum et al., 2019)

Table 1.3: Regulatory action for Flame retardants (Blum et al., 2019)

Flame retardants covered	Action	Jurisdiction/ Year/ Policy
PentaBDE, OctaBDE	Bans products containing more than 1/10 of 1% of the flame retardants pentaBDE or octaBDE, by mass.	CA/ 2003/AB 302
PentaBDE, OctaBDE	Prohibits marketing or use of these PBDEs	EC/ 2003/ Directive 2003/11/EC
PentaBDE, OctaBDE	Agreement between US EPA and manufacturers to phase out manufacture and import by 2004	US/ 2003/phase out agreement
DecaBDE	Restricts certain products containing DecaBDE including mattresses and televisions/ computers	WA/ 2007/ HB 1024
PentaBDE, OctaBDE	These regulations prevent the manufacture of these PBDEs and restrict their use in Canada. Note: these regulations were subsequently repealed and replaced with the Prohibition of Certain Toxic Substances Regulations, 2012, to the same effect.	Canada/ 2008/ Polybrominated Diphenyl Ethers Regulations
PentaBDE, OctaBDE	Elimination of production, use, import, export by all countries party to the treaty, with exemptions for recycling of articles	Stockholm Convention/ 2009/ SC-4/18 and SC-4/14
DecaBDE	Agreement between US EPA and some manufacturers to phase out manufacture and import by 2013	US/ 2009/ phase out agreement
TCEP	Prohibits foam padded children's products with this flame retardant	Canada/ 2010/ Canada Consumer Product Safety Act
TCEP, TPhP, TDCIPP, TCIPP, V6, IPTPP	Requires manufacturers to report these flame retardants in children's products to the state	WA/ 2011/ Children's Safe Products Act
TDCIPP	Requires warnings for exposures that exceed the No Significant Risk Level	CA/ 2011/ Proposition 65
TCEP	Limits this flame retardant in children's products	MD/ 2013/ House Bill 99
TDCIPP	Limits this flame retardant in children's products	MD/ 2014/ House Bill 229

All flame retardants	Requires labelling of furniture that contains flame retardants above 1000 ppm	CA/ 2014/ Senate Bill 1019
TCEP, TDCIPP, TCIPP	Limits these flame retardants to 5 mg/ kg in children's toys	EU/ 2014/ Commission Directive
TCEP, TDCIPP, TCIPP	Limits these flame retardants to 1000 ppm in children's products, furniture and mattresses and specifies that safer alternatives must be used	MN/ 2015/ HF 1100
TCEP	Generally prohibits the use of this flame retardant	EU/ 2015/ REACH Authorization List
DecaBDE	Adds DecaBDE to the list of prohibited PBDEs.	Canada/ 2016/ Regulations Amending the Prohibition of Certain Toxic Substances Regulations, 2012
Flame retardants with specific health hazards including: oral toxicity, dermal sensitization, gene mutation, and tumorigenicity	Prohibits the use of these flame retardants in children's loose-fitting sleepwear	Canada/ 2016/ Children's Sleepwear Regulations
DecaBDE, IPTPP	US EPA is required to propose rules to reduce exposures to the extent practicable by June, 2019	US/ 2016/ Toxic Substances Control Act
TDCPP, TCEP, and flame retardants with the following health hazards: carcinogenicity; developmental or reproductive toxicity; endocrine disruption; neurotoxicity	Limits these flame retardants to 0.1% in furniture and children's products.	Washington DC/ 2016/ B21-0143
DecaBDE	Elimination of production, use, import, export by all countries party to the treaty, with exemptions for specific uses	Stockholm Convention/ 2017/ SC-8/10
TCEP, TDCIPP	Reporting required for manufacturers of children's foam-padded sleeping products with these flame retardants	CA/ 2017/ Safer Consumer Products Program rule

Organohalogen flame retardants	Limits these flame retardants to 100 ppm in children's products, bedding and furniture	RI/ 2017/ H5082
TCEP, TDCIPP	Limits these flame retardants to 1000 ppm in children's products and residential furniture	WA/ 2017/ Children's Safe Product Act
All halogenated OPFRs and all other additive, non-polymeric organohalogen flame retardants	Initiated rulemaking to prohibit these flame retardants in children's products, furniture, mattresses and electronics cases; issued guidance to manufacturers and consumers warning about health concerns of organohalogen flame retardants	US/ 2017/ Consumer Product Safety Commission
DecaBDE	Prohibits the manufacture and use in Japan.	Japan/ 2018/ Ministry of Economy, Trade and Industry
All OPFRs and most other flame retardants	Limits these flame retardants to 1000 ppm in children's products, mattresses and furniture	CA/ 2018/ Assembly Bill 2998
All flame retardants	Limits these flame retardants to 1000 ppm in furniture	ME/ 2018/ LD 182
Halogenated flame retardants prohibition; all flame retardants for labelling	Prohibits the use of halogenated flame retardants in the enclosure or stand of covered electronic displays; requires that components containing flame retardants be labelled with a code to identify the flame retardant used	EU/ 2018/ D059740/02
TCEP, TPHP	These flame retardants proposed as high priority chemicals which would undergo risk evaluation.	US/ 2019/ Toxic Substances Control Act

1.11 Research aims and objectives.

The above material identifies several research gaps related to the magnitude of human exposure to OPEs in the UK and Africa. In particular, there are no data on intake of OPEs via the diet or drinking water in UK and in Africa, nor any information on the presence of OPEs in indoor dust in Nigeria. To address these gaps, the aims of the current study are to:

(i) Review the current global database on human dietary exposure on OPEs and evaluate the importance of this pathway as a contributor to overall human exposure to these contaminants;

(ii) Investigate the magnitude of UK dietary exposure to OPEs;

(iii) Evaluate the extent of UK human exposure to OPEs via drinking water;

(iv) Assess human exposure to OPEs via ingestion of indoor dust from Nigeria;

(v) Determine concentrations of OPEs in selected foodstuffs of Nigerian origin collected from major stores in UK and in Nigeria. These data will be used to perform a preliminary dietary exposure assessment;

(vi) Evaluate the overall health risk of current UK exposure to OPEs.

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CHAPTER II

A Critical Review of Human Exposure to Organophosphate Esters with a Focus on Dietary Intake

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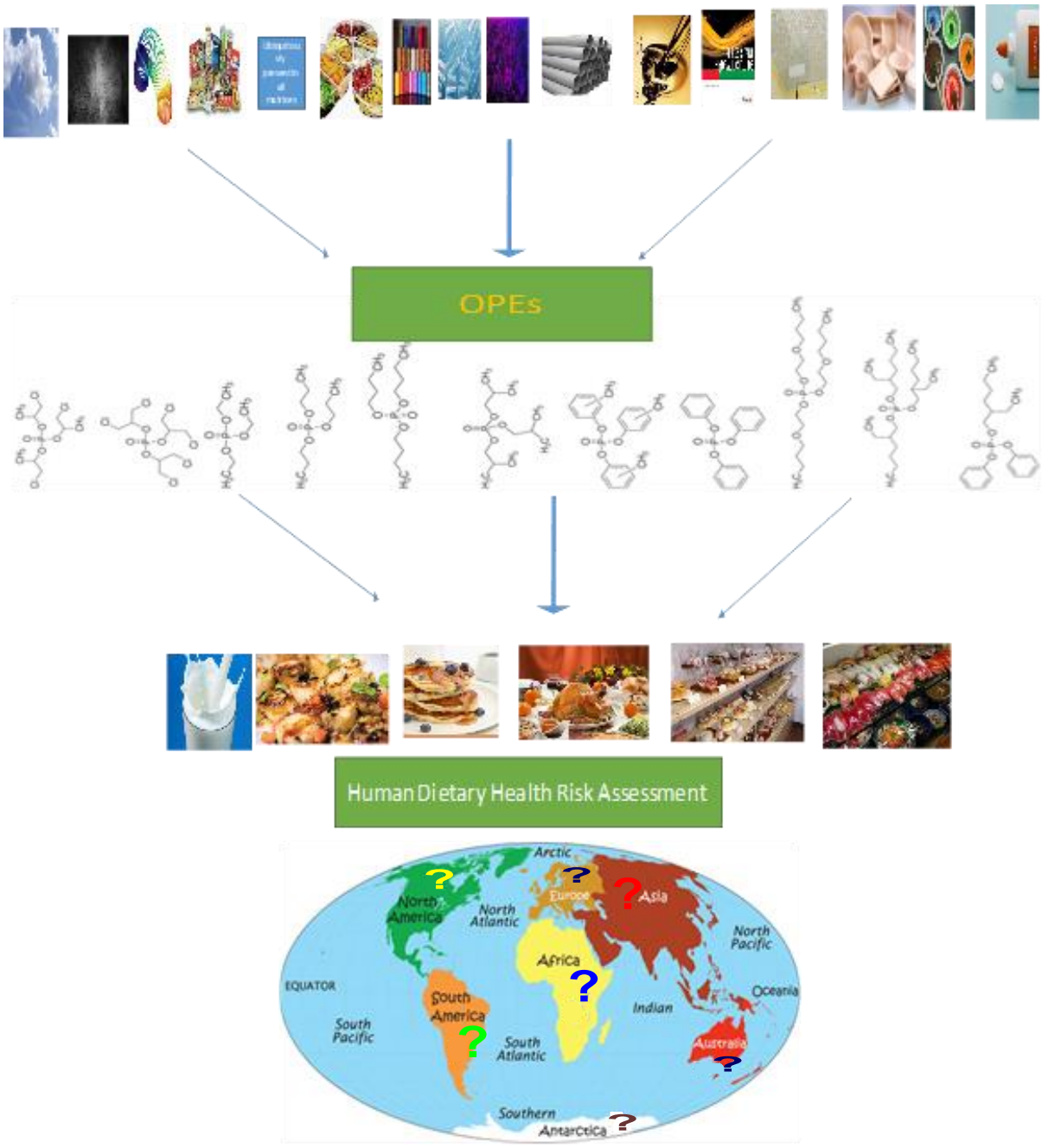
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Graphical Abstract



2.1 Abstract

Organophosphate esters (OPEs) are common additives in a wide range of commercial and industrial products. Elevated and prolonged exposure to OPEs may induce several adverse effects. This is concerning as they are ubiquitous in air, indoor dust, drinking water, and other environmental matrices. However, information on the presence of OPEs in foodstuffs and consequent health risks remains scant. This review critically evaluates available information

on levels and sources of OPEs in food, discusses the relative significance of diet as a pathway of human exposure, identifies knowledge gaps, and suggests directions for future research. For toddlers, dermal uptake from dust ingestion appears the predominant pathway of exposure to chlorinated OPEs, as well as EHDPP and TPHP. In contrast, diet was identified as the main pathway of exposure to all eight OPEs considered for adults, and for TnBP, TEHP, and TBOEP for toddlers. While summed exposures via all pathways are within published reference dose (RfD) values, they do not include high-end exposure estimates, and for highly-exposed individuals, the margin between exposure and the RfD values will be smaller. Moreover, this review's exposure estimates are based on a meta-analysis of multiple exposure assessments conducted over a range of points in space and time. There is thus an urgent need for assessments of human exposure to OPEs that examine all relevant pathways in a spatially and temporally-consistent fashion. Given our finding that food is an important exposure pathway to OPEs, regular monitoring of their presence as well as their metabolites (that may have toxicological significance) in foodstuffs is recommended. While dermal uptake from indoor dust is revealed as an important human exposure pathway, no evaluations exist of exposure via dermal uptake from OPE-containing products such as foam-filled furniture. This review also highlights very few data exist on OPEs in drinking water.

Keywords: Organophosphate esters; Foodstuffs; Indoor dust; Indoor air; Drinking water; Dermal uptake

2.2 Introduction

Organophosphate esters (OPEs) are a class of anthropogenic organic compounds found ubiquitously in many environmental media due to their release from commercial and industrial products (ATSDR, 2012). Widely used as flame retardants in furniture, textiles, building materials, electronics and other processing chemicals, they are also often used as plasticisers in floor polish and wax, coatings, engineering thermoplastics, and epoxy resins (Greaves and Letcher, 2014). In common with other chemical contaminants, human exposure to OPEs can potentially occur via inhalation, ingestion of food, water and/or dust, as well as through dermal contact with dust, soil and/or consumer products (ATSDR, 2012).

Chemically, OPEs comprise a heterogeneous class of phosphoric acid esters in which the hydrogen in the phosphate group is replaced by an alkyl, aryl, or chlorinated alkyl group (Guo et al., 2016). OPEs are usually employed as additive flame retardants (FRs) in various consumer products, i.e. they are physically added to materials rather than chemically bonded to the matrix. Further to their use as FRs there are several applications to which OPEs are added including textiles, rubber, antistatic agent, cellulose, polyurethane foam, electronic equipment, cotton, cutting oils, etc. (Veen and de Boer, 2012). OPEs such as TPHP, TBOEP are used in unsaturated polyester resins, floor wax and stabilizers for anti-foaming and as additives to floor polishes, lubricants, lacquers and hydraulic fluids. For instance, the common chlorinated OPEs (i.e., TCEP, TCIPP and TDCPP) are applied in flexible and rigid PUFs (Wei et al., 2015)

Consequently, they are susceptible to release into the environment via leaching, volatilisation, as well as abrasion (Guo et al., 2016; Pang et al., 2017). Following release into the environment, they may accumulate in indoor environments and following release from such environments ultimately be transported over long distances by air and water (Hou et al., 2016). As a result, there has been widespread detection of OPEs in air, water, soil, indoor environments, and biota, including humans (Gao et al., 2014).

Owing to their persistent, bio-accumulative, and toxic properties, several brominated flame retardants (BFRs) have been listed under the Stockholm Convention on Persistent Organic Pollutants (POPs) (Stockholm Convention on POPs, 2013). In 2018, the global consumption of FRs reached 2.6 million tonnes and is predicted to approach 3.1 million tonnes by 2023 (BCC Research, 2018). The global production and used of OPEs is increasing rapidly in recent years. It is likely therefore that the use of OPEs has increased as replacements for restricted BFRs, with OPEs increasing worldwide consumption projected to reach 860000 t in 2023 from 680,000 t in 2015 to 816000 t in 2018 (BBC Research, 2018; Wang et al., 2015a). The uses OPEs which account for 20 % of the total consumption of FRs in Western Europe increased from 58,000 tons in 1998 to 91,000 tons in 2006 (Wei et al., 2015).

Unfortunately, some OPEs, especially those that are chlorinated, are thought to be persistent in the environment (Lai et al., 2015), with human exposure demonstrated by their detection in human milk (Kim et al., 2014). Concerns about such exposure are compounded by toxicological studies revealing that high concentrations and prolonged exposure to OPEs can induce adverse effects including carcinogenicity, neurotoxicity, kidney toxicity, reproductive toxicity, liver toxicity, and endocrine disruption (Hou et al., 2016; Wei et al., 2015). The presence and concentrations of OPEs in various biotic and abiotic environmental matrices has been reviewed (Wei et al., 2015; Sugeng et al., 2017; Hou et al., 2016; Greaves and Letcher, 2017). However, information on the worldwide presence of OPEs in foodstuffs remains scant and the sources of contamination, i.e. whether the presence of OPEs in food is due to migration from food packaging, bioaccumulation, uptake from the agricultural environment, contamination during industrial processing, or some other sources, remain unclear. Currently, data on concentrations of OPEs in food is restricted to samples from China, USA, Belgium, Sweden, and Australia (Zhao et al., 2019; Zhang et al., 2016; Wang and Kannan, 2018; Poma et al., 2017; 2018; He et al., 2018a), while there exists no data from other European countries,

North America, South America, and Africa. It is on this premise that this critical review will: (a) discuss the pathways of human exposure to OPEs; (b) assess the current state-of-knowledge on OPEs in diet; and (c) evaluate the relative significance of dietary exposure compared to other human exposure pathways.

2.3 Methodology

The search for research articles, reviews, book, conference proceedings and other online resources was carried out between November 20, 2018 to October 20, 2020 using the following electronic databases: Scopus, ScienceDirect and Web of Science core collection. The search terms used were: "organophosphate esters (OPEs)", "organophosphorus flame retardants" "foodstuffs" and "human exposure" and only articles published between 2014 and 2020were selected. ScienceDirect and Scopus returned a total of 2506 and 1105 publications respectively, with a further 554 articles located on Web of Sciences core collection. Further screening based on suitability of the titles and abstracts of articles, identified 121 full-text articles from ScienceDirect, 95 full text articles from Scopus and 103 full-text articles from Web of Science core collection respectively. After duplicate studies (n=130) were removed, 189 publications were left for further screening. After full text screening, 114 articles were excluded based on factors such as article not written in English, full text not available, as well the nature of the samples analysed, the sampling methodology, statistical data presented, articles with no human exposure data and those not related to risk assessment of OPEs. This left 75 articles consisting of 66 research papers, 5 review papers and four official reports. In addition, screening of references cited in these 75 articles, identified a further 15 publications (comprising 14 research articles and one official report published before 2014). In total therefore, 90 articles were included in this review.

2.4 Physicochemical properties and pathways of human exposure to OPEs

Several key physicochemical properties essentially define the environmental behaviour and fate of OPEs; in particular, their availability for uptake by biota and routes of human exposure. As well as the ambient temperature experienced by OPE-treated materials, emissions of OPEs via volatilisation will depend on their vapour pressure and concentrations in the treated products (Carlsson et al., 1997; Ni et al., 2007). Meanwhile, the extent of OPE bioaccumulation is dependent on their octanol: water partition coefficient (K_{OW}) and the rate at which they metabolise in biota (Regnery and Püttmann, 2010). For example, halogenated OPEs were reported to be more persistent in the environment and more resistant to degradation than alkyl and aryl OPEs (Marklund et al., 2005; Bester, 2006).

The three main pathways via which humans are exposed to chemicals, are ingestion, inhalation, and dermal absorption. These broad categories may further be broken down into sub-categories such as ingestion of dust, food, and drink, as well as dermal uptake resulting from contact with dust and with products containing chemicals. The relative contribution that each pathway makes to overall exposure depends *inter alia* on the physicochemical properties and commercial applications of the chemicals, as well as lifestyle and demographic factors related to the exposed individual. Evidence to date has demonstrated that human exposure to OPEs can occur via dermal contact (Abdallah et al., 2016), ingestion of contaminated dust (Abdallah and Covaci, 2014), inhalation of air (Schreder et al., 2016), and more recently diet (Poma et al. 2018; Zhao et al., 2019) (Fig. 2.1).

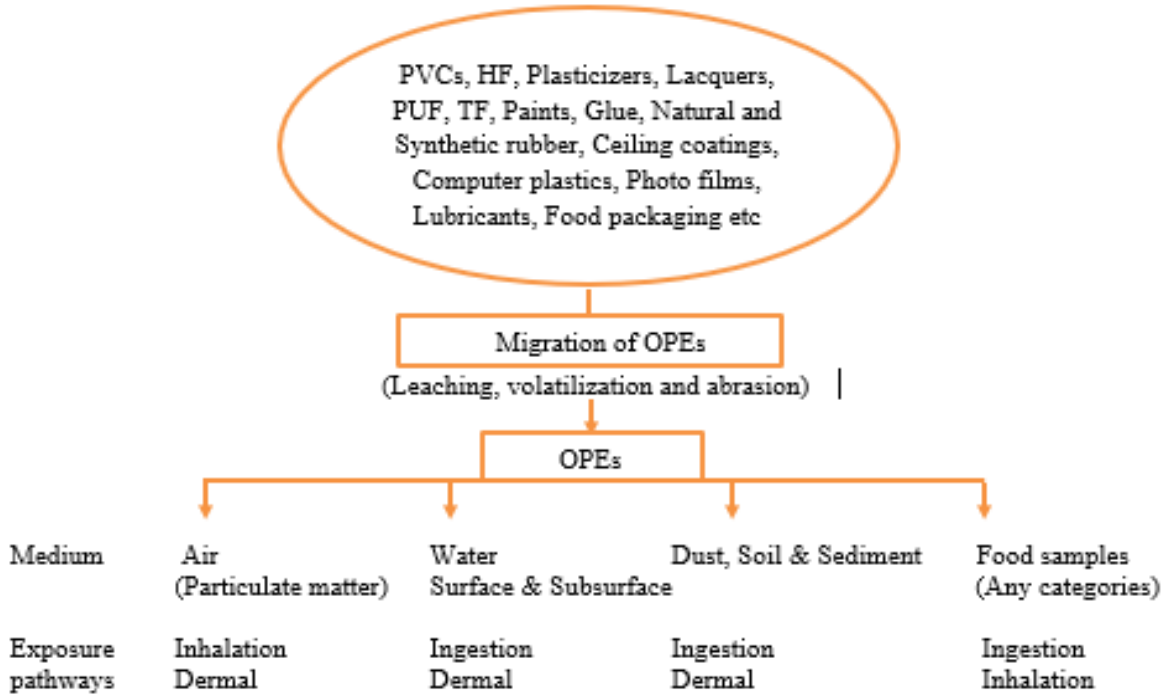


Fig. 2.1: Schematic representation of the pathways of transmission of OPEs from treated products to humans

2.4.1 Human Exposure to OPEs via Inhalation

A summary of studies reporting concentrations of OPEs in indoor air are provided as supplementary information (see appendix 2.1), with a summary of estimated daily intakes (EDIs) of OPEs through air inhalation reported in various studies presented in appendix 2.2. Schreder et al. (2016) observed that estimated exposure to OPEs via inhalation exceeded estimated exposure from dust ingestion. Adult inhalation intake of tris (2-chloroisopropyl) phosphate (TCIPP) was estimated at 4540 ng/day, which was 31 times that from dust ingestion for TCIPP in the studied population (Schreder et al., 2016). Moreover, in a study carried out examining exposure via indoor air inhalation, dust ingestion, and dermal uptake in Albany, New York, USA; Kim et al. (2019) reported TCIPP (27–43 %) and TEP (11–33 %) were the two major contributors of total human exposure via inhalation. In a similar study carried out

by Cao et al. (2019), inhalation was shown to be one of the main human exposure routes for volatile OPEs such as TiBP, TnBP, TCIPP, and TEP. Moreover, in a study of exposure occurring via air inhalation, indoor dust ingestion and dermal uptake, Zhou et al. (2017) reported that under a median exposure scenario, air inhalation contributed 5.7 ng ΣOPEs.kg $bw^{-1}.day^{-1}$ representing 73 % of total exposure for German adults. A similarly high contribution of inhalation was reported for adults in a study of living rooms of private homes in Norway by Xu et al. (2016). According to Xu et al. (2016), the estimated inhalation exposure to ΣOPEs has the highest median value among all pathways considered (median = 34 ng.kg $bw^{-1}.day^{-1}$), followed by dust ingestion (median = 13 ng.kg $bw^{-1}.day^{-1}$). Xu et al. (2016) showed that inhalation is the major exposure pathway for low molecular weight, relatively more volatile OPEs, like TCEP and TCIPP, while dust ingestion is the main route for less volatile OPEs such as TBOEP, TPHP, and TMPP. Fig. 2.2 shows the range of mean estimates of human exposure via inhalation found in the literature for four individual OPEs clearly indicating that human exposure via inhalation for children and adults follows the order TCIPP >> TCEP > TDCIPP > TPHP.

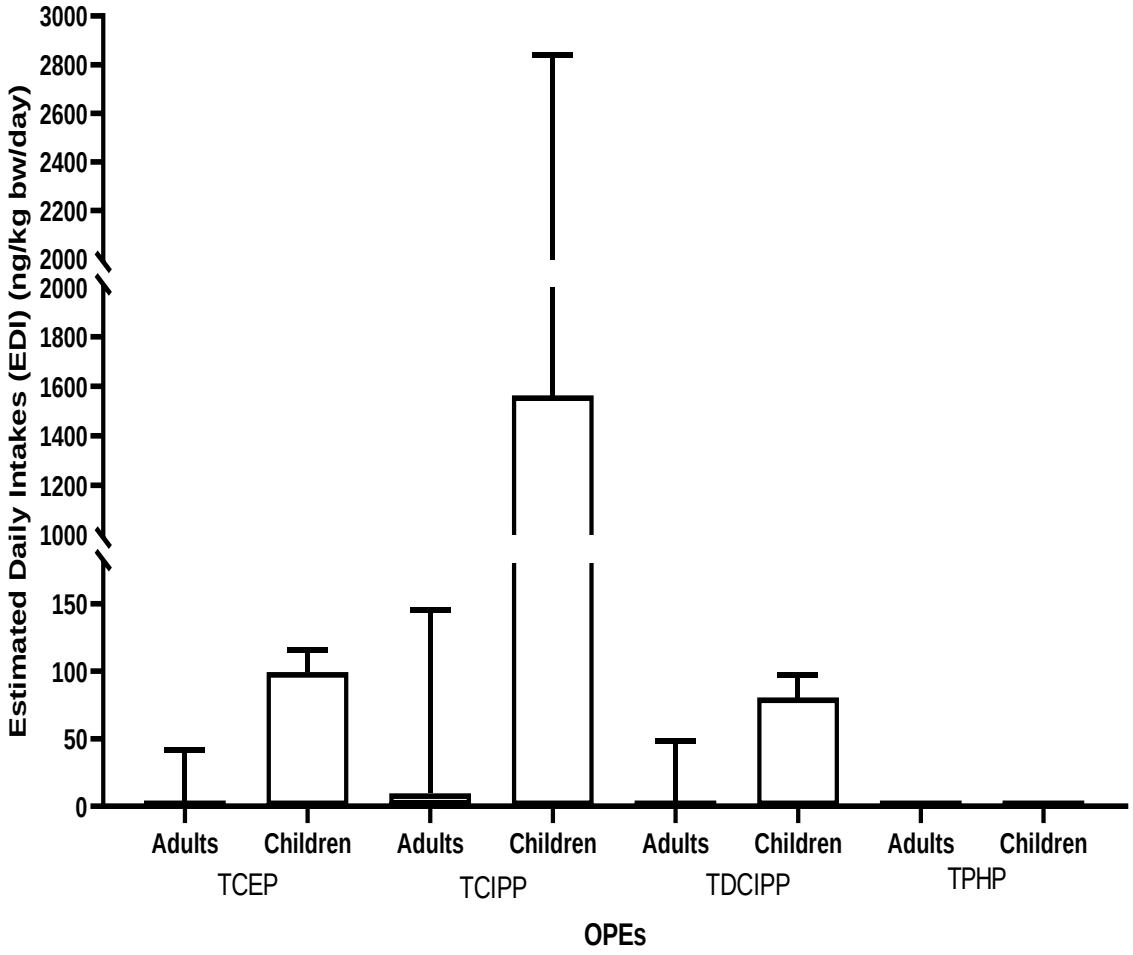


Fig. 2.2: Box-plot showing the range of mean estimates of human exposure to TCEP, TCIPP, TDCIPP, and TPHP via air inhalation.

2.4.2 Human Exposure to OPEs via Dust Ingestion

A summary of concentrations of OPEs reported in indoor dust is provided in supplementary material (see appendix 2.3), while EDIs from ingestion of indoor dust are collated in Table S5. Several studies have showed that ingestion of dust (indoor and outdoor) is an important human exposure pathway to OPEs (Brommer et al., 2012; 2015; Abdallah and Covaci et al., 2014; Stubbings et al., 2018; Cao et al., 2019; Kim et al., 2019). According to Cao et al. (2019) assuming that toddlers stay at home all the time, while adults spend only 62.5 % of their time

at home; the mean estimated daily intakes (EDIs) for toddlers and adults for Σ_{14}OPEs were 35 and 6.7 ng. kg bw^{-1}. day^{-1}, respectively. The 95th percentile EDIs for toddlers and adults were 91 and 33 ng. kg bw^{-1}. day^{-1}, respectively (Cao et al., 2019). The estimated EDIs for this study are comparable with those of 160 and 32 ng. kg bw^{-1}. day^{-1} calculated for toddlers and adults respectively in Germany (Brommer et al., 2012). Similar values were reported for toddlers and adults from New Zealand (median: 17.5 ng. kg bw^{-1}. day^{-1} and 1.2 ng. kg bw^{-1}. day^{-1}) (Ali et al., 2012), and Sweden (median: 18 ng. kg bw^{-1}. day^{-1} and 0.85 ng. kg bw^{-1}. day^{-1}) (Luongo and Ostman, 2015). These EDIs are lower than those reported in the U.S. for adults (median: 13 ng. kg bw^{-1}. day^{-1}) (Xu et al., 2016), in Japan for toddlers (median: 112 ng. kg bw^{-1}. day^{-1} and 115 ng. kg bw^{-1}. day^{-1}) based on ingestion of floor and elevated surface dust respectively (Tajima et al., 2014), and Egypt (median: 52 ng. kg bw^{-1}. day^{-1} and 13 ng. kg bw^{-1}. day^{-1}) for toddlers and adults respectively (Abdallah and Covaci, 2014). In a study carried out by He et al. (2015), the median EDIs of Σ_{12}OPEs for adults and toddlers via dust ingestion in an e-waste recycling area were 7.02 ng. kg bw^{-1}. day^{-1} and 80.2 ng. kg bw^{-1}. day^{-1}. These values were substantially higher than the EDIs for adults and toddlers in urban locations (2.06 ng. kg bw^{-1}. day^{-1} and 23.5 ng. kg bw^{-1}. day^{-1}), rural areas (2.0 ng. kg bw^{-1}. day^{-1} and 22.6 ng. kg bw^{-1}. day^{-1}) and college dormitories (3.2 ng. kg bw^{-1}. day^{-1} and 2.06 ng. kg bw^{-1}. day^{-1}) in China (He et al., 2015) (see appendix 2.4). Zhou et al. (2017) also reported that under a median dust exposure scenario, dust ingestion was the most significant exposure pathway to Σ_{10}OPEs for toddlers contributing 69 % (41 ng. kg bw^{-1}. day^{-1}) of their total exposure followed by dermal uptake which contributes 27 % (16 ng. kg bw^{-1}. day^{-1}), and air inhalation 4 % (2.4 ng. kg bw^{-1}. day^{-1}) (see appendix 2.4). Figure 2.3 summarises visually the range of reported mean estimates of human exposure via dust ingestion for four major OPEs for adults and toddlers. These results show that – normalised to body weight - toddlers are more highly exposed to these four OPEs than adults.

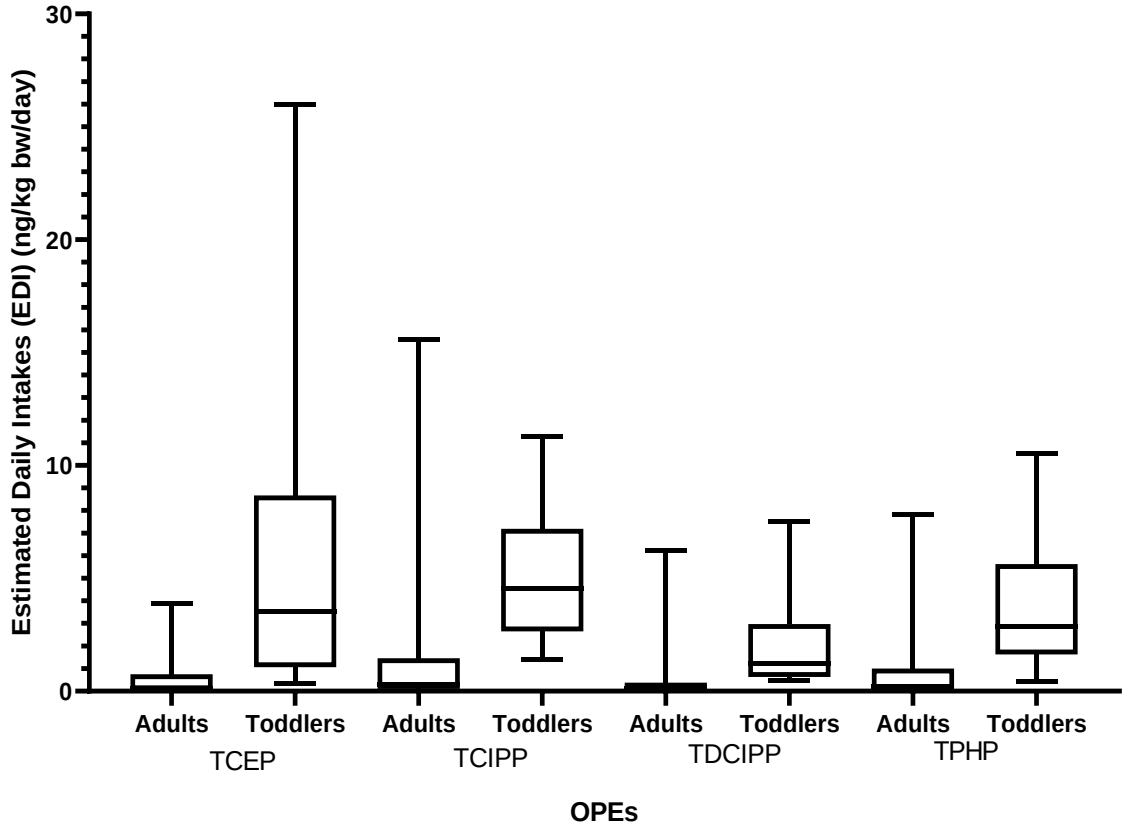


Fig. 2.3: Box plot showing the range of mean reported estimates of human exposure via dust ingestion to TCEP, TCIPP, TDCIPP, and TPHP

2.4.3 Human dermal uptake of OPEs

Recently, a few studies have raised concerns about dermal absorption as a potentially significant pathway of exposure to OPEs (Abdallah et al., 2016; Mendelsohn et al., 2016; Liu et al., 2017a, b; Bello et al., 2018; Frederiksen et al., 2018). Data in appendix 2.5 summarises estimates of dermal exposure to OPEs published to date. Hoffman et al. (2015) found a significant positive association between levels of TDCIPP and TPHP on hand wipes and the concentrations of their metabolites in urine, suggesting that hand-to-mouth contact and/or dermal absorption may be important exposure pathways to OPEs. More recently, a study examining the exposure to TPHP through nail polish application, suggested the primary

exposure route of TPHP is dermal absorption (Mendelsohn et al., 2016). Similarly, in a study carried out by Bello et al. (2018), high levels of urinary biomarkers of TCIPP were detected in spray polyurethane foam applicators post-shift, indicating dermal absorption as an important exposure pathway to TCIPP to such individuals.

In addition, *in vitro* skin absorption studies (Abdallah et al., 2016; Hughes et al., 2001) reveal that a relatively high percentage of TCEP, TCIPP, and TDCIPP can be absorbed by human or mouse skin. Assessments of dermal exposure to OPEs are however, limited. Two studies reported OPE intakes via dermal absorption from contact with indoor dust (Cequier et al., 2014; Abdallah et al., 2016). Abdallah et al. (2016) investigated human dermal uptake of Σ_3OPEs using human *ex vivo* and cultured EPISKIN^{TM} 3-D human skin equivalent (3D-HSE) models. They reported that the median EDIs via dermal absorption of Σ_3OPEs (TCEP, TCIPP, and TDCIPP) for toddlers and adults via indoor dust ingestion were 36 ng.kg bw^{-1}. day^{-1} and 4.1 ng. kg bw^{-1}. day^{-1} which were lower than the reported values of 108 ng.kg bw^{-1}. day^{-1} and 23 ng. kg bw^{-1}. day^{-1} (Σ_8OPEs) for school children and women by Cequier et al. (2014). Abdallah et al. (2016) also investigated the impact of hand-washing on reducing dermal exposure to OPEs. They found that depending on the physicochemical properties of the OPEs, hand-washing reduces the overall human dermal uptake of the OPEs (Abdallah et al., 2016). The same authors noted that as well as from adhered indoor dust, OPEs on the skin surface might also arise from dermal contact with flame-retarded consumer products (i.e. fabrics, mobile phones), which may constitute a more significant exposure route due to high concentrations of OPEs in these products (Abdallah et al, 2016, 2018). In summary, the evidence to date suggests that human exposure to selected individual OPEs via dermal absorption occurs in this order: TPHP >> TCIPP > TDCIPP > TCEP (Fig. 2.4). This contrasts with the situation for air

inhalation for which such exposure was greater for the chlorinated OPEs. Figure 4 also shows that toddlers are much more exposed than adults.

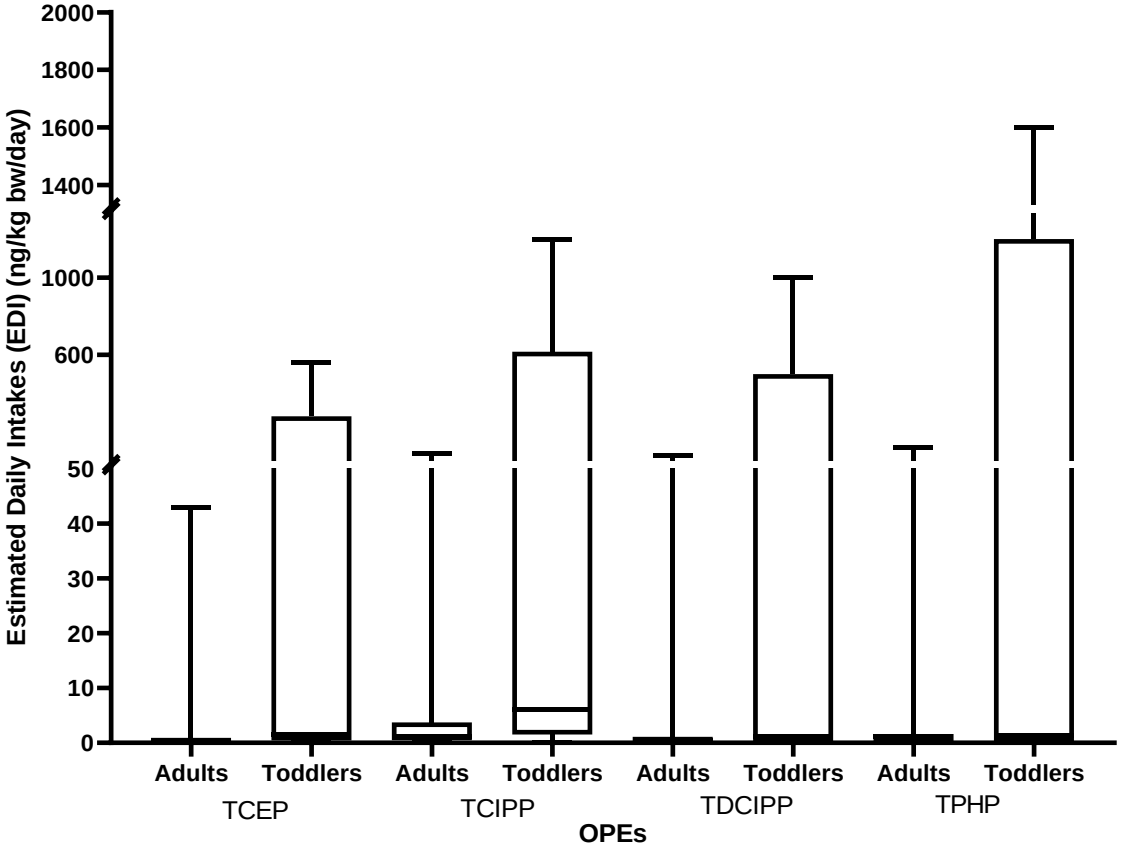


Fig. 2.4: Box plot showing the range of reported mean estimates of human exposure to TCEP, TCIPP, TDCIPP, and TPHP via dermal absorption from indoor dust.

2.4.4 Human Exposure to OPEs via drinking water

To date, several studies have reported concentrations of OPEs in drinking water (Liu et al., 2019; Benotti et al., 2009; Rodil et al., 2012; Li et al., 2014; Ding et al., 2015; Lee et al., 2016; Kim and Kannan, 2018; Park et al., 2018). Reported concentrations of individual OPEs are shown in appendix 2.6. Concentrations of Σ_{14}OPEs range in the USA between 3.02 and 366 ng/L for tap water (Kim and Kannan, 2018), and 8-720 ng/L for source and finished water

(Benotti et al., 2009). In China, concentrations in municipal water from Nanjing ranged between 3.6-180 ng/L (Liu et al., 2019), while in Hangzhou they fall in the range 123-338 ng/L in tap water, 0.9-11.2 ng/L in bottled water, and 17.2-126 ng/L in filtered drinking water (Ding et al., 2015). Elsewhere, concentrations in surface and tap water from Spain range between 40-140 ng/L (Rodil et al., 2012) (see appendix 2.6).

The level of human exposure to OPEs received via drinking water has been evaluated in only a small number of studies (Kim and Kannan, 2018; He et al., 2019; Lee et al., 2016; Liu et al., 2019; Ding et al., 2015). According to He et al. (2019), who assumed water ingestion rates of (0.322 L/day, 0.502 L/day and 1.0445 L/day) for toddlers, older children, and adults in Chongqing, China; the mean EDIs for the same age groups for Σ_{11}OPEs were 1.02, 0.684 and 0.939 ng. kg $bw^{-1}.day^{-1}$, respectively. The value obtained for toddlers exceeded the 0.22 ng. kg $bw^{-1}.day^{-1}$ obtained for Σ_{14}OPEs under a typical drinking water exposure scenario in the USA (Kim and Kannan, 2018). For Σ_{14}OPEs under a high exposure scenario, Kim and Kannan (2018) obtained an EDI value that ranged between 1.17 ng.kg $bw^{-1}.day^{-1}$ and 9.65 ng. kg $bw^{-1}.day^{-1}$ depending on the age group considered. In Korea, Lee et al. (2016) found that the median EDI values via drinking water for Σ_{10}OPEs for toddlers, children, teenagers and adults were: 2.55 ng. kg $bw^{-1}.day^{-1}$, 2.10 ng. kg $bw^{-1}.day^{-1}$, 1.27 ng. kg $bw^{-1}.day^{-1}$, and 1.81 ng. kg $bw^{-1}.day^{-1}$ respectively. These values were about 12 times higher than those obtained in the USA by Kim and Kannan (2018).

Kim and Kannan (2018) observed that TCIPP and TBOEP combined contributed > 50% of the total EDI via water ingestion among the Σ_{14}OPEs evaluated. They also reported that indirect water ingestion during swimming can contribute to a total OPE exposure of up to 15.8 ng/swimming event for children and 9.28 ng/swimming event for adults. In Hangzhou and Quzhou, Eastern China, Ding et al. (2015) found that at 7.07 ng.kg $bw^{-1}.day^{-1}$ and 6.95 ng. kg

$bw^{-1}.day^{-1}$ for adults and children, the mean EDIs for Σ_9OPEs via tap water, exceeded those via filtered water (2.22 ng. kg $bw^{-1}.day^{-1}$ and 2.19 ng. kg $bw^{-1}.day^{-1}$), well water (0.17 ng. kg $bw^{-1}.day^{-1}$ and 0.16 ng. kg $bw^{-1}.day^{-1}$) and barrelled water (1.06 ng. kg $bw^{-1}.day^{-1}$ and 1.05 ng. kg $bw^{-1}.day^{-1}$) respectively. In Nanjing, China, Liu et al. (2019) found median EDIs for Σ_5OPEs for male and female adults were in the range 4.2-7.1 ng. kg $bw^{-1}.day^{-1}$ and 3.6-6.1 ng. kg $bw^{-1}.day^{-1}$ respectively. Liu et al. (2019) also observed that for individual OPEs, TEP, TCEP, and TCPP made the biggest contributions to human exposure via water ingestion. Under a high exposure scenario, assuming ingestion of water contaminated at the 95th percentile concentration, Liu et al. (2019) found the EDI value for ΣOPEs to vary between 45.2-64.8 ng.kg $bw^{-1}.day^{-1}$ and 38.9-55.7 ng.kg $bw^{-1}.day^{-1}$ for male and female adults. These values exceed substantially estimates of high ΣOPE exposure scenarios (95th percentile) via ingestion of tap water in Korea (8.23-16.5 ng.kg $bw^{-1}.day^{-1}$) (Lee et al. 2016) and in Eastern China at high exposure scenario (median) (6.8-11.56 ng.kg $bw^{-1}.day^{-1}$) (Ding et al. 2015). Data in appendix 2.7 summarises human exposure data via water ingestion, while Figure 5 illustrates the range of mean estimates of the exposure of adults and children to TCEP, TCIPP, and TBOEP via water ingestion. This clearly shows that children are more exposed to these OPEs via water ingestion than adults.

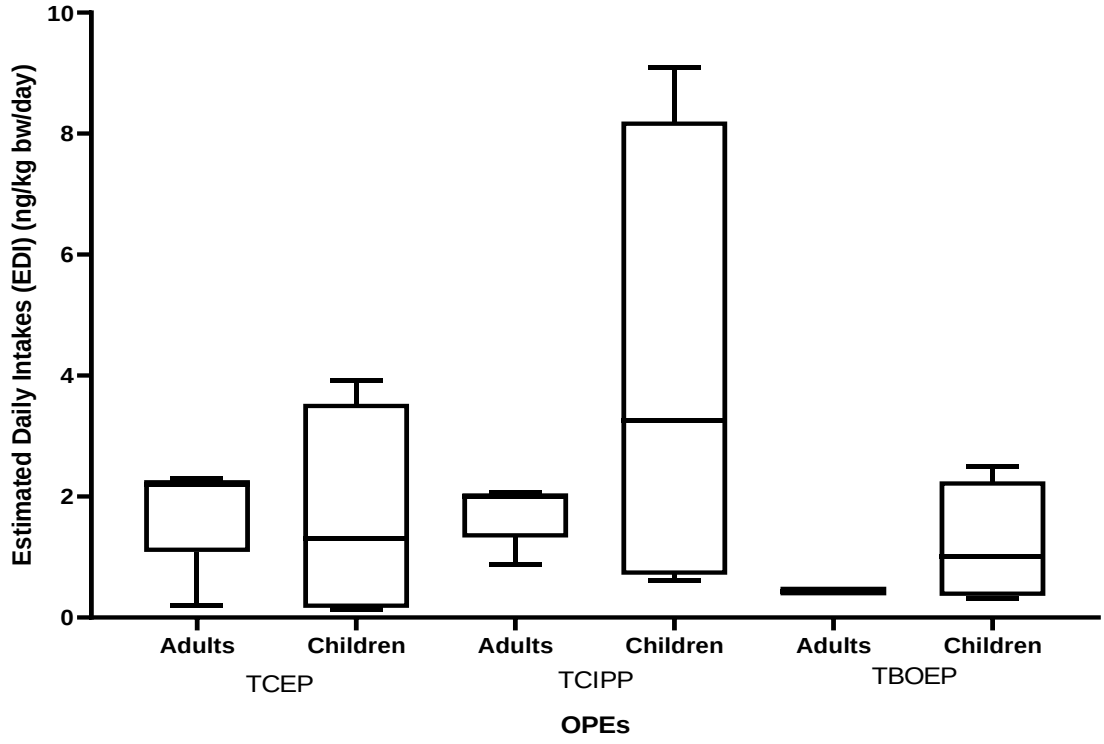


Fig. 2.5: Box-plot showing the range of mean estimates of human exposure to TCEP, TCIPP, and TBOEP via water ingestion

2.4.5 Infant Exposure to OPEs via breast milk

There is growing concern over the presence of OPEs in human milk, which serves as the main source of nutrition for breast-fed infants (Beser et al, 2019). A small number of studies have reported concentrations of several OPEs in human breast milk. In a study carried out by He et al. (2018b) in South East Queensland, Australia; TCEP, TBP, and TEHP were measured in human milk at concentration ranges of <0.13–0.47, 0.26–2.1, and 1.2–6.2 ng/mL, respectively. Similarly, Ma et al. (2019) reported concentrations of $\sum_{12}$OPEs ranging from 0.67 to 7.8 ng/mL with a mean value of 3.6±1.4 ng/mL (see appendix 2.8). This was consistent with the average concentration of Σ_{11}OPEs (3.4 ng/g) reported by Sundkvist et al. (2010) in pooled human milk samples from Sweden.

Concentrations of OPEs in human milk vary with several factors including mother's age and diet (Kim et al., 2014). Assuming a daily intake of 450 mL breast milk for infants 0–1 year old, He et al. (2018b) found that breastfeeding would result in average estimated daily intakes (EDIs) of 4.6, 26 and 76 ng.kg $bw^{-1}.day^{-1}$ for TCEP, TBP, and TEHP respectively. According to Ma et al. (2019), the respective mean and the high-end EDIs of ΣOPEs via human milk were 542 and 911 ng.kg $bw^{-1}.day^{-1}$ for infants less than 1 month of age; 505 and 850 ng.kg $bw^{-1}.day^{-1}$ for infants from 1 to 3 months of age; 397 and 668 ng.kg $bw^{-1}.day^{-1}$ for infants from >3 to 6 months of age; and 300 and 504 ng.kg $bw^{-1}.day^{-1}$ for infants from >6 to 12 months of age (see appendix 2.9). The decreasing EDI with increasing infant age was attributed to increasing body weight and decreasing milk ingestion level with age. Data in appendix 2.9 shows the reported data on infant exposure to individual OPEs via human milk. Analysis of these data show nursing infant exposures to individual OPEs fall in the order: TDCIPP > TCEP > > TPHP > TCIPP (Fig. 2.6).

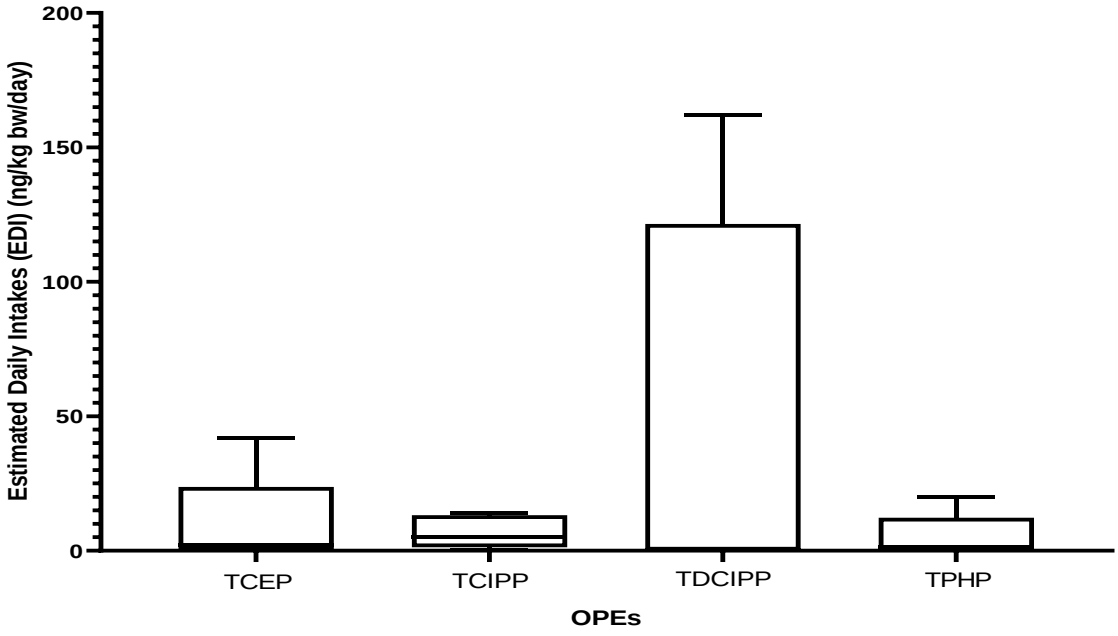


Fig. 2.6: Box-plot showing the range of mean estimates of breast-fed infant exposure to TCEP, TCIPP, TDCIPP, and TPHP via ingestion of human milk

2.4.6 Human Dietary Intake of OPEs

OPEs enter the human diet primarily via two routes. First, via bioaccumulation into plants and animals from contaminated air, soil, water, animal diet etc. 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 as well as in food contact and packaging materials (Campone et al., 2010; Ding et al., 2018; Poma et al., 2018; Wang and Kannan, 2018). Moreover, cooking processes may reduce the levels of OPE contamination in food (Ding et al., 2018; Zhao et al., 2019). Data in appendix 2.10 summarises the concentrations of OPEs detected in foodstuffs to date.

In surveys of fish worldwide, concentrations of ΣOPEs have been reported to be as high as 15,000 ng g^{-1} (lipid weight - lw) (Sundkvist et al., 2010) (Table S11). Rice was reported as a significant source of exposure to OPEs in China (Zhang et al., 2016). In the study of Poma et al. (2018), fish-oil food supplements were the most contaminated food samples with a total mean ΣOPE concentration of 225 ng.g^{-1} (wet weight – ww), followed by grain, cheese, and other food (meat and chicken stocks) with concentrations of 36.9, 20.1, and 18.8 ng.g^{-1} ww respectively (see appendix 2.10). These observed values exceeded those detected in duplicate diet samples by Xu et al. (2017) who found the sum of the average concentrations of four OPEs (EHDPP, TCEP, TPHP, and TCIPP) to be 7.7 ng.g^{-1} ww (Xu et al., 2017). In the Philippines, Kim et al., (2011) reported concentrations of the sum of nine OPEs (including TCEP, TCIPP, and TDCIPP) in fish from Manila Bay to range between 110 to 1900 ng.g^{-1} lw.

Data in appendix 2.11 summarises reported human dietary intakes of OPEs from several studies from different countries. According to Malarvannan et al. (2015), mean dietary intakes of TCIPP, TPHP, EHDPP, TBOEP, TDCIPP, and TCEP through eel consumption were: 0.10, 0.034, 0.028, 0.017, 0.012, and 0.10 ng.kg bw^{-1}.day^{-1} respectively; while high-end intake

estimates were: 2.5, 0.84, 0.74, 0.43, 0.29, and 0.25 ng.kg $bw^{-1}.day^{-1}$, respectively (see appendix 2.11).

Looking beyond exposure via consumption of specific foodstuffs and considering overall dietary exposure, estimated dietary exposures to ΣOPEs at different locations vary, including between the United States (adults: 25.1 ng.kg $bw^{-1}.day^{-1}$, children: 56.6 ng.kg $bw^{-1}.day^{-1}$) (Wang and Kannan, 2018), China (adults: 55 ng.kg $bw^{-1}.day^{-1}$, children: 98 ng.kg $bw^{-1}.day^{-1}$) (Ding et al., 2018), (male adults: 539 ng.kg $bw^{-1}.day^{-1}$, female adults: 600 ng.kg $bw^{-1}.day^{-1}$) (Zhang et al., 2016), (Chinese adults: 44.3 ng.kg $bw^{-1}.day^{-1}$) (Zhao et al., 2019), Sweden (adults: 85 ng.kg $bw^{-1}.day^{-1}$) (Poma et al., 2017), and Belgium (adults: 103 ng.kg $bw^{-1}.day^{-1}$) (Poma et al., 2018) (see appendix 2.11). EDI values for toddlers, children, and teenagers exceed those for adults.

Fig. 2.7 depicts the range of estimates of dietary exposure of adults and children to four selected individual OPEs, showing clearly that children's exposure via diet occurs in the order: TCIPP > > TPHP >TCEP > TDCIPP (Fig. 2.7). In contrast, adult dietary exposure is of a broadly similar level for TCIPP, TDCIPP, and TPHP, but slightly lower for TCEP. Importantly, while this figure suggests that the average dietary exposure data obtained from ten studies for adults exceeded those for children; only two studies evaluated the EDI for children and in both these studies (Wang and Kannan, 2018; Ding et al., 2018), the EDIs for children were higher than those for adults measured in the same study.

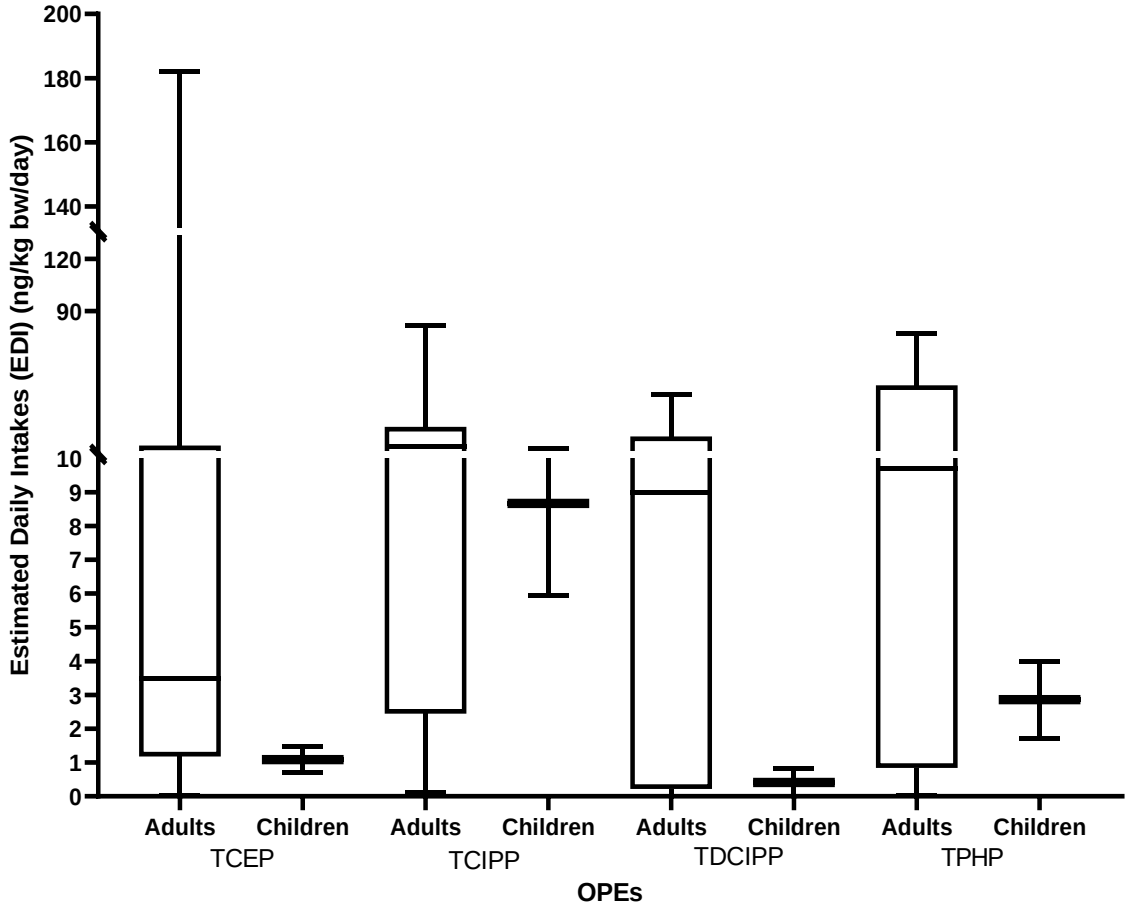


Fig. 2.7: Box-plot showing the range of mean estimates of dietary exposure to TCEP, TCIPP, TDCIPP, and TPHP

2.5. Relative Significance of Different Exposure Pathways to OPEs

As highlighted above, measurable exposure to OPEs occurs through ingestion of contaminated house dust and food, inhalation of contaminated air, and dermal absorption. While Ji et al. (2014) argued that exposure via contact with dust, air and water should not be underestimated or ignored and that indoor air and water may be more important than diet as pathways of human exposure to OPEs; some recent studies have highlighted the importance of diet as a pathway of human exposure to OPEs (Zhang et al., 2016; Poma et al., 2017; Ding et al., 2018; Wang and Kannan, 2018).

This section examines the significance of food ingestion in the context of its contribution to total human exposure to the following OPEs based on available literature data: TCEP, TCIPP, TDCIPP, TPHP, TnBP, TBOEP, TEHP, and EHDPP. The average of the reported mean human exposure estimates for each of these eight OPEs via dust, water, human milk and food ingestion, air inhalation, and dermal absorption, were used to evaluate the relative significance of each exposure pathway for both toddlers and adults. These average EDI values for each exposure pathway considered for adults and toddlers are listed in Table 2.1 and their relative contributions to overall exposure to each individual OPE illustrated in Figure 2.8 for toddlers and Figure 2.9 for adults.

Table 2.1: Obtained mean estimated daily intake (EDI) values for adults and toddlers for all exposure pathways

		Mean EDI values (ng.kg bw^{-1}.day^{-1})							
Exposure pathway	**Age group**	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**TnBP**	**TBOEP**	**TEHP**	**EHDPP**
Air inhalation	Adults	3.63	16.9	4.20	0.124	1.57	9.66	0.354	0.0996
	Toddlers	0.37	1.80	0.06	0.090	1.17	0.0164	0.040	0.214
Dust ingestion	Adults	2.36	9.37	2.83	0.980	0.090	2.36	0.521	0.315
	Toddlers	4.04	4.49	1.77	3.11	0.694	21.0	1.52	2.17
Dermal uptake	Adults	4.53	10.2	9.63	17.8	0.110	3.20	0.319	7.84
	Toddlers	103	208	221	401	0.420	2.03	0.280	227
Food ingestion	Adults	32.2	21.3	11.9	27.0	4.31	12.7	47.2	12.8
	Toddlers	3.61	12.4	2.91	3.65	12.0	46.8	7.23	0.940
Water ingestion	Adults	1.52	1.49	0.151	-	0.850	0.202	-	-
	Toddlers	0.239	0.618	0.0164	-	0.293	0.220	-	-
Human milk ingestion	Infants	4.40	65.3	4.00	14.5	57.2	152	38.9	5.13
Total EDI (∑exposure pathways)	Adults	44.2	59.3	28.7	45.9	6.93	28.1	48.4	21.1
	Toddlers	111	227	226	408	14.6	70.1	9.07	230

Total Carcinogenic risk (TCR)	Adults Toddlers	9.72x10^{-7} 2.44x10^{-6}	- -	- -	- -	6.24x10^{-8} 1.31x10^{-7}	- -	1.55x10^{-7} 2.90x10^{-8}	- -
RfD values (ng.kg bw^{-1}.day^{-1})	-	7000 [a]	10000 [a]	20000 [a]	-	10000 [a]	-	100000 [a]	-
SFO ((ng/kg bw/day)$^{-1}$)	-	2x10^{-8} [b]	-	-	-	9x10^{-9} [b]	-	3.2x10^{-9} [b]	-

[a] Reference dose (RfD) values were calculated by USEPA (2017).
[b] Oral cancer slope factor (SFO) values were obtained from (USEPA, 2017; Li et al., 2018)

This data analysis shows that for toddlers, dermal uptake of OPEs from indoor dust was the major exposure pathway for all the chlorinated OPEs i.e. TCEP (103 ng.kg bw^{-1}.day^{-1}, 93 %), TCIPP (208 ng.kg bw^{-1}.day^{-1}, 92 % Σexposure), and TDCIPP (221 ng.kg bw^{-1}.day^{-1}, 98 %); as well as for aryl OPEs such as TPHP (401 ng.kg bw^{-1}.day^{-1}, 98%) and EHDPP (227 ng.kg bw^{-1}.day^{-1}, 98 %). It should be noted here that this high contribution of dermal uptake from indoor dust for these OPEs is driven very substantially by the mean exposure estimates via this pathway reported in a single study of childcare centres in the USA (Stubbings et al, 2018). This illustrates that the estimates provided here are averages across a number of different studies conducted at different points in time and space.

Consequently, the contributions made by different exposure pathways will vary considerably between individuals depending on lifestyle factors. In contrast, the diet (excluding human milk ingestion) was found to be the principal pathway of exposure for toddlers to alkyl OPEs such as TnBP (12 ng.kg bw^{-1}.day^{-1}, 84 %), TBOEP (47 ng.kg bw^{-1}.day^{-1}, 67 %), and TEHP (7.2 ng.kg bw^{-1}.day^{-1}, 80 %) followed by dust ingestion and air inhalation, with dermal uptake least important (Fig. 2.8).

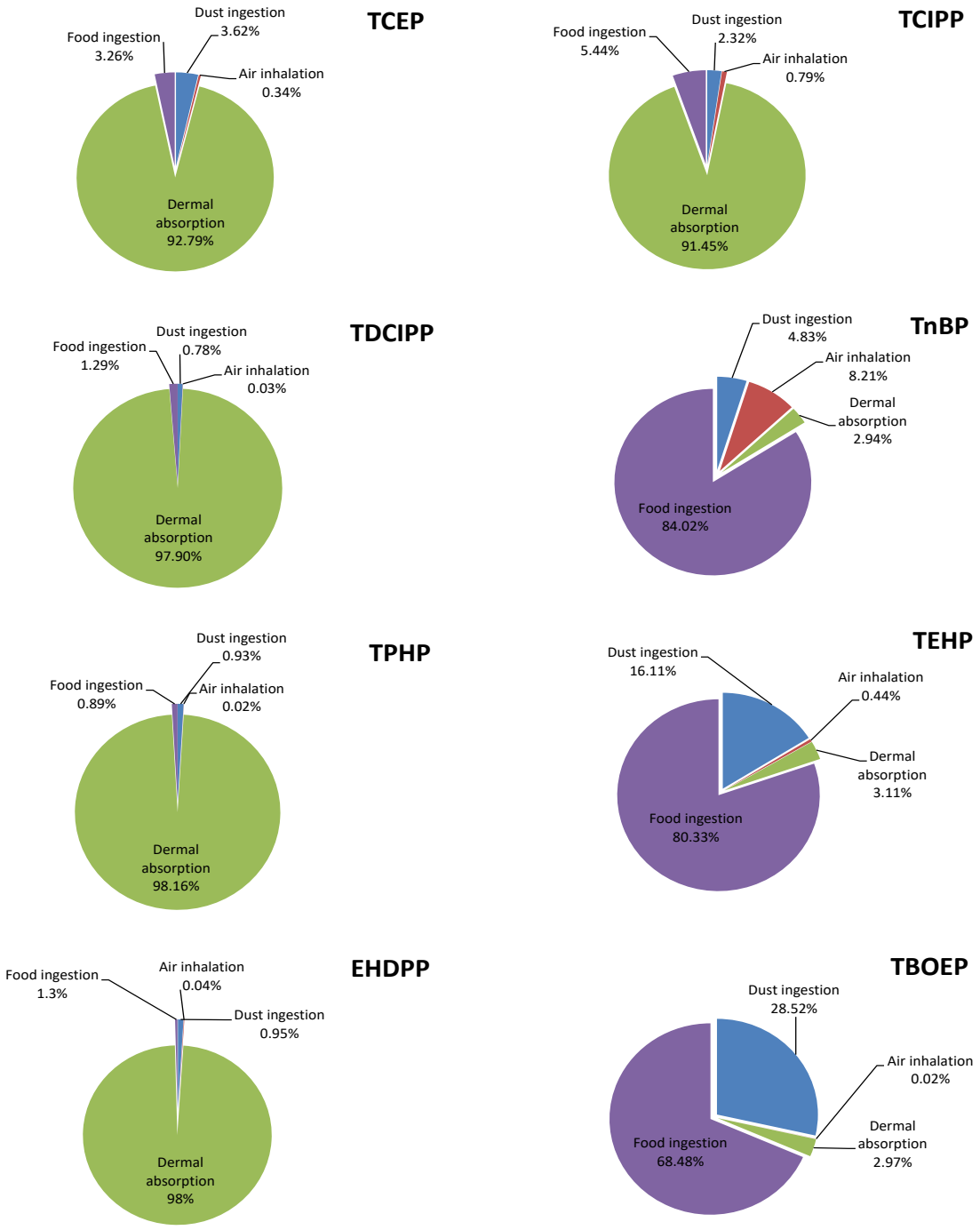


Fig. 2.8: Relative significance of exposure of toddlers via air inhalation, dermal uptake, diet, and dust ingestion for individual OPEs

For adults, food ingestion appears the main human exposure pathway for all eight OPEs evaluated, contributing 32.2 ng.kg bw^{-1}. day^{-1} and 75% Σexposure for TCEP, 21.3 ng.kg bw^{-1}.

day^{-1}, 37% for TCIPP, 11.9 ng.kg bw^{-1}. day^{-1}, 42 % for TDCIPP, 4.31 ng.kg bw^{-1}. day^{-1}, 71% for TnBP, 27.0 ng.kg bw^{-1}. day^{-1}, 59 % for TPHP, 47.2 ng.kg bw^{-1}. day^{-1}, 97% for TEHP, 12.8 ng.kg bw^{-1}. day^{-1}, 61% for EHDPP, and 12.7 ng.kg bw^{-1}.day^{-1}, 46 % for TBOEP (Fig. 2.9).

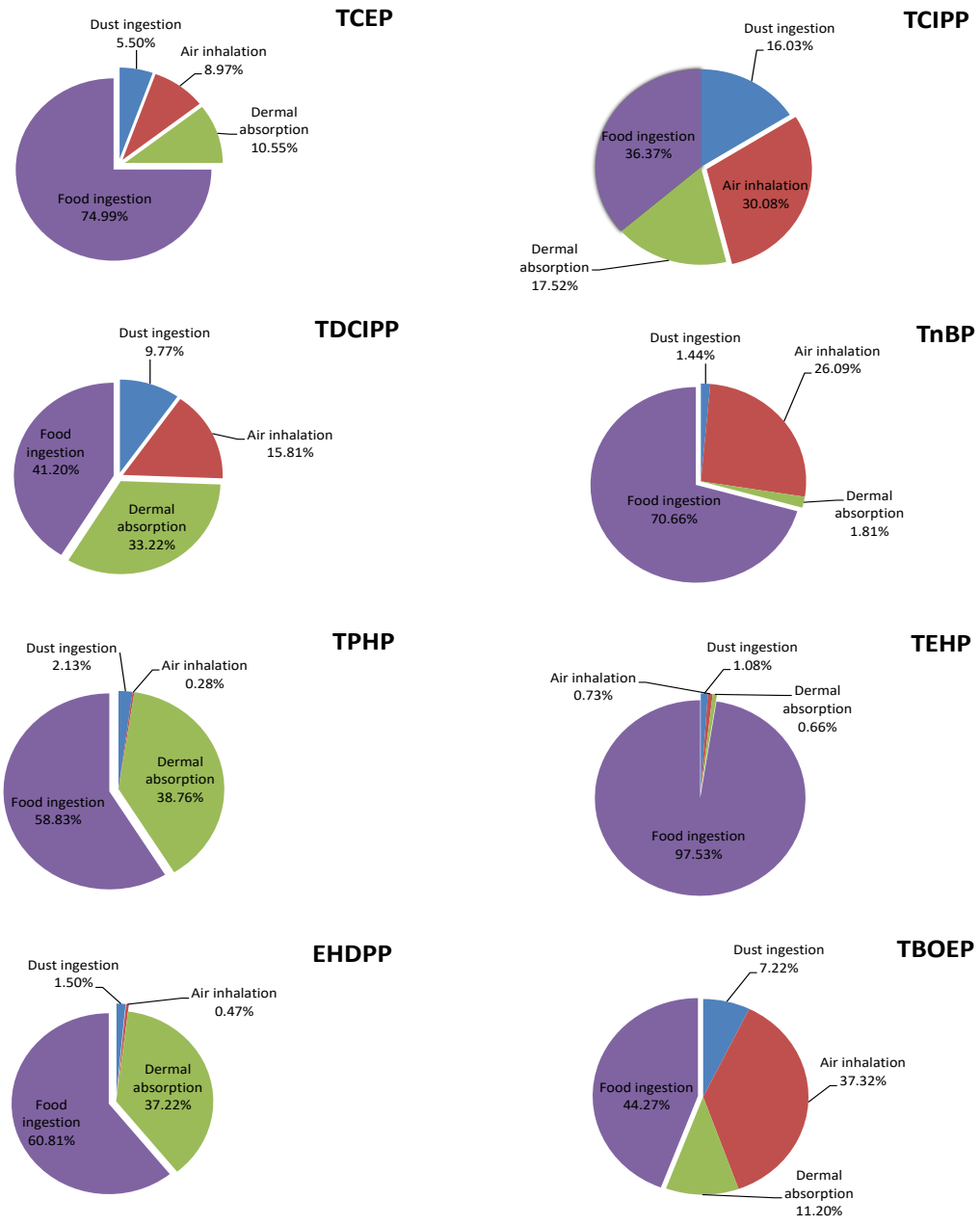


Fig. 2.9: Relative significance of exposure of adults via air inhalation, dermal uptake, diet, and dust ingestion for individual OPEs

For water ingestion, only five OPEs (TCEP, TCIPP, TDCIPP, TnBP, and TBOEP) have been evaluated in any depth. For adults and toddlers, the mean EDIs of these five OPEs are in the

order: TCEP > TCIPP > TnBP > TBOEP > TDCIPP and TCIPP > TnBP > TCEP > TBOEP > TDCIPP respectively (see appendix 2.12). This shows that the chlorinated OPEs are the main OPEs both adults and toddlers are exposed to via water ingestion. In addition, data on infant exposure to OPEs via human milk ingestion as shown in (appendix 2.12), reveals that TBOEP, TCIPP, TnBP and TEHP are the main OPEs infants are exposed to through breast feeding.

The EDI (ng.kg $bw^{-1}.day^{-1}$) values of OPEs were either compared with the oral reference dose (RfD ng.kg $bw^{-1}.day^{-1}$) which is an indicator of risk assessment of human exposure to non-carcinogenic toxic substances proposed by the U.S. EPA (2014). Based on the availability of laboratory animal exposure data from several organ/system specific RfD, USEPA (2017) derived a revised RfDs value for each OPEs was derived through calculation by dividing the human equivalent dose (HED) by uncertainty factor (UF). This HED is obtained by multiply the no observed adverse effect level (NOAEL) by dosimetric adjustment factor (DAF) (Li et al., 2018, USEPA, 2017) (Table 2.1).

The sum of the average EDIs via all exposure pathways for toddlers and adults for the eight OPEs evaluated were used to evaluate the risk of such overall exposure via comparison with the corresponding reference dose (RfD) values (Fig. 2.10 and Fig. 2.11). This comparison indicated that EDI values of the sum of all exposure pathways for each OPE determined for toddlers and adults were lower than the established reference dose values by (USEPA, 2017; Li et al., 2018).

The carcinogenic effects from chronic daily exposure to the OPEs in the foodstuffs for adults and toddlers using the oral cancer slope factor (SFO) of OPEs adopted from (USEPA, 2017; Li et al., 2018). The carcinogenic risk of OPEs were obtained by multiply the estimated daily intake (EDI) with the oral cancer slope factor (SFO). Currently, only the SFO for TCEP, TnBP and TEHP were available (USEPA, 2017; Li et al., 2018). The value obtained in this review for the total carcinogenic risk (TCR) through all pathways for adults for three OPEs TCEP,

TnBP and TEHP were below the acceptable risk value of ($1x10^{-6}$) (Ding et al., 2015), while for TCEP, the TCR ($2.44x10^{-6}$) obtained for toddlers were higher than the acceptable risk value (Table 2.1). This shows that there is a high carcinogenic risk from TCEP to toddler through all the exposure pathways considered in this review.

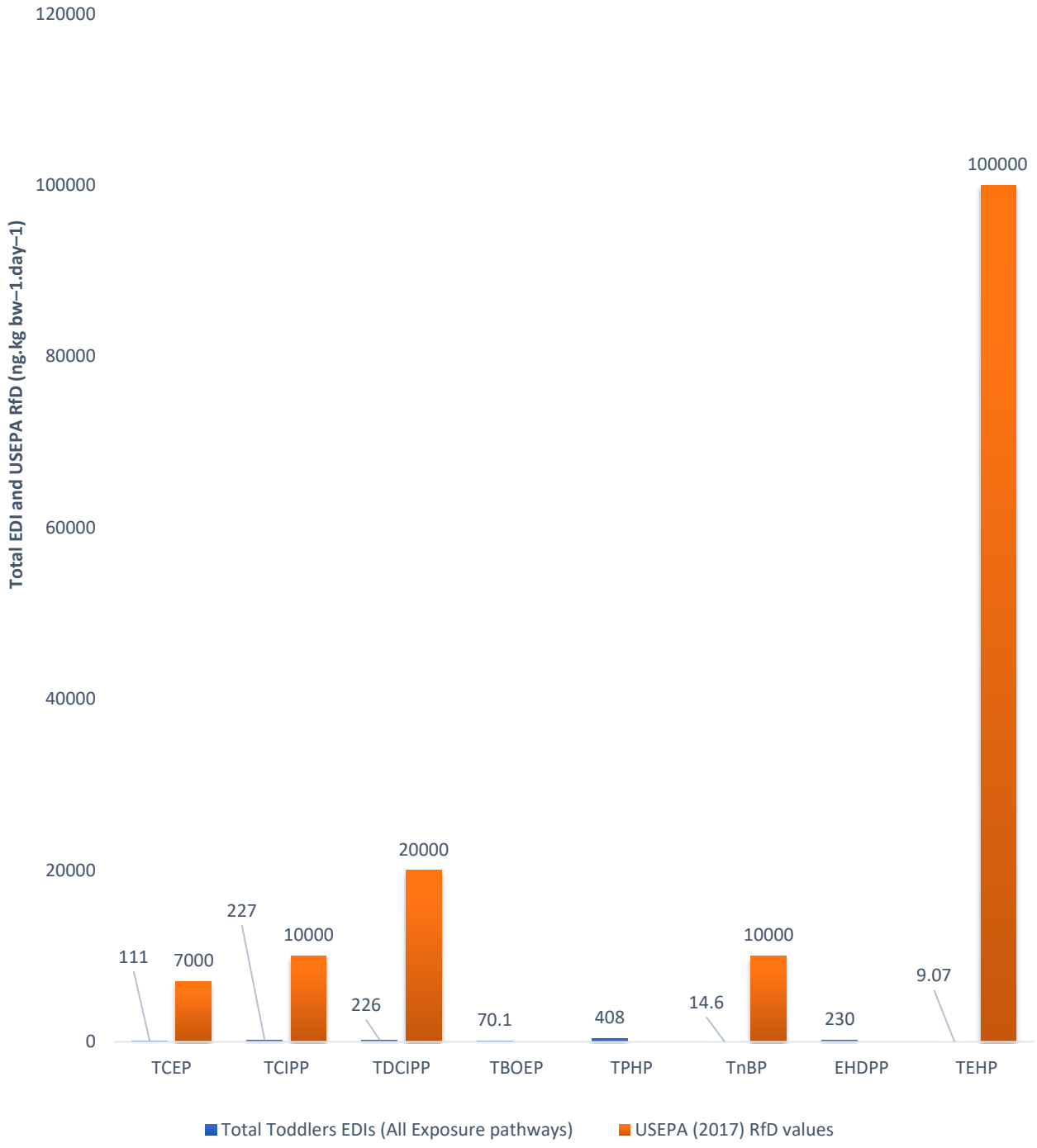


Fig. 2.10: Comparison of average estimated daily intake (EDI) values via all exposure pathways for selected OPEs for toddlers with the corresponding reference doses (RfDs ng.kg bw^{-1}.day^{-1}) adopted from USEPA (2017)

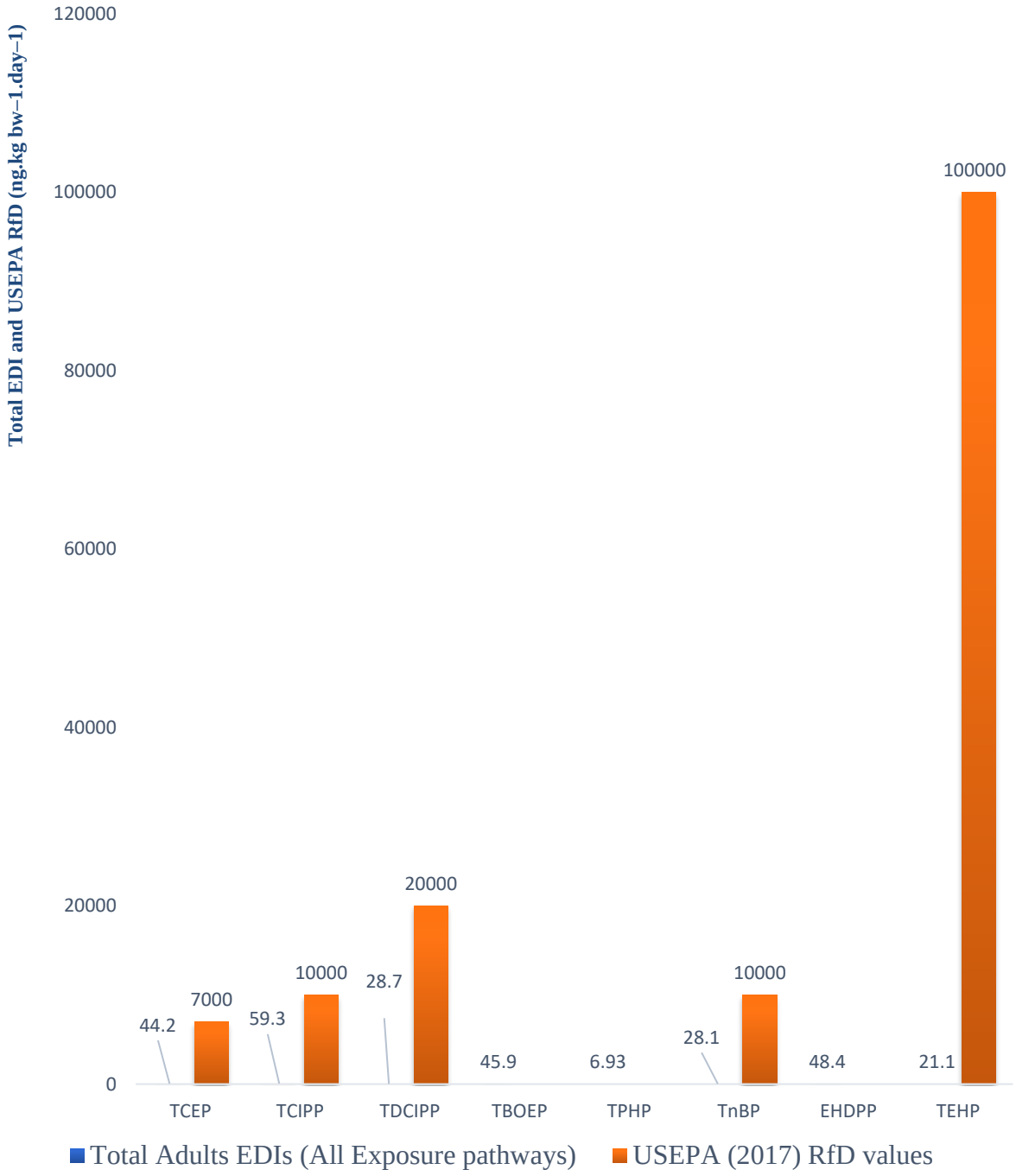


Fig. 2.11: Comparison of average estimated daily intake (EDI) values via all exposure pathways for selected OPEs for adults with the corresponding reference doses (RfDs ng.kg bw^{-1}.day^{-1}) adopted from (USEPA, 2017; Li et al., 2018)

2.6 Conclusions, research priorities, gaps, and future directions

This study summed the average of the mean estimates of exposure to OPEs via a range of pathways and used these to derive estimates of the relative contributions of each pathway to overall exposure to individual OPEs for both adults and toddlers. For toddlers, dermal uptake from dust ingestion was highlighted as the predominant pathway of exposure to chlorinated OPEs, as well as EHDPP and TPHP. In contrast, diet was identified as the main pathway of exposure to all eight OPEs considered for adults, and for TnBP, TEHP, and TBOEP for toddlers. Reassuringly, these summed exposures were below the reference dose (RfD) values obtained by (USEPA, 2017). However, it is important to stress that our summed exposures do not include high-end exposure estimates and that for highly-exposed individuals, the margin between exposure and the RfD values will be smaller. A further caveat is that this review relied on a meta-analysis of mean exposure estimates from multiple exposure assessments conducted over a range of points in space and time, with concomitant uncertainty in both the magnitude and the relative contribution of different exposure pathways. Therefore, there is an urgent need for comprehensive assessments of human exposure to OPEs that examine all relevant pathways in a spatially and temporally-consistent fashion.

This review reveals that relatively few studies have determined the magnitude of human dietary exposure to OPEs. Given our finding that food is an important exposure pathway to these chemicals, regular monitoring of the presence of OPEs in foodstuffs is recommended. Moreover, the currently available literature reveals that human dietary exposure to OPEs occurs principally via industrially processed food groups, such as grains, oils, and dairy products (Li et al., 2019; Poma et al., 2018). For this reason, surveillance of OPEs in processed foodstuff samples should likely have higher priority compared to raw foodstuffs in future studies. This is especially important for EHDPP, which is capable of migrating from packaging materials to

the foodstuffs (Wang and Kannan, 2018; Poma et al., 2018; Li et al., 2019). Moreover, several studies have highlighted that OPE derivatives can be generated by enzyme-catalysed metabolism of OPEs in biota as well as through other degradation routes, such as microbial metabolism/biotransformation, base-catalysed hydrolysis, and photodegradation (Li et al., 2019; Cequier et al., 2015; Greaves et al., 2016). This suggests 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 compared to their parent OPE triesters, such metabolites/degradation products are more biologically active with respect to several toxicological endpoints (Li et al., 2019; Su et al., 2014). However, to date, there is to our knowledge only two published reports on OPE derivatives/by-products in foodstuffs that reported the presence of OPEs metabolites in diet samples (Poma et al., 2019; He et al., 2018a). Thus, inclusion of possible OPE metabolites in future dietary exposure studies is recommended.

While dermal uptake from indoor dust is revealed as an important human exposure pathway, there appear to date to be no evaluations of exposure via dermal uptake from OPE-containing products such as foam-filled furniture. Given the widespread use of chlorinated OPEs at percent concentrations in furniture foam (Stubbings et al, 2018), investigation of this exposure pathway seems prudent. This review also highlights that there are very few data on OPEs in drinking water and more research is needed to ascertain the level and human exposure to these compounds through water ingestion.

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CHAPTER III

Organophosphate Esters in UK Diet; Exposure and Risk Assessment

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Graphical Abstract



3.1 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 $\sum_8$OPEs = 18.4 ng/g wet weight (ww)) in milk and milk products, followed by those in cereal and cereal products (mean $\sum_8$OPEs = 15.9 ng/g ww), with concentrations lowest in chickens'

eggs (mean $\sum_8$OPEs = 1.61 ng/g ww). Interestingly, concentrations in animal-derived foods (mean $\sum_8$OPEs = 44.2 ng/g ww) were statistically indistinguishable ($p>0.05$) from plant-derived foods (mean $\sum_8$OPEs = 36.8 ng/g ww). Estimated daily dietary intakes (EDIs) of $\sum_8$OPEs 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 $\sum_8$OPEs 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.

Keywords: food, ingestion, organophosphate esters, dietary exposure.

3.2 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 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 more than 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 et al., 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 1.6; 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 ∑OPEs/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.

3.3 Materials and Methods

3.3.1 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%), iso-octane (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 hours in a muffle furnace prior to use, to minimise residual organic contamination.

3.3.2 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 (see appendix 3.1). 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.

3.3.3 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 x 1 min vortexing, followed by 15 mins 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 iso-octane: 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 mins 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.

3.3.4 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 appendix 3.2).

3.3.5 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 3.1). 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 hrs) 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 3.1), 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 3.2). Average recoveries of the ISs spiked into Na_2SO_4 ranged between 63 and 114 % (Table 3.1). 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 0.016-0.059 ng/g dw) for TCEP only (Table 3.1).

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 3.1; see appendix 3.3). However,

for TCEP with procedural blank contamination the LOD and LOQ was calculated as 3 & 10 times the standard deviation of the blanks (Table 3.1, see appendix 3.3).

Table 3.1: Instrumental performance, procedural blanks, and instrument detection limits (IDLs) for target OPEs

Target OPEs	RT (min)	Calibration range (ng/µL)	Linear (R^2)	Isotope labelled IS	Relative Response factors (RRFs)	IS Recovery (%) (n=40) (50 ng/µL)	Na_2SO_4 IS Recovery (%) (n=5) (50 ng/µL)	Procedural blank (ng/g) (dw) (n=32)	Instrument detection limit (IDL) (LOD) (pg/injection)
TCEP	8.87	0.05-0.75	0.9983	d27-TnBP	0.13±0.02	74.9 – 86.2 (mean = 79.4, RSD = 7.3)	63-96	0.016-0.059	0.67
TCIPP	9.07	0.05-0.75	0.9974	d27-TnBP	0.04±0.01	74.9 – 86.2 (mean = 79.4, RSD = 7.3)	63-96	ND	0.75
TDCIPP	12.16	0.05-0.75	0.9975	d15-TPHP	0.04±0.01	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	89-114	ND	0.74
TPHP	12.75	0.05-0.75	0.9958	d15-TPHP	0.53±0.03	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	89-114	ND	1.01
EHDPP	12.99	0.05-0.75	0.9981	d15-TPHP	1.45±0.11	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	89-114	ND	1.04
TnBP	8.17	0.05-0.75	0.9987	d27-TnBP	1.11±0.11	74.9 – 86.2 (mean = 79.4, RSD = 7.3)	63-96	ND	1.01
TBOEP	12.58	0.05-0.75	0.9998	d15-TPHP	0.45±0.05	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	89-114	ND	0.27
TMTP	14.40	0.05-0.75	0.9815	d15-TPHP	0.24±0.01	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	89-114	ND	0.50

R^2 = regression coefficient

Table 3.2: Standard recoveries (SRs) and relative standard deviation (RSD) of target OPEs measured in spiked vegetable oil and egg samples

OPEs	Vegetable oil (n=5)			Egg (n=5)		
	Standard recovery (%)	Mean	RSD (%)	Standard recovery (%)	Mean	RSD (%)
TCEP	76.4 – 114.1	93.5	17.7	60.2 – 83.2	73.7	12.0
TCIPP	72.9 – 123.5	95.5	18.8	55.6 – 89.3	75.2	16.5
TDCIPP	76.2 – 112.8	99.5	19.8	59.6 – 86.1	71.4	13.6
TnBP	63.8 – 78.6	73.1	8.1	73.9 – 116.1	85.8	20.0
EHDPP	55.9 – 111.2	91.1	23.2	75.9 - 111.2	95.1	13.9
TPHP	70.3 – 80.2	75.5	4.6	75.7 – 115.8	84.2	21.7
TBOEP	64.0 – 116.7	85.2	24.8	63.1 – 108.1	86.6	24.7
TMTP	76.8 – 119.7	98.9	17.9	87.3 – 109.9	99.6	8.8

3.3.6 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 3.3); 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 and plant-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).

Table 3.3: KMO and Bartlett's Test

Kaiser-Meyer-Olkin Measure of Sampling Adequacy.		.722
Bartlett's Test of Sphericity	Approx. Chi-Square	87.382
	Df	28
	Sig.	<.001

3.3.7 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 3.4; see appendix 3.4) (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 equation 1 (Zhao et al., 2019)

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

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 3.4 and see appendix 3.4).

Table 3.4: Average UK Daily food consumption data (g/day) (Standard deviation, high end exposure in parenthesis) (National Diet and Nutrition Survey (NDNS) report Published by Public Health England and the Food Standards Agency (2014)

Cereals and cereal products	Toddlers (1.5-3 yrs)	Children (4-18 yrs)	Adults (19-64 yrs)	Elderly (65+ yrs)
White bread	32	65	65	61
Pasta	11.6	28.8	27.5	16.8
Rice	11.6	28.8	27.5	16.8
Pizza	11.6	28.8	27.5	16.8
Brown bread	28	41	43	47
Noodles	11.6	23	22	13.5
Burger bread	14	34	31	34
Average (SD, High-end exposure)	**17 (7, 30)**	**36 (6, 48)**	**35 (7, 49)**	**29 (13, 56)**
Pastries				
Croissants	9	17	18	20.5
Cakes	9	17	18	20.5
Puddings	42	48	51	69
Biscuits	15	26	22	19
Average (SD, High-end exposure)	**18.8 (15.8, 50.3)**	**27 (14.6, 56.3)**	**27.3 (15.9, 59.1)**	**32.3 (24.5, 81.3)**
Savoury Snacks				
Mini pretzel	2.25	4.75	3.75	2.5
Corn chips	2.25	4.75	3.75	2.5
Bacon Rasher	2.25	4.75	3.75	2.5
Onion ring	2.25	4.75	3.75	2.5
Mini pretzel	2.25	4.75	3.75	2.5
Average (SD, High-end exposure)	**2.44 (0.38, 3.19)**	**4.81 (0.13, 5.06)**	**3.81 (0.13, 4.06)**	**2.63 (0.25, 3.13)**
Milk and milk products	192	154	129	165
Semi skimmed	335	110	114	141

Skimmed	280	152	121	188
Whole	51.3	20.8	12.3	12.3
Evaporated milk	51.3	20.8	12.3	12.3
Banana milk/Chocolate milk	192	154	129	165
Ice cream	21	31	27	31
Fresh cream and spray cream	51.3	20.8	12.3	12.3
Cheddar cheese	10	18	20	19
Cottage Cheese	26	37	30	25
Desserts	29	27	36.5	38
Average (SD, High-end exposure)	**99 (114, 328)**	**55.6 (54.8, 165)**	**47.9 (48.0, 144)**	**59.6 (68.8, 197)**
Baby food	**280 (215, 710)**	-	-	-
Egg and egg dishes	**23 (9, 41)**	**35 (23, 81)**	**41 (38, 117)**	**33 (24, 81)**
Fish and fish dishes				
Cod	4.2	7.4	10.2	10.4
Tilapia	4.2	7.4	10.2	10.4
Tuna	4.2	7.4	10.2	10.4
Prawns	4.2	7.4	10.2	10.4
Basa	4.2	7.4	10.2	10.4
Salmon	7	10.8	16	14
Mackerel	7	10.8	16	14
Trout	7	10.8	16	14
Average (SD, High-end exposure)	**5.25 (1.45, 15.2)**	**8.68 (1.76, 30.5)**	**12.4 (3.00, 74.3)**	**11.8 (1.86, 43.8)**
Fat spreads (Fats and oils)				
Fat spread	6	9	10	13

Butter	5	8	10	14
Cooking oils	0.5	1	1.5	1.5
Average (SD, High-end exposure)	**3.83 (2.93, 9.69)**	**6.00 (4.36, 14.7)**	**7.17 (4.91, 17.0)**	**9.50 (6.95, 23.4)**
Meat and meat products				
Lamb	34	60	76	65
Beef	39	79	96	91
Pork	27	36	55	38
Chicken	12.5	34.5	45.5	34.5
Turkey	12.5	34.5	45.5	34.5
Average (SD, High-end exposure)	**25 (12.2, 49.4)**	**48.8 (20.1, 88.9)**	**63.6 (22.0, 108)**	**52.6 (25.0, 103)**
Vegetables	6.86	10.9	14.4	15.4
Sweetcorn	6.86	10.9	14.4	15.4
Broccoli	6.86	10.9	14.4	15.4
Carrot	6.86	10.9	14.4	15.4
Mixed pepper	6.86	10.9	14.4	15.4
Mushrooms	11	15.5	28.5	29
Lettuce	6.86	10.9	14.4	15.4
Spinach	11	15.5	28.5	29
Salad	6.86	10.9	14.4	15.4
Mixed vegetable	6.86	10.9	14.4	15.4
Average (SD, High-end exposure)	**7.78 (1.83, 11.4)**	**11.9 (2.03, 16.0)**	**17.5 (6.22, 30.0)**	**18.4 (6.00, 30.4)**
Potatoes (all)				
Average (SD, High-end exposure)	**32 (25, 82)**	**58 (40, 138)**	**69 (51, 171)**	**79 (68, 215)**

Non-alcoholic Beverages – (Fruit juice)				
Average (SD, High-end exposure)	**114 (81, 276)**	**170 (132, 434)**	**132 (114, 360)**	**133 (92, 317)**
Fruits				
Apple, banana, strawberry, oranges, mango/melon				
Average (SD, High-end exposure)	**106 (68, 242)**	**84 (70, 224)**	**120 (103, 326)**	**143 (115, 373)**
Sweet, Sugar, and chocolate confectionery				
Chocolate	9	22	20	15
Sweet	13	20	12	11
Sugar	7	10	17	20
Average (SD, High-end exposure)	**9.67 (3.06, 15.8)**	**17.3 (6.43, 30.2)**	**16.3 (4.04, 24.4)**	**15.3 (4.51, 24.4)**
Nuts				
Nut	9 (3, 15)	11 (5,21)	14 (8, 30)	11 (7, 25)

Source: National Diet and Nutrition Survey, 2014 (NDNS: results from Years 1 to 4 (combined) - GOV.UK (www.gov.uk)

3.4 Results and discussion

3.4.1 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 (appendix 3.5). 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 (see appendix 3.5). 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) (see appendix 3.5). 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. 3.2). 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 and Letcher, 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 $\sum_8$OPEs = 18.4 ng/g ww), followed by cereals and cereal products (CRL) (average $\sum_8$OPEs = 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 (see table in appendix 3.5, Fig. 3.2). While in this study, the highest concentrations of $\sum_8$OPEs (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 $\sum_8$OPEs = 44.2 ng/g

ww) display concentrations that are statistically indistinguishable ($p > 0.05$) from those detected in plant-derived foods (mean $\sum_8$OPEs = 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 $\sum_8$OPEs for egg and egg products, meat and meat products, and fish respectively (Fig. 2.2). 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 – 65 % of the total mean concentrations of $\sum_8$OPEs 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 $\sum_8$OPEs (Fig. 2.2). The higher concentration of TBOEP found in these foods

was responsible for the overall higher concentration observed in Figure 3.1 with greater concentration spread as shown by the error bar. However, the actual distribution of OPEs in various food groups are shown in Figure 3.2. 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 (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% $\sum_8$OPEs) and EHDPP (1.76 ng/g ww, 25%) (see appendix 3.5; Fig. 3.2). 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 – 45 % and 34 - 42 %, were the dominant OPEs in baby food and meat and meat products (see appendix 3.5; Fig. 3.2). EHDPP and TPHP also made substantial contributions to $\sum_8$OPEs 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%) (see appendix 3.5 and 3.6; Fig. 3.2). 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)

3.4.1.1 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 $\sum_8$OPEs 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) (see appendix 3.5). 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 – 65 % of $\sum_8$OPEs concentrations in non-alcoholic beverages, fruits, vegetables, and cereals and cereal products (Fig. 3.2, see appendix 3.6). 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) (see appendix 3.6). 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) (see appendix 3.5 and 3.6). 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.

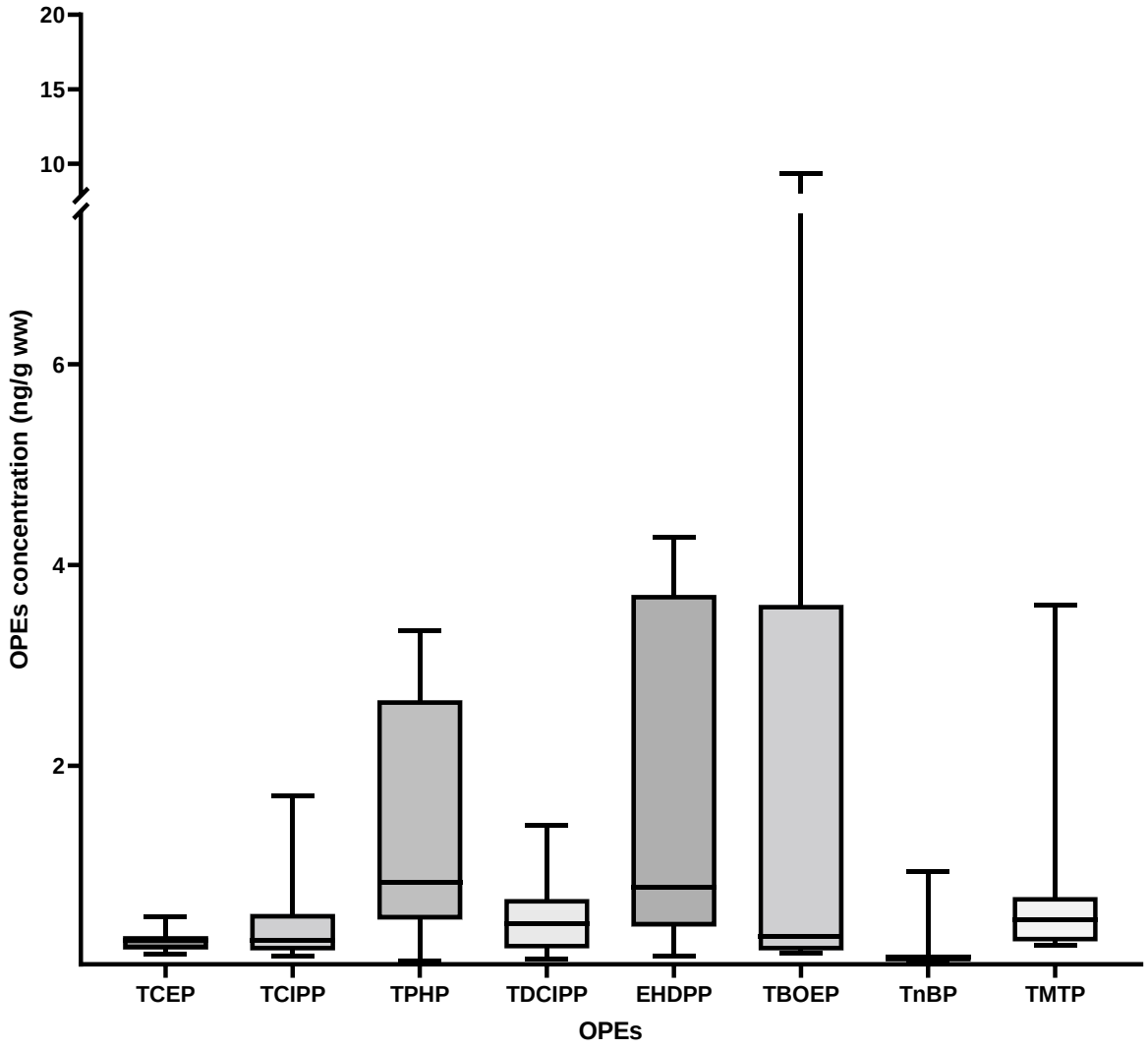


Fig. 3.1: Box plots of OPE concentrations (ng/g, ww) in UK foodstuffs [NB: the middle line of the box is the median OPE concentrations, the top and bottom lines of the box represent the 75th percentile and 25th percentile OPE concentrations, while the top and bottom lines of the y-error bars represent the maximum and minimum OPE concentrations]

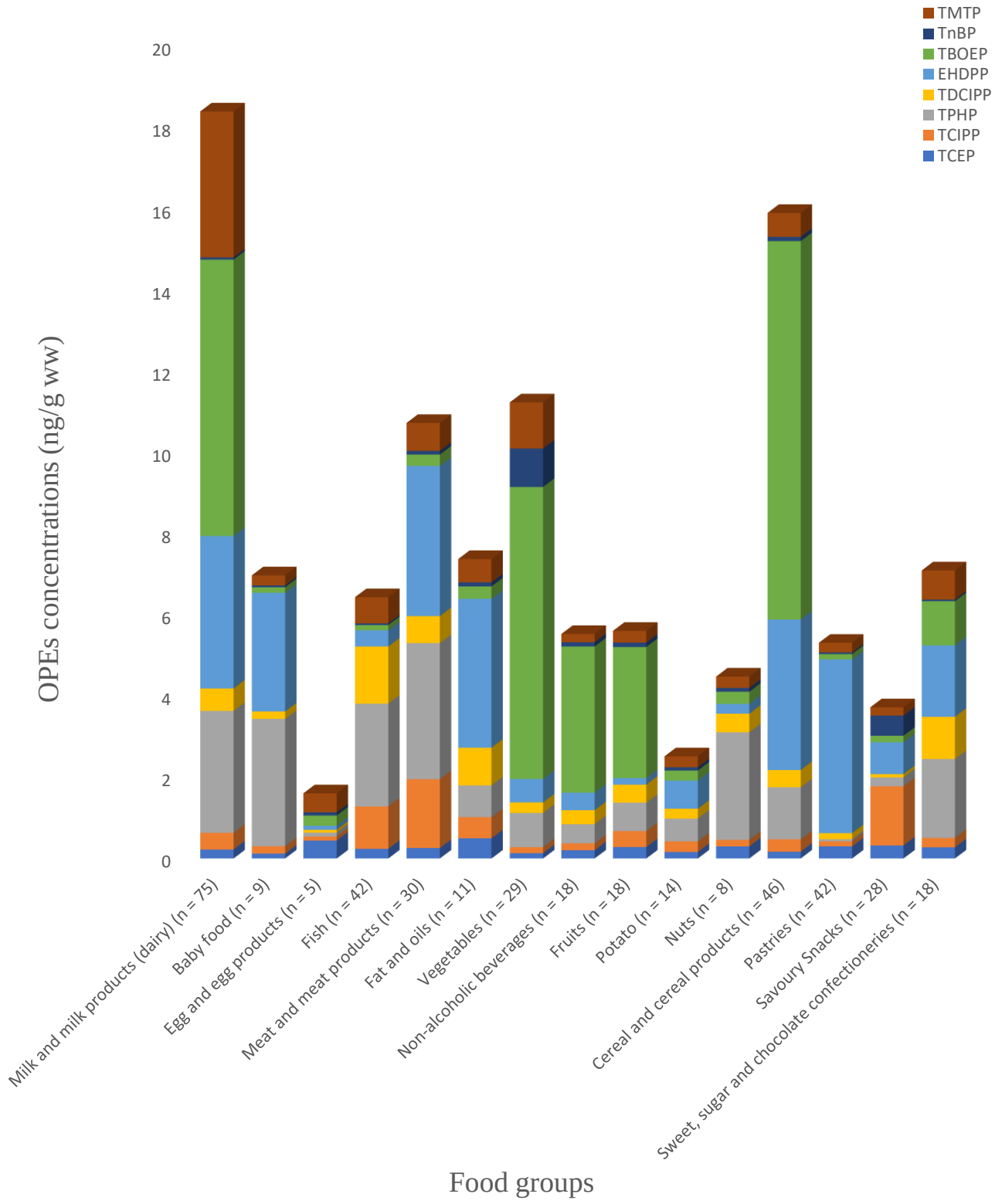


Fig. 3.2: Mean distribution of individual OPEs (ng/g ww) in different UK Food Groups

3.4.1.2 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 3.5). TCEP also correlated significantly with TnBP and TMTP at ($r = 0.748$, $p < 0.01$) (Table 3.5). 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 3.5).

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 ($r = 0.964$, $p < 0.01$) (Table 3.5). 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 3.5). This finding was broadly corroborated by principal component analysis (PCA). In PCA, three components were extracted (Table 3.6) 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 3.6). 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 3.6) 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.

Table 3.5: Spearman's rank correlation coefficient between concentration of target OPEs in UK Food samples from Major Groceries

Correlations										
			TCEP	TCIPP	TPHP	TDCIPP	EHDPP	TBOEP	TnBP	TMTP
Spearman's rho	TCEP	Correlation Coefficient	1.000	.609*	.077	.595*	.326	.326	.748**	.748**
		Sig. (2-tailed)	.	.016	.785	.019	.236	.236	.001	.001
	TCIPP	Correlation Coefficient		1.000	.477	.598*	.476	.345	.583*	.590*
		Sig. (2-tailed)		.	.072	.018	.073	.208	.023	.021
	TPHP	Correlation Coefficient			1.000	.659**	.267	.450	.327	.343
		Sig. (2-tailed)			.	.007	.336	.092	.234	.211
	TDCIPP	Correlation Coefficient				1.000	.186	.539*	.560*	.493
		Sig. (2-tailed)				.	.508	.038	.030	.062
	EHDPP	Correlation Coefficient					1.000	.313	.310	.421
		Sig. (2-tailed)					.	.257	.261	.119
	TBOEP	Correlation Coefficient						1.000	.562*	.595*
		Sig. (2-tailed)						.	.029	.019
	TnBP	Correlation Coefficient							1.000	.964**
		Sig. (2-tailed)							.	<.001
	TMTP	Correlation Coefficient								1.000
		Sig. (2-tailed)								.
**. Correlation is significant at the 0.01 level (2-tailed)										
*. Correlation is significant at the 0.05 level (2-tailed).										

Table 3.6: Principal component analysis (after varimax rotation) indicating the contribution of statistical dominant variables measured to ascertain the contamination sources of the OPEs

Variables	Principal loading factors			Communalities
	PC1	PC2	PC3	
TMTP	**0.938**	-0.097	-0.048	0.892
TCIPP	**0.919**	0.212	0.088	0.897
TnBP	**0.648**	0.364	0.575	0.884
TCEP	**0.645**	0.563	0.372	0.872
TPHP	-0.055	**0.767**	0.017	0.592
EHDPP	0.131	**0.713**	0.062	0.529
TDCIPP	0.307	**0.700**	0.385	0.732
TBOEP	0.005	0.076	**0.953**	0.914
Eigenvalue	2.674	2.097	1.539	-
% Of variance explained	33.431	26.217	19.235	-
Cumulative (%)	33.431	59.648	78.883	-

3.5 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 $\sum_8$OPEs 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 3.7, appendix 3.7 (a-d); Fig 3.3 and Fig. 3.4). The estimated mean EDI values for the $\sum_8$OPEs 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 $\sum_8$OPEs 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 ∑EDIs for six OPEs (TCEP, TCIPP, TDCIPP, TPHP, EHDPP and TnBP) for adults in our study with the values obtained from previous studies (Fig. 3.6). 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 (He et al., 2018), slightly above those reported in USA (Wang and Kannan, 2018) and below those from other studies with which ∑EDIs is compared (Fig. 3.6).

Interestingly, the mean ∑EDI values of $\sum_6$OPEs (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 $\sum_6$OPEs 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; 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) (see appendix 3.8). In contrast, our mean ∑EDI values for $\sum_6$OPEs 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) (see appendix 3.8). In addition, our estimated ∑EDIs for diet for the $\sum_6$OPEs 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) (see appendix 2.9). 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) (see appendix 3.8). Overall, our data on UK dietary exposure corroborate the conclusion of our critical review that human exposure to ∑OPEs through food ingestion is of comparable importance to that received via other exposure pathways (Gbadamosi et al., 2021).

3.5.1 Contributions of different food types to overall UK dietary exposure to OPEs

Baby food is a major source of $\sum_8$OPEs exposure for toddlers (mean: 163 ng/kg bw/day, 39%; high-end exposure: 230 ng/kg bw/day, 15%) (Fig. 3.3 and Fig. 3.4); 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 ∑OPE 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 $\sum_8$OPEs (see appendix 3.7b, Fig. 3.3 and Fig. 3.4). Interestingly, cereal and cereal products were the main dietary source of $\sum_8$OPEs for adults (mean: 15.6 ng/kg bw/day, 25%), while fruits were the main dietary source of the $\sum_8$OPEs 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. 3.3 and Fig. 3.4). For toddlers, the mean and high exposure ∑EDI values for $\sum_8$OPEs 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. 3.5). However, there are statistically significant differences ($p<0.05$) between EDIs of $\sum_8$OPEs 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 $\sum_8$OPEs considered in this study. In a study carried by Zhao et al. (2019), the EDI of $\sum_9$OPEs 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 $\sum_9$OPEs assigned to foods of animal origin (9 ng/kg bw/day) was comparable to our adult EDI (17.2 ng/kg bw/day) of $\sum_8$OPEs 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 $\sum_{15}$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 ∑EDIs 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 ∑OPEs exposure for adults (Poma et al., 2018; Chen et al., 2021b). Our mean adult EDI of ∑OPEs 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 attributed to fish and seafood (300±54 ng/kg bw/day) in Belgium (Poma et al., 2018). Surprisingly, UK dietary exposure to ∑OPEs 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 $\sum_8$OPEs (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. 3.3, see appendix 3.7 a-d).

3.5.2 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 3.7, Fig. 3.3, and Fig. 3.4). The overall 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 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).

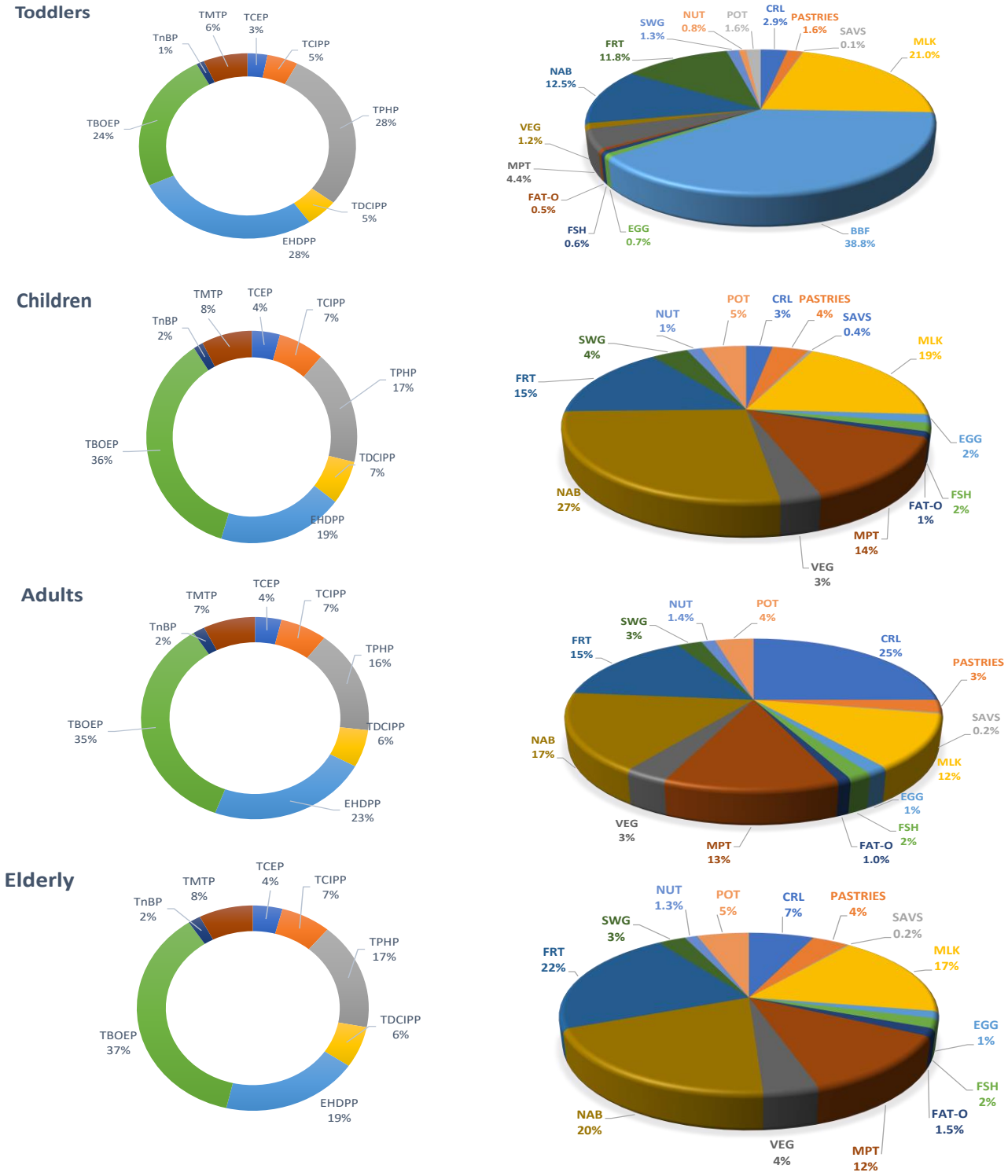


Fig. 3.3: The contribution of individual OPEs and food groups to estimated daily intakes (EDI) of Σ_8OPEs for various age groups in the UK [MPT= meat and meat products, FAT-

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]

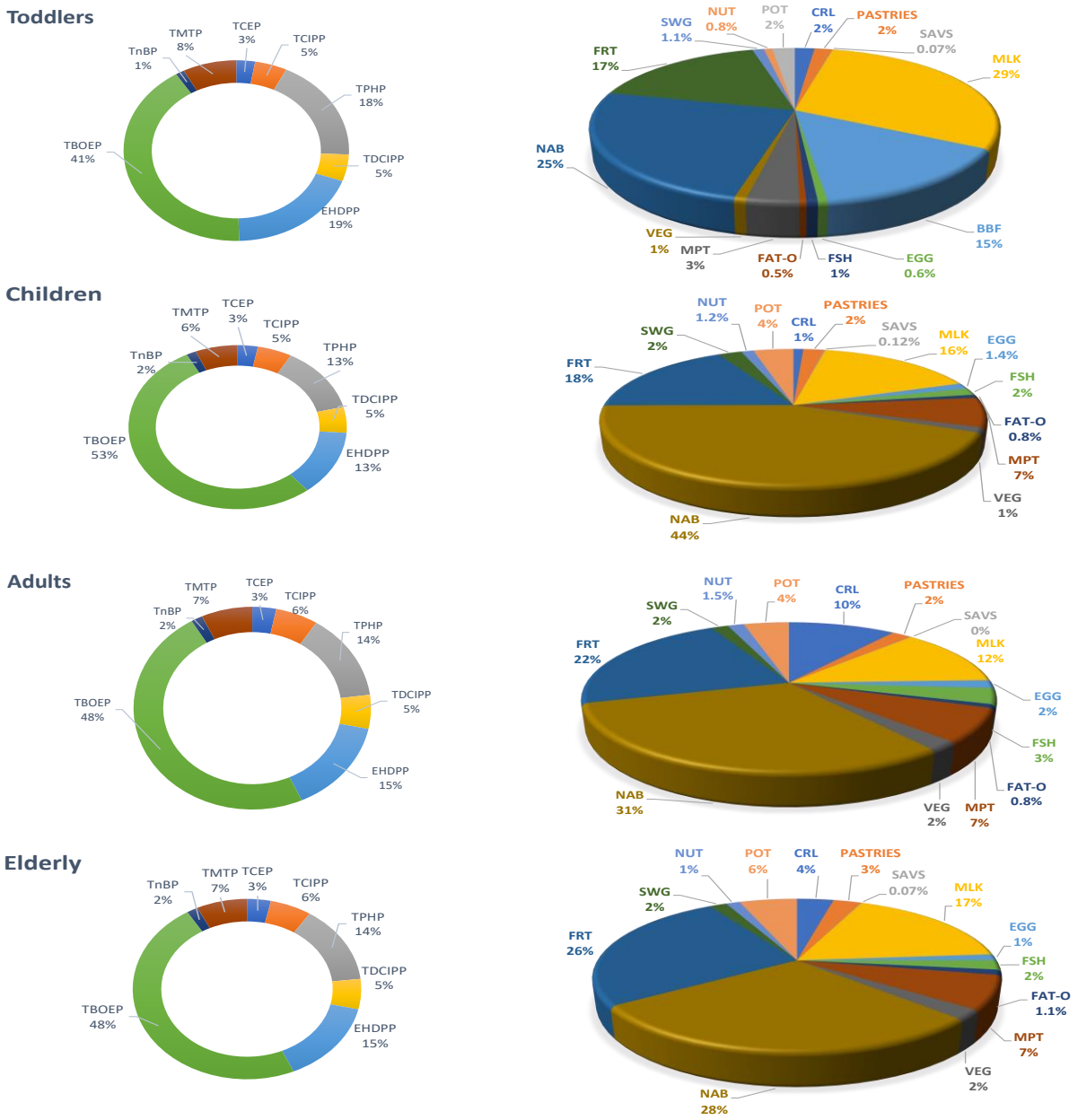


Fig. 3.4: High-end EDI for individual OPEs for various food group for the four-age group

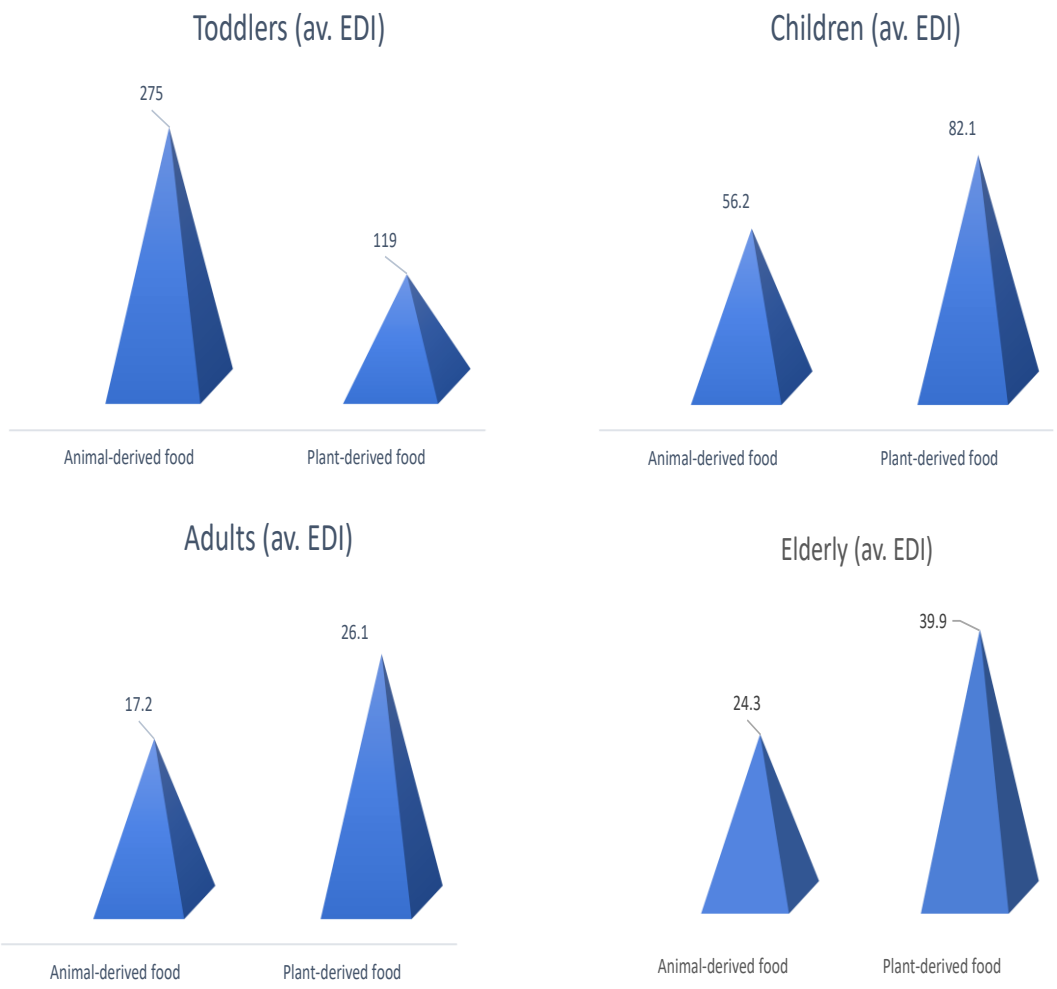


Fig. 3.5: Contributions of the two broad food categories (animal-derived and plant-derived food) to the total average dietary EDIs for four age groups in the UK

3.5.3 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 (7,000 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 (2,200 ng/kg bw/day), TCIPP (8,000 ng/kg bw/day),

TDCIPP (1,500 ng/kg bw/day), TPHP (7,000 ng/kg bw/day), TBOEP (1,500 ng/kg bw/day), and TnBP (2,400 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 (3,600 ng/kg bw/day) for TCIPP was obtained from Saito et al. (2007) (Table 3.7). 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 1,000. 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 3.7). 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 3.7).

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) (see appendix 3.9a). For toddlers, the mean and high-end exposure scenario EDIs for the Cl-OPEs were: TCIPP (296 and 1,339 ng/kg bw/day) > TDCIPP (23.6 and 123 ng/kg bw/day) > TCEP (17.2 and 94.4 ng/kg bw/day) (see appendix 3.9c). Interestingly, for toddlers the HQ for TCIPP is 0.37 using the lowest TCIPP RfD value of 3,600 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) (see appendix 3.9b). 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) (see appendix 3.9b), 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 (see appendix 3.9c). 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 (see appendix 3.9 a-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 3.7). 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 (∑EDIs <<< RfDs) (see appendix 3.9 a-c, Table 23.7). 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, the 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 (see appendix 3.9 a-c).

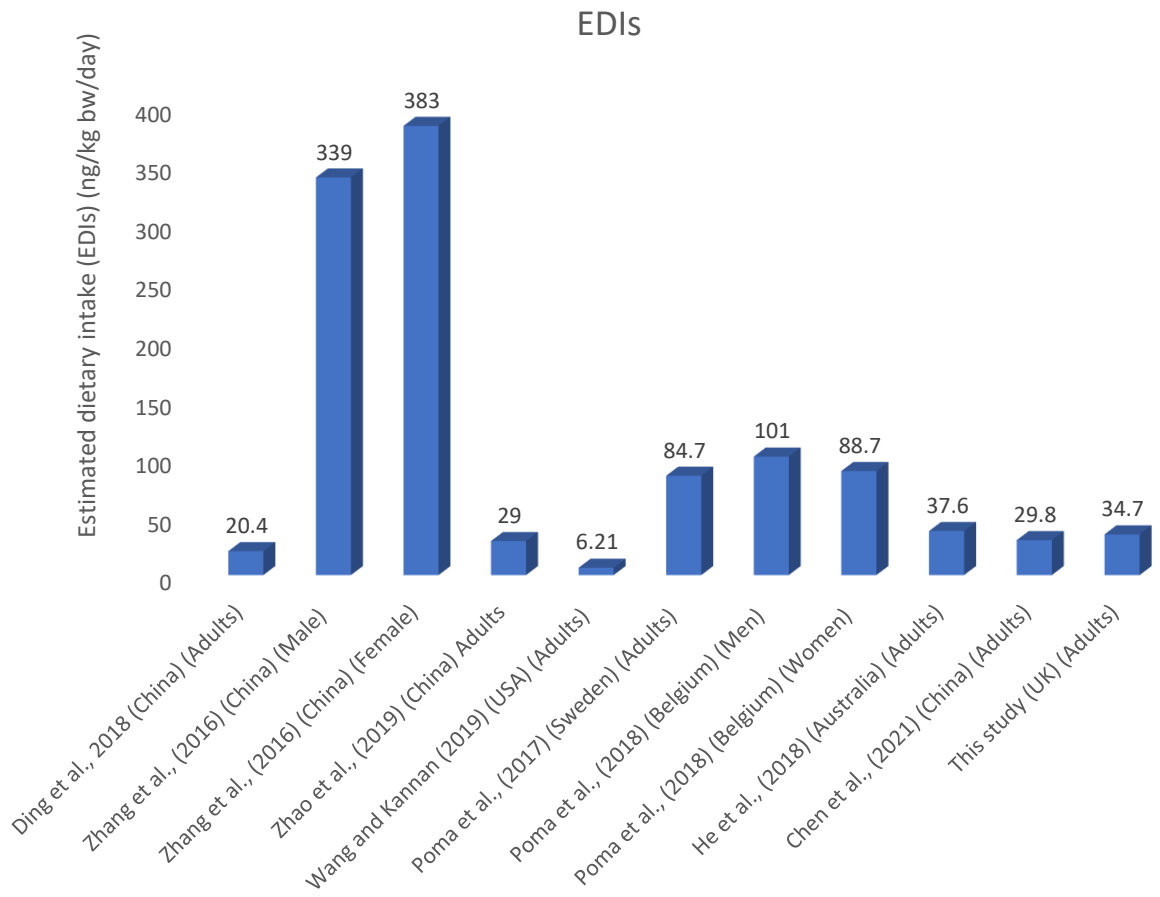


Fig. 3.6: Comparison of the mean dietary intake of Σ_6OPEs (TCEP, TCIPP, TDCIPP, TPHP, EHDPP, and TnBP) for UK adults with previous studies from other countries

Table 3.7. 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	∑OPEs
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]	7,000	10,000	20,000	NA	NA	NA	10,000	NA	
RfD (ng/kg bw/day) [b]	2,200	8,000	1,500	7,000	600 [d]	1,500	2,400	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	3,600	NA	NA	NA	NA	NA	NA	

[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)

RfD = Reference dose

NA = not available

3.6 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 – 28 % of the total mean concentration of $\sum_8$OPEs in such foodstuffs. By comparison, in plant-derived foods such as: vegetables, non-alcoholic beverages, and fruits; TBOEP was predominant, representing between 58 – 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 $\sum_8$OPEs 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.

3.7 References

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CHAPTER IV

Concentrations of organophosphate esters in drinking water from the United Kingdom: Implications for human exposure

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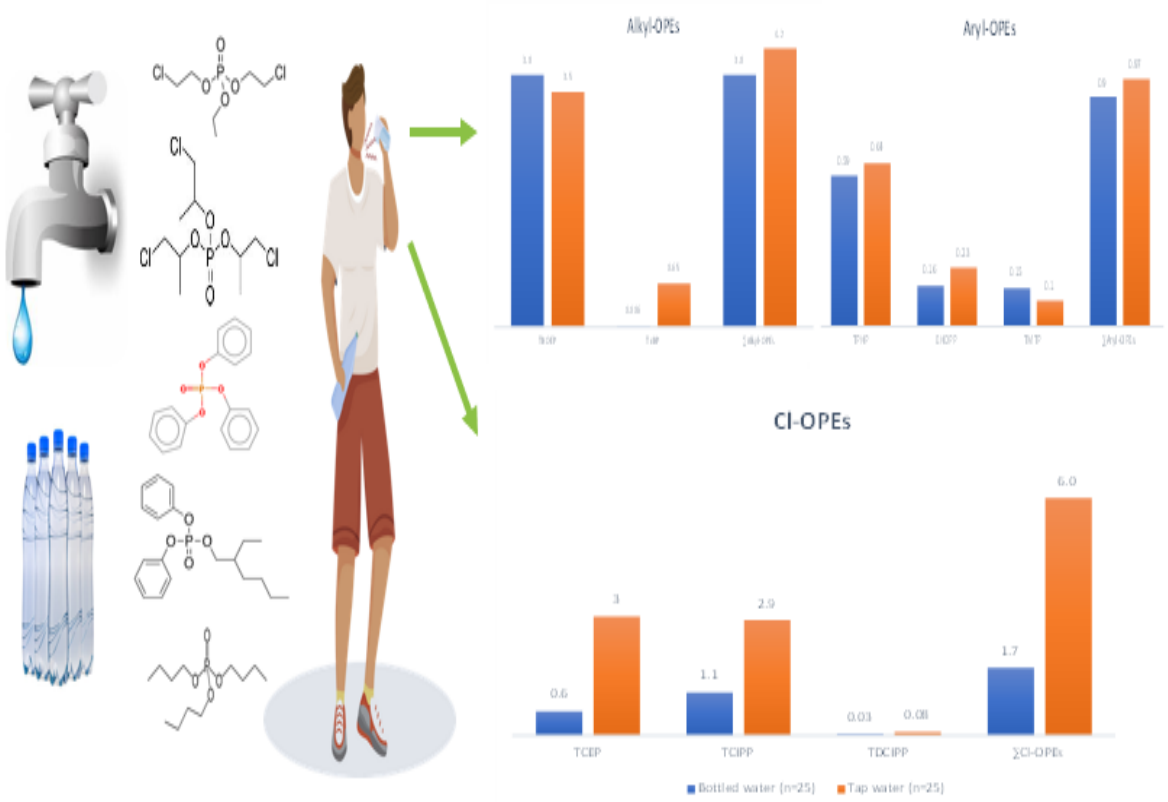
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Graphical Abstract



4.1 Abstract

Data on the presence of organophosphate esters (OPEs) in drinking water and its significance as a pathway of exposure are limited. In this study, we measure for the first time, concentrations of eight OPEs in 50 UK drinking water samples. Arithmetic mean concentrations of $\sum_8$OPEs were: 6.4 and 11 ng/L in bottled (n=25) and tap water samples (n=25), respectively. The predominant OPEs detected were: tris (butoxyethyl) Phosphate (TBOEP), tris (2-chloroethyl) phosphate (TCEP), and tris(2-chloroisopropyl) Phosphate (TCIPP) with arithmetic mean concentrations in the two water sample types ranging between (3.5 – 3.8 ng/L), (0.60 – 3.0 ng/L), and (1.02 – 2.9 ng/L), respectively. Estimated daily intakes (EDIs) (mean and high-end exposure) via drinking water for different sectors of the UK population were: infants (0.93 and

6.4 ng/kg bw/day) > toddlers (0.46 and 3.1 ng/kg bw/day) > children (0.35 and 2.3 ng/kg bw/day) > adults (0.28 and 2.1 ng/kg bw/day). Based on these data, exposure to Σ_8OPEs via drinking water is much lower than via: food, indoor dust ingestion, inhalation, and dermal uptake for adults and toddlers. Reassuringly, our EDIs were lower than relevant reference dose (RfD) values. However, combining our drinking water ingestion data with exposure via other pathways revealed overall exposure to 2-ethylhexyl diphenyl phosphate (EHDPP) and TCIPP to approach health-based limit values for UK toddlers under a high-end exposure scenario.

Keywords: daily intakes, tap water, reference dose and high-end exposure scenario.

4.2. Introduction

Organophosphate esters (OPEs) have been widely used as a flame retardant (FR) in various industrial and consumer products [1]. Other uses include as stabilisers, plasticisers, antifoaming, and wetting agents, as well as additives in lubricants and hydraulic fluids [2,3]. OPEs are used as additive FRs, meaning that they are not chemically bound to consumer products [4], thus these compounds can be released during production, use, and end of life product management by leaching, volatilisation, and abrasion [5]. Global usage of OPEs as a replacement for restricted BFRs has increased rapidly in recent years from 680,000 t in 2015 to 2,800,000 t in 2018 [1,6]. In western Europe, OPEs have been estimated to account for 20% of total FR consumption [3]. Such widespread and substantial use has led to the detection of OPEs in various environmental matrices including: food, water, air, dust, and sediment, as well as in human tissues such as: breast milk, placenta, blood serum, urine, hair, and nails [7-11]. Such evidence of human exposure is of potential concern given reports that OPEs can cause adverse effects. For instance, tri(2-chloroethyl) phosphate (TCEP) has been reported to decrease red blood cell cholinesterase activity, disrupt the thyroid endocrine system, and elicit

neurotoxicity; while triphenyl phosphate (TPhP) has been linked to decreased red blood cell cholinesterase activity, along with neurotoxicity, contact allergenic effects, and impaired fertility. Moreover, tributoxyethyl phosphate (TBOEP) was associated with decreased red blood cell cholinesterase activity, and triethyl phosphate (TEP) linked with disruption of the thyroid endocrine system [2,3]. Also of concern, both TCEP and tris (1-chloro-2-propyl) phosphate (TCIPP) are potentially carcinogenic [3,12]. The presence of OPEs in human tissues demonstrates that human exposure occurs, but while research to date has highlighted that this arises via: dermal contact, dust ingestion, inhalation, and dietary intake [7]; relatively few studies have examined drinking water as a pathway of exposure to OPEs. Such studies are, hitherto, limited to: China [13-17], the United States [18,19], Spain [20], and South Korea [21,22]. Against this background, the current study reports concentrations of eight OPEs in 52 samples of drinking water collected in the UK, with the primary objective to assess the significance of drinking water as an exposure pathway of the UK population to OPEs. To the best of our knowledge, this is the first study of the occurrence of OPEs in UK drinking water, and as such will form a valuable baseline against which efforts to minimise this occurrence may be evaluated.

4.3 Materials and Methods

4.3.1 Chemicals and materials

Eight reference OPE standards Tri-n-butyl phosphate (TnBP), Tri(2-chloroethyl) phosphate (TCEP), Tris(1-chloro-2-propyl) phosphate (TCIPP), Tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), Triphenyl phosphate (TPHP), 2-Ethyl hexyl diphenyl phosphate (EHDPP), Tris(-2- butoxyethyl) phosphate (TBOEP), and Tri-m-tolyl phosphate (TMTP) with two isotopically-labelled internal standards of deuterated TBP (d_{27}-TBP, 98%) and TPHP (d_{15}-TPHP, 98%) (50 µg/mL in toluene) and 2,3,4,6-tetrachlorobiphenyl (PCB-62) used as a recovery determination

(or syringe) standard were purchased from Wellington laboratories, (Guelph, ON, Canada). All organic solvents used were HPLC grade which include dichloromethane (DCM, 99.8%), iso-octane (ISOC, 99.5), methanol (MEOH, 99.9%), acetonitrile (ACN, 99.8%), and n-hexane (HEX, 95%) were purchased from Fisher scientific (Loughborough, UK). Oasis® HLB extraction cartridges (200 mg, 6 cm^3) were purchased from Waters Corporation (Milford, MA, USA). The nitrogen gas used for solvent evaporation was purchased from BOC Gases, UK. All glassware were baked at 450 °C overnight and rinsed before each use with DCM (three times), hexane, and acetonitrile.

4.3.2 Sampling details

(a) Tap water: Tap water was sampled from the kitchen of families and laboratory tap water by running the tap for 3 – 5 mins before collection, no water filter or purifier was used.

(b) Bottled water: Bottled water of different brands (spring, lake, stream, natural etc) packaged in 550 – 1000 mL polyethylene terephthalate bottlers were purchased from major grocery stores within Birmingham.

4.3.3 Sample collection and preparation

Fifty drinking water samples comprising: tap water (n = 25), bottled water (n = 25) were collected from three major cities within the West Midlands conurbation of the UK, between July and August 2021. One litre tap water samples were collected from the kitchen of 25 different homes located within different conurbations (Birmingham, Walsall, and Coventry) in the UK West Midlands; while 25 bottled water samples consisted of single 500 - 1,500 mL polyethylene terephthalate bottles of popular brands purchased from major grocery stores within Birmingham. A detailed description of how drinking water samples were taken is

provided in the supplementary information. Following collection, all samples were stored at 4 °C prior to extraction, which was conducted within 24 h of sample collection.

Approximately 200 mL of drinking water were spiked with 10 ng of isotopically-labelled internal (surrogate) standards (d_{27}-TnBP and d_{15}-TPHP) and extracted using an Oasis® HLB solid phase extraction cartridge (200 mg, 6 cm^3; Waters). The cartridges were preconditioned by a sequence of 10 mL each of dichloromethane, methanol, and Milli-Q purified water. After sample loading, cartridges were dried under a gentle nitrogen gas stream, and eluted with 6 mL of dichloromethane. The eluent was concentrated under a gentle stream of nitrogen to incipient dryness. This was reconstituted with 100 µL of iso-octane containing 10 ng of PCB-62 as recovery determination (syringe) standard (RDS). The final sample concentrate was transferred to an amber vial prior to analysis on an Agilent 5975C GC-MS operated in selected ion monitoring electron ionisation mode and fitted with a 30 m DB-5 MS GC column (0.25 mm ID, 0.25 µm film thickness) (Restek, USA). Detailed information on the instrumental analysis conditions is described in our previous work [7]

4.3.4 Quality assurance and quality control

All laboratory glassware was washed, rinsed with deionised, distilled Milli-Q water, heated at 460 °C for at least 2 hours, then rinsed sequentially with hexane, acetone, and dichloromethane prior to use. For all target analytes, the relative standard deviation of the relative response factors (RRFs) in the five calibration standards (0.05 – 0.75 ng/µL) were below 8%. Two procedural blanks (n = 2) were included for every batch of five samples with only TCEP detected in blanks at an average concentration of 0.10 ± 0.08 ng/L (Table 4.1). Concentrations of TCEP in each batch of samples were therefore blank-corrected (by subtracting the average concentrations in the two procedural blanks detected with the samples from each batch). In the absence of an appropriate certified reference material, matrix spiked samples (Milli-Q water)

(n = 5) containing 10 ng of each target OPE (equivalent to 50 ng/L in the water sample) were analysed to evaluate method performance. Recoveries of our eight target OPEs in spiked samples ranged from 67 – 123% (Table 4.1). Moreover, recoveries of the two internal standards were 92 ± 17% and 89 ± 11% for d_{27}TnBP and d_{15}TPHP respectively (Table 4.1). The limit of detection (LOD) and the limit of quantification (LOQ) were calculated as the amounts of an analyte that yielded signal to noise ratios (S/N) of 3 and 10 respectively based on 11 injections of the lowest concentration calibration standard (0.05 ng/µL, Table 4.1). For exposure assessment purposes, OPE concentrations below the LOQ were assumed to be present at either zero (lower bound (LB)) or the LOQ (upper bound (UB)).

Table 4.1: Internal standard recovery, blank concentrations, and limit of detection (LOD) and limit of quantification of OPEs

Target OPE	Internal standard	Range of IS Recovery (%) (mean, RSD) (n=5)	Na_2SO_4 Native Recovery (%) (n=5) (50 ng/µL)	Procedural Blanks (ng/L) (n=20)	LOD (ng/L)	LOQ (ng/L)
TnBP	d_{27}-TnBP	78 – 118 (92, 18)	88.7 ± 10.1	ND	0.006	1.63
TCEP	d_{27}-TnBP	78 – 118 (92, 18)	75.9 ± 12.1	0.10 ± 0.08	0.001	0.13
TCIPP	d_{27}-TnBP	78 – 118 (92, 18)	67.2 ± 12.4	ND	0.006	1.48
TDCIPP	d_{15}-TPHP	83 – 107 (89.3, 12)	81.9 ± 9.91	ND	0.004	1.01
TPHP	d_{15}-TPHP	83 – 107 (89.3, 12)	123 ± 6.71	ND	0.003	0.70
EHDPP	d_{15}-TPHP	83 – 107 (89.3, 12)	112 ± 11.2	ND	0.002	0.52
TBOEP	d_{15}-TPHP	83 – 107 (89.3, 12)	83.9 ± 10.2	ND	0.013	3.28
TMTP	d_{15}-TPHP	83 – 107 (89.3, 12)	79.2 ± 12.7	ND	0.004	1.08

4.3.5 Statistical analysis

Descriptive and multivariate statistical analyses were performed using IBM SPSS Statistics 28 (USA) for Windows and Microsoft Excel 365. The data were $\log_{10}$ transformed prior to analysis after a Shapiro-Wilk test showed that the data were not normally distributed. Such data transformation is necessary due to the sensitivity of principal component analysis (PCA) to non-uniformly distributed data [23]. A t-test was used to investigate significant differences in OPE (chlorinated, aryl and alkyl OPEs) concentrations between tap and bottled water. The Spearman rank correlation coefficient (r) is used to reflect the linear correlation between the analytes as well as the correlation between OPE concentrations in bottled, tap and dispensed water, while PCA was carried out after fulfilling the condition of data to be normally distributed. PCA was performed to investigate the possible factors driving OPE concentrations in the three drinking water sample types. This was carried out based on varimax orthogonal rotation with eigen-value > 1 after determining the Kaiser-Meyer OIkin (KMO) test that measured sampling adequacy and Bartlett's Test of sphericity was adequate and found to be significant ($p<0.01$) for the variables [23]. The first four principal components (PCs) with (eigen-values > 1) which explained > 75% of the total variance were retained as the most significant components.

4.4 Exposure and risk estimation

The estimated daily intake (EDI) expressed as nanograms per kilogram of body weight per day of OPEs via ingestion of drinking water was calculated for infants, toddlers, children, and adults using the following equation (1)

$$EDI = C_{water}\, x\, Ingestion\ rate\ (IR) \qquad 1$$

Where C_{water} is the concentrations of a given OPE or combination of OPEs in drinking water (ng/L), IR is the average drinking water ingestion rate (L (kg of bw)$^{-1}$day^{-1}) which is 0.05 L (kg of bw)$^{-1}$day^{-1} for infants, 0.026 L (kg of bw)$^{-1}$day^{-1} for toddlers, 0.02 L (kg of bw)$^{-1}$day^{-1} for children and 0.016 L (kg of bw)$^{-1}$ day^{-1} for adults [24] (Table 4.2). Both a "normal" exposure scenario (assuming the water consumed was contaminated at the arithmetic mean OPE concentration) and a high-end exposure scenario (assuming the water consumed was contaminated at the 95th percentile OPE concentration) were evaluated for each of the age groups considered.

Table 4.2: The drinking water ingestion rates (IRs) for various age groups.

Age group	**Water Mean ingestion rate (IR) (L/kg bw/day)**	**95th percentile ingestion rate (IR) (L/kg bw/day)**
Birth to < 1 month	0.137	0.238
1 to < 3 months	0.119	0.285
3 to < 6 months	0.08	0.173
6 to < 12 months	0.053	0.129
1 to < 2 years	0.027	0.075
2 to < 3 years	0.026	0.062
3 to < 6 years	0.021	0.052
6 to < 11 years	0.017	0.047
11 to < 16 years	0.012	0.035
16 to < 18 years	0.01	0.030
18 to < 21 years	0.011	0.036
≥ 21 years	0.016	0.042
> 65 years	0.018	0.043
All ages	0.016	-

US EPA Exposure factors handbook (2011)

4.5 Results and discussion

4.5.1 Concentration of OPEs in drinking water

A statistical summary of concentrations of our target OPEs are shown as Table 4.3. Similar to previous studies [14,17-22,25-29], TCEP was detected in all the studied drinking water samples (detection frequency (DF) = 100%). In contrast, TCIPP, TDCIPP, TPHP and EHDPP displayed varying DFs ranging from 44 - 96% in tap water and 16 – 92% in bottled water (Table 4.3). TnBP displayed the lowest DF, ranging from 0% in bottled water to 16 % in tap water. With respect to TMTP and TBOEP, DFs were between 28 - 72% and 20 – 72%, in tap water and bottled water, respectively (Table 4.3). The higher DFs observed for TCEP, TCIPP, TPHP, and TBOEP may be associated with the wide past and current application of these OPEs in the UK [21,26], as well as their physicochemical properties. Both TCEP and TCIPP have been used widely in: polyurethane carpet backing, furniture foam, and polystyrene building insulation [3]. Meanwhile, TPHP is used as an additive in food packaging materials [30], while TBOEP is widely used in floor polish/wax and as a plasticiser in vinyl plastics and rubber stoppers [3,31]. Moreover, TCEP, TCIPP, and TBOEP have relatively higher water solubilities (exceeding 1000 mg/L at 25 °C) in comparison to other OPEs (see appendix 4.1). Average concentrations of target individual OPEs across the two drinking water categories examined (bottled and tap water) were: TBOEP (7.3 ng/L) > TCIPP (3.9 ng/L) > TCEP (3.6 ng/L) > TPHP (1.2 ng/L) > TnBP (0.66 ng/L) > EHDPP (0.39 ng/L) > TMTP (0.25 ng/L) > TDCIPP (0.11 ng/L) accounting for 42%, 23%, 21%, 7%, 4%, 2%, 1%, and 0.7% of $\sum_8$OPEs, respectively. Thus, TCEP and TCIPP were the predominant chlorinated OPEs (Cl-OPEs), TPHP and EHDPP the predominant aryl-OPEs, while TBOEP was the dominant alkyl-OPE (Fig. 4.1).

Several studies have reported higher concentrations of TCEP, TCIPP, and TBOEP in drinking water samples than in our study; specifically in China [13-17,25,28-29], in Korea [21,22], and the USA [19]. The mean (95^{th} percentile) concentrations of the chlorinated OPEs, TCEP and TCIPP in UK tap water (TCEP: 3.0 (7.3 ng/L), TCIPP: 2.9 (960 ng/L)) and bottled water (TCEP: 0.60 (1.6 ng/L), TCIPP: 1.0 (1.8 ng/L)) in our study; were lower than the average concentrations reported for drinking water from China (TCEP: 38.8 ng/L;TCIPP: 67.0 ng/L) [21], (TCEP: 9.1 ng/L; TCIPP: 6.7 ng/L) (Ding et al., 2015), (TCEP: 18.7 ng/L; TCIPP: 20.0 ng/L) [28], (TCEP: 27.8 ng/L; TCIPP: 218 ng/L) (Huang et al., 2022), in Korea (TCEP: 39.5; TCIPP; 49.4 ng/L) [22], in US (TCEP: 150 ng/L) [18] and TCIPP (40 ng/L) in drinking water from Spain (Rodil et al., 2012) (Table 4.4). However, our mean concentrations for the aryl OPEs: TPHP (0.64 and 0.59, ng/L) and EHDPP (0.23 and 0.16) in tap and bottled water, respectively (Table 4.3) were comparable to those reported in China for TPHP (0.14 and 0.28 ng/L) for ambient temperature water and hot water, respectively [17] but lower than the values reported in other studies from China (TPHP: 21.3 ng/L) [28], (TPHP: 1.11 ng/L) (Huang et al., 2022). Meanwhile, our arithmetic mean concentrations of TBOEP (3.5 and 3.8 ng/L) in tap and bottled water were comparable to those reported in Eastern China [14] and below that reported in eight major metropolitan cities in China (26.1 ng/L) [21]. Among our target OPEs, TBOEP was present at the highest average concentration in: bottled water (3.8 ng/L) and tap water (3.5 ng/L) followed by TCEP with a mean concentration of 3.0 ng/L in tap water and 0.60 ng/L in bottled water (Table 4.3).

4.5.2 Differences in OPE concentrations between drinking water categories

The average $\sum_8$OPEs concentration in tap water (11 ng/L) exceeded those in bottled water (6.4 ng/L) (Table 4.3). A t-test revealed a significant difference between $\sum_8$OPEs concentrations in bottled water (mean: 6.4 ng/L) and tap water (mean: 11 ng/L) ($p < 0.01$). In contrast, the

average sum of the three chlorinated OPEs (TCEP, TCIPP, and TDCIPP) in tap water (6.0 ng/L), bottled water (1.7 ng/L) and dispensed water (0.79 ng/L) showed a significant difference ($p < 0.05$) (Fig. 4.1). This indicated that tap water was the most contaminated with chlorinated OPEs (Fig. 4.1). This is consistent with what was reported in China [14,21,28,29], where tap water displayed higher concentrations of chlorinated OPEs than the other drinking water types considered. For the aryl OPEs such as TPHP, EHDPP and TMTP, mean concentrations in tap water (TPHP: 0.64 ng/L; EHDPP: 0.23 ng/L; TMTP: 0.10 ng/L) were slightly higher (but not significantly) than those obtained from bottled water (TPHP: 0.59 ng/L; EHDPP: 0.16 ng/L; TMTP:0.15 ng/L). Moreover, mean concentrations of alkyl-OPEs: TBOEP and TnBP in bottled water (3.8 and <LOD) and tap water (3.5 and 0.65 ng/L), respectively (Fig. 4.1) were not significantly different.

Table 4.3: Statistical summary of OPE concentrations (ng/L) and detection frequency (DF, %) in the three drinking water categories examined in our study

		Tap water (n=25)			Bottled water (n=25)		
OPE	**LOD**	**DF (%)**	**Range (mean)**	**95th Percentile**	**DF (%)**	**Range (mean)**	**95th Percentile**
TCEP	0.001	100	0.37 – 7.6 (3.0)	7.3	100	0.12 – 2.3 (0.60)	1.6
TCIPP	0.006	96	<LOD – 9.9 (2.9)	7.5	92	<LOD – 2.5 (1.02)	1.8
TDCIPP	0.004	68	<LOD – 0.40 (0.08)	0.18	36	<LOD – 0.17 (0.03)	0.14
TPHP	0.003	84	<LOD – 2.5 (0.64)	1.94	92	<LOD – 3.6 (0.59)	0.98
EHDPP	0.002	44	<LOD – 2.4 (0.23)	1.06	16	<LOD – 2.1 (0.16)	0.83
TnBP	0.006	16	<LOD – 5.5 (0.65)	4.2	0	<LOD	<LOD
TBOEP	0.013	72	<LOD – 13 (3.5)	12	72	<LOD – 11 (3.8)	8.4
TMTP	0.004	28	<LOD – 0.50 (0.10)	0.45	20	<LOD – 1.7 (0.15)	1.2
$\sum_8$OPEs			0.41 – 42 (11)	35		0.15 – 23 (6.4)	15

LOD: limit of detection

Table 4.4: Comparison of arithmetic mean (unless indicated otherwise) concentrations (ng/L) of OPEs in drinking water measured in this study with mean concentrations reported from other countries

Country (Sampling year)	Water type (n)	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TnBP	TBOEP	TMTP	Reference
China (2012)	Bottled water (n=8)	0.43	6.58	ND	6.95	ND	1.16	31.7	-	[16]
China (2014) [a]	Bottled water (n=23)	0.5	0.6	0.6	0.8	-	0.1	0.2	-	[14]
Korea (2014)	Bottled water (n=10)	16.4	79.6	-	0.99	-	4.24	64.4	-	[21]
United Kingdom (2022)	**Bottled water (n=25)**	**0.60**	**1.1**	**0.03**	**0.59**	**0.16**	**<0.01**	**3.8**	**0.15**	**This study**
China (2014)	Tap water (n=21)	48.5	43.0	5.8	1.4	-	9.5	3.7	-	[14]
China (2014)	Tap water (n=39)	14.1	20.3	ND	5.17	ND	3.39	3.67	-	[16]
Korea (2014)	Tap water (n=75)	25.3	10.7	-	1.98	-	4.29	10.7	-	[21]
USA (2016-2017)	Tap water (n=58)	0.45	11.6	4.76	3.72	0.29	2.47	10.2	-	[19]
Korea (2017)	Tap water (n=44)	39.5	49.4	2.00	23.0	-	11.8	43.9	-	[22]
China (2020)	Tap water (n=1)	0.31	8.99	-	7.47	0.63	6.15	-	-	[26]
China (2022) *	Tap water (n=47)	18.7	20.0	3.21	21.3	-	19.6	1.04	-	[28]
United Kingdom (2022)	**Tap water (n=25)**	**3.0**	**2.9**	**0.08**	**0.64**	**0.23**	**0.65**	**3.5**	**0.10**	**This study**
China (2014) [a]	Filtered drinking water (n=17)	9.1	6.7	0.5	0.2	-	0.9	0.3	-	[14]
USA (2006-2007) [a]	Drinking Water (n=15)	150	220	-	-	-	-[b]	-	-	[18]

Country (Sampling year)	Water type (n)	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TnBP	TBOEP	TMTP	Reference
China (2021) [a]	Drinking water (n=38)	27.8	218	NQ	1.11	ND	29.6	3.09	-	[29]
Spain (2008) [a]	Drinking water (n=28)	5	40	-	-	-	32	-	-	[20]
Korea (2014)	Drinking water (n=127)	38.8	67.0	4.46	2.12	0.54	3.40	26.1	-	[21]
China (2020)	Drinking water (n=25)	45.7	46.9	13.1	1.63	0.65	15.6	-	0.62	[27]
China (2014) [a]	Well water (n=19)	0.5	2.5	0.1	0.2	-	0.2	0.2	-	[14]
China (2014) [a]	Barrelled water (n=19)	6.9	8.0	0.5	0.2	-	0.1	ND	-	[14]
China (2020-2021)	Barrelled water (n=28)	0.16	0.14	-	-	-	-	-	-	[17]
China (2020-2021	Normal temperature water (n=53)	1.31	22.4	0.28	0.14	-	0.34	-	-	[17]
China (2020-2021	Hot water (n=53)	3.74	65.0	0.50	0.28	-	0.37	-	-	[17]

[a] Median value

ND = not detected

NQ = Not quantified (concentrations above the MLOD but lower that the method limit of quantification (MLOQ) is defined as NQ

- Publication year was assumed as the sampling year unless stated otherwise by the study authors

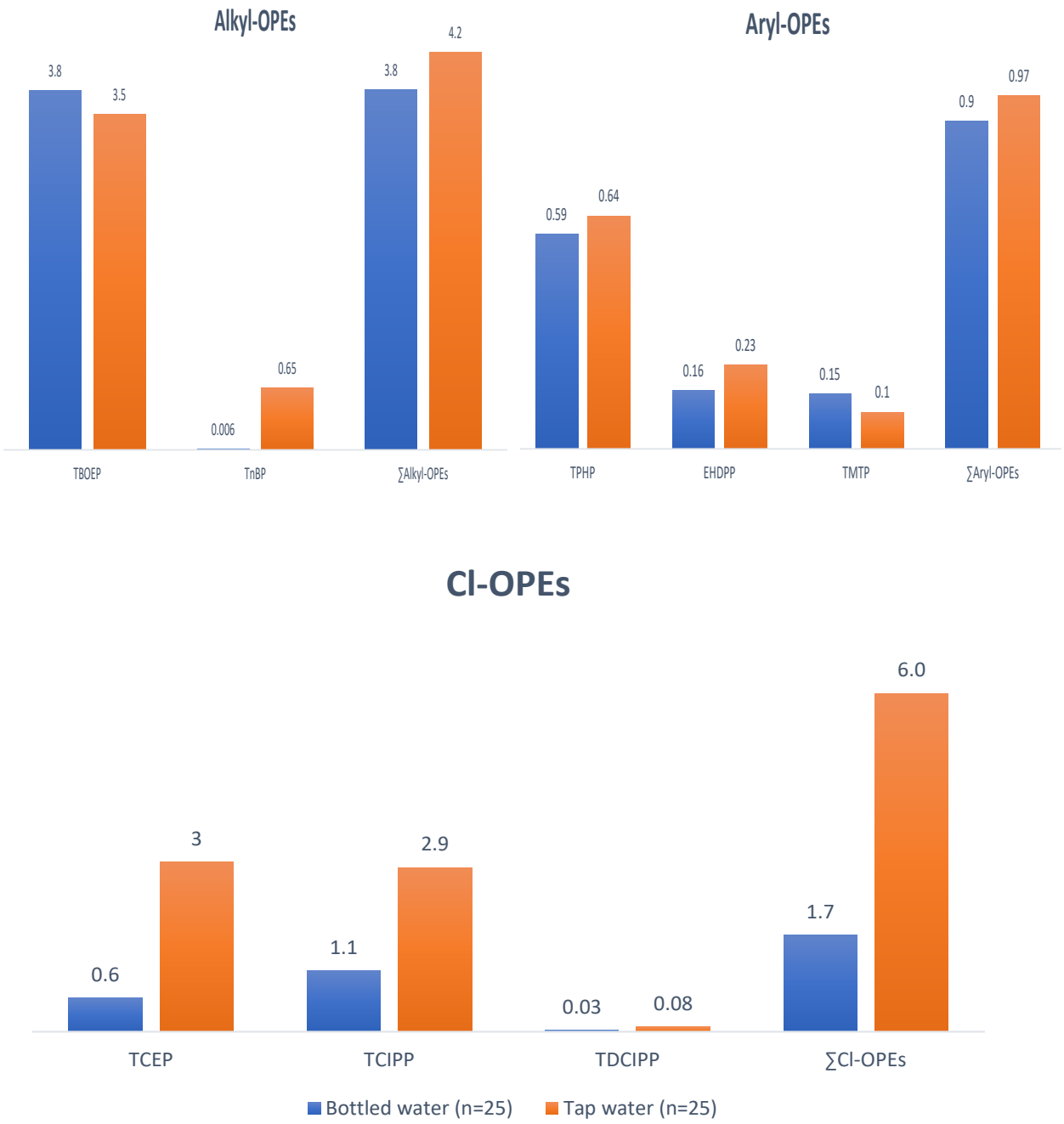


Fig. 4.1: Comparison of arithmetic mean concentrations (ng/L) of different categories of OPEs (chlorinated, aryl and alkyl) in two types of UK drinking water.

4.5.3 Potential sources of OPEs in UK drinking water

Spearman's correlation coefficients for the OPEs determined in the drinking water samples are presented in Table 4.5. Spearman's correlation has been used previously for OPE source

identification in the environment [32,33]. Most of the OPEs showed a positive correlation with each other. Significant positive correlations were observed between TCEP and: TCIPP ($r = 0.562$, $p < 0.01$), EHDPP ($r = 0.458$, $p < 0.01$), and weak but not significant correlation with TDCIPP, TPHP and TnBP ($r = 0.243$-0.277) (Table 4.5), suggesting that these OPEs likely originate from a common source or shared similar transport mechanism in drinking water [32,34]. This is similar to reports for drinking water in China [26] where TCEP and TCIPP correlated significantly ($r = 0.40$, $p < 0.05$). Moreover, we also observed positive correlation between TDCIPP and: TPHP ($r = 0.323$, $p < 0.05$), EHDPP (0.366, $p < 0.01$), and TMTP ($r = 0.381$, $p < 0.01$), as well as a negative correlation between TDCIPP and TnBP ($r = -0.281$, $p < 0.05$) (Table 4.5). In contrast, TBOEP does not correlate with any other OPE measured, indicating the source(s) of TBOEP differ from those of the other OPEs targeted. These results were also corroborated with PCA results where the initial dimensional reduction and transformation of the data produces four components which explained 79.3% of the data variation (Table 4.6). The first principal component (PC-1) accounts for 23.8% of the total variation and was heavily loaded on three OPEs: TCEP (0.87), TCIPP (0.74) and EHDPP (0.61) (Table 4.6). This suggests similar contamination sources of these OPEs, which for the Cl-OPEs likely reflects their widespread use in polyurethane foam (PUF) for furniture, upholstery, and mattresses, and for building insulation [3]. The second component (PC-2) explains 21.1% of the total variance (Table 4.6) and is driven primarily by a high positive loading of 0.86 for TPHP and a strong negative loading of -0.81 for TnBP. The third component (PC-3) has high positive loadings for TMTP (0.92) and TDCIPP (0.63) and accounted for 18.9% of total variance. Figure 4.2 plots the first three PCs. In addition, the fourth component (PC-4) was driven substantially only by TBOEP (0.95) and explained 15.5% of the total variation (Table 4.6). This is consistent with the results of our correlation analysis and likely

reflects the use of TBOEP in floor polish, which is an application distinct from those of our other target OPEs.

Table 4.5: Spearman's correlation coefficients between OPEs in UK drinking water

Correlations									
OPEs		TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TnBP	TBOEP	TMTP
TCEP	Correlation Coefficient	1.000	.562**	.243	.276	.458**	.277	.051	-.071
	Sig. (2-tailed)		<.001	.089	.052	<.001	.051	.727	.625
TCIPP	Correlation Coefficient		1.000	.198	.069	.278	.235	-.132	-.086
	Sig. (2-tailed)			.174	.639	.053	.104	.367	.557
TDCIPP	Correlation Coefficient			1.000	.323*	.366**	-.281*	.013	.381**
	Sig. (2-tailed)				.022	.009	.048	.926	.006
TPHP	Correlation Coefficient				1.000	.074	-.212	.045	-.179
	Sig. (2-tailed)					.611	.139	.756	.213
EHDPP	Correlation Coefficient					1.000	.181	.047	.211
	Sig. (2-tailed)						.209	.747	.142
TnBP	Correlation Coefficient						1.000	.000	-.163
	Sig. (2-tailed)							1.000	.257
TBOEP	Correlation Coefficient							1.000	-.147
	Sig. (2-tailed)								.309
TMTP	Correlation Coefficient								1.000
	Sig. (2-tailed)								.
**. Correlation is significant at the 0.01 level (2-tailed).									
*. Correlation is significant at the 0.05 level (2-tailed).									

Table 4.6: Principal component analysis (after varimax rotation) showing contribution of statistically significant variables (in bold)

OPEs	Component				Communalities
	1	2	3	4	
TCEP	**0.869**	-0.084	-0.078	0.115	0.782
TCIPP	**0.741**	0.255	-0.017	-0.289	0.698
EHDPP	**0.608**	-0.357	0.371	0.268	0.707
TPHP	0.187	**0.855**	-0.205	-0.041	0.809
TnBP	0.227	**-0.807**	-0.296	-0.096	0.800
TMTP	-0.113	-0.073	**0.918**	-0.121	0.875
TDCIPP	0.357	0.320	**0.631**	0.384	0.775
TBOEP	-0.017	0.021	-0.018	**0.947**	0.898
Eigen-value	2.034	1.708	1.512	1.090	
% of variance explained	23.78	21.12	18.93	15.48	
Cumulative (%)	23.78	44.90	63.83	79.30	

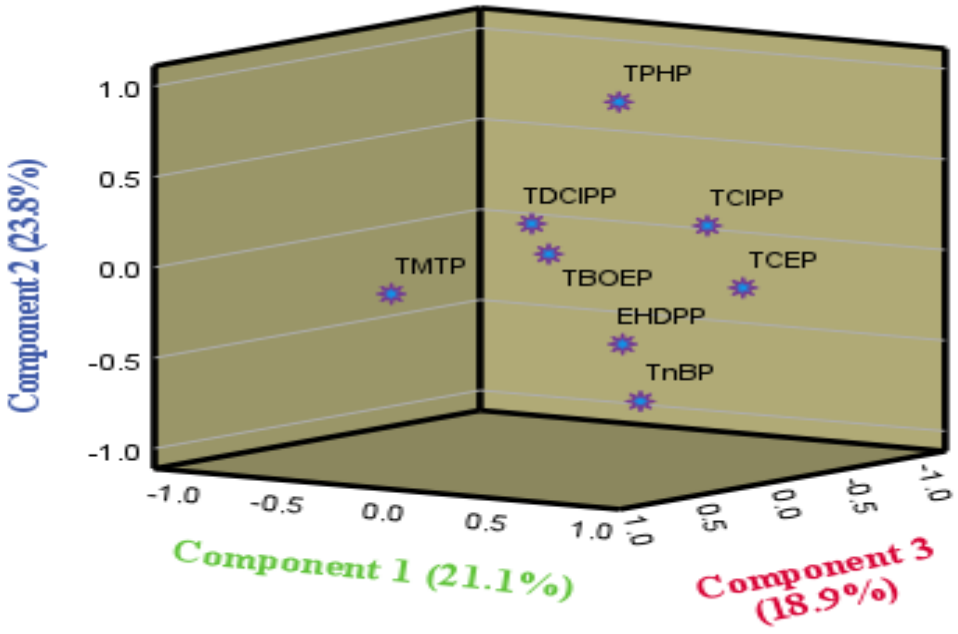


Fig. 4.2: Graphical representation of principal component analysis of OPE concentrations in UK drinking water

4.6 Exposure assessment of OPEs via drinking water

To evaluate the potential health risk of OPE exposure via ingestion of UK drinking water, the estimated daily intake (EDI) of OPEs was calculated (Table 4.7a-b, Fig 4.3). Under a normal exposure scenario (using mean concentrations), EDIs of $\sum_8$OPEs for infants, toddlers, children, and adults were 0.59, 0.29, 0.22 and 0.18 ng (kg of bw)$^{-1}$ day^{-1} for tap water and 0.34, 0.17, 0.13, and 0.10 ng (kg of bw)$^{-1}$ day^{-1} for bottled water respectively (see appendix 4.2 and 4.3). The relative contribution of the individual OPEs to the total EDI via the ingestion of the drinking water for the four age-groups are presented in Fig. 4.4 and Fig. 4.5 Daily intakes of $\sum_8$OPEs via tap water ingestion for the four age groups was between 41 - 44 % higher than those for bottled water (Table 4.7a and 4.7b). This concurred with several other studies that reported higher daily intake of $\sum$OPEs for tap water in China (7.07 – 7.7 ng (kg of bw)$^{-1}$ day^{-1}) [14,16,28], and in South Korea (254 ng/person/day) [22]. Our mean EDIs for $\sum_8$OPEs in tap water for adults (0.18 ng (kg of bw)$^{-1}$ day^{-1}) and children (0.22 ng (kg of bw)$^{-1}$ day^{-1}) were below those reported in drinking water from China [14] for adults (7.07 ng (kg of bw)$^{-1}$ day^{-1}) and children (boy: 6.95 ng. kg of bw)$^{-1}$ day^{-1}; girl: 6.8 ng kg of bw)$^{-1}$ day^{-1}, respectively. Table 4.8 compares our EDIs with those reported for drinking water from other studies, as well as EDIs for other exposure pathways in UK. Our data reveals that infants (mean exposure: 0.93 ng/kg bw/day; high-end exposure: 6.4 ng/kg bw/day) have a higher daily exposure to our target OPEs via drinking water than toddlers (mean: 0.46 ng/kg bw/day; high-end exposure: 3.1 ng/kg bw/day) and children (mean: 0.35 ng/kg bw/day; high-end: 2.3 ng/kg bw/day) with the least exposed being adults (mean: 0.28 ng/kg bw/day; high-end exposure: 2.1 ng/kg bw/day), respectively (Table 4.9; Table 4.10). This exposure risk trend is essentially driven by differences between the age groups in the water consumption rates normalised to body weight. The total estimated daily intake of $\sum_8$OPEs attributable to UK drinking water were lower than

those reported from different other countries (Table 4.8). Moreover, the fact that higher EDIs were reported in the drinking water from other countries than the UK, may be because of the small sample size in this study. Therefore, analysis of a greater number of UK drinking water samples is required. We also compared our data for exposure of the UK population to individual OPEs via drinking water with other pathways of human exposure to OPEs. A summary of our drinking water ingestion exposure data in comparison with other exposure pathways is presented in Table 4.8. This shows that UK population's exposure to OPEs via drinking water for all age groups was below the reported values for other exposure pathways but nonetheless represents an appreciable human exposure pathway, especially for infants, toddlers, and children.

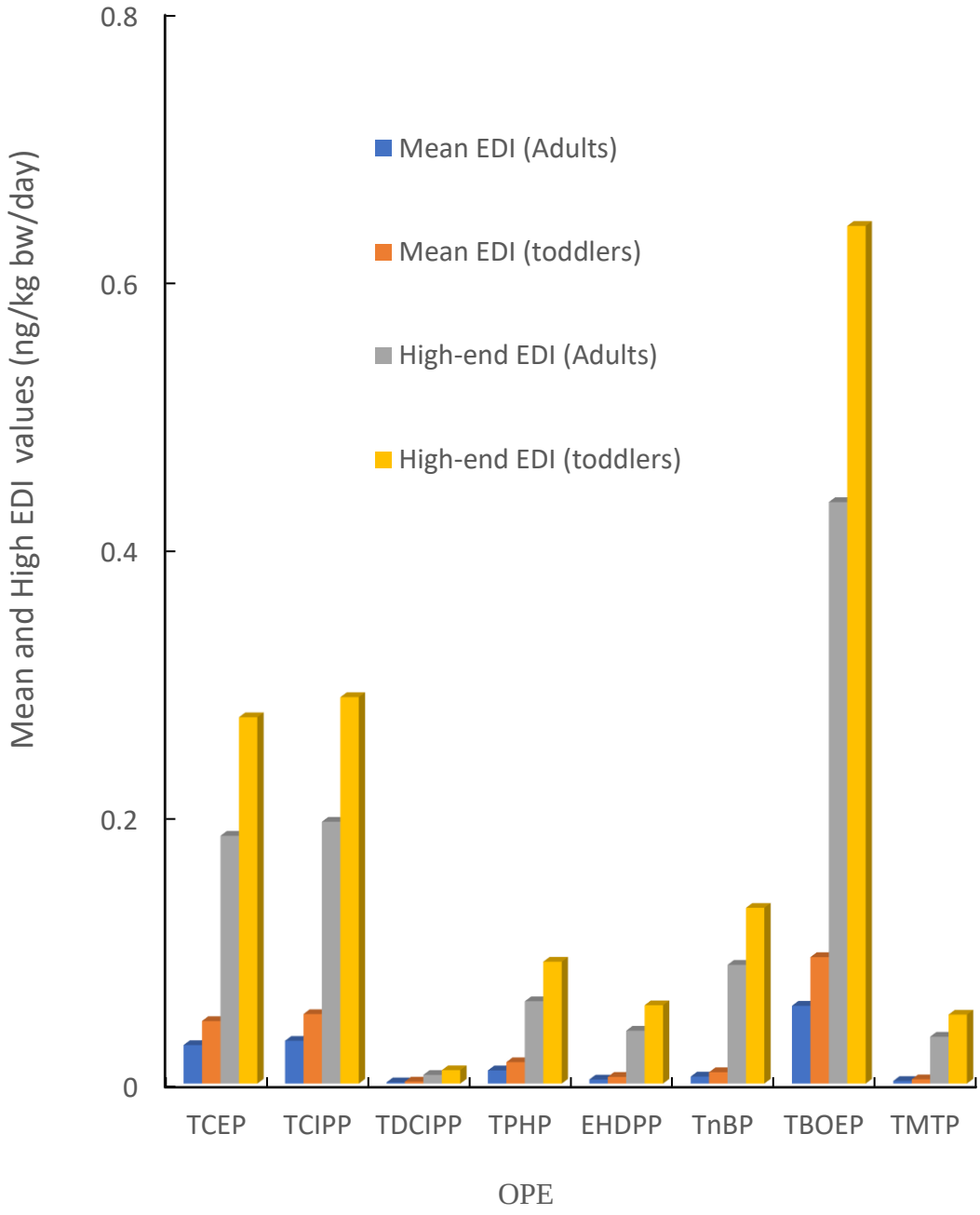


Fig. 4.3: Average and high exposure EDI values (ng/kg bw/day) of individual OPEs via drinking water for adults and toddlers (EDIs plotted represent the average of those obtained for ingestion of tap and bottled water)

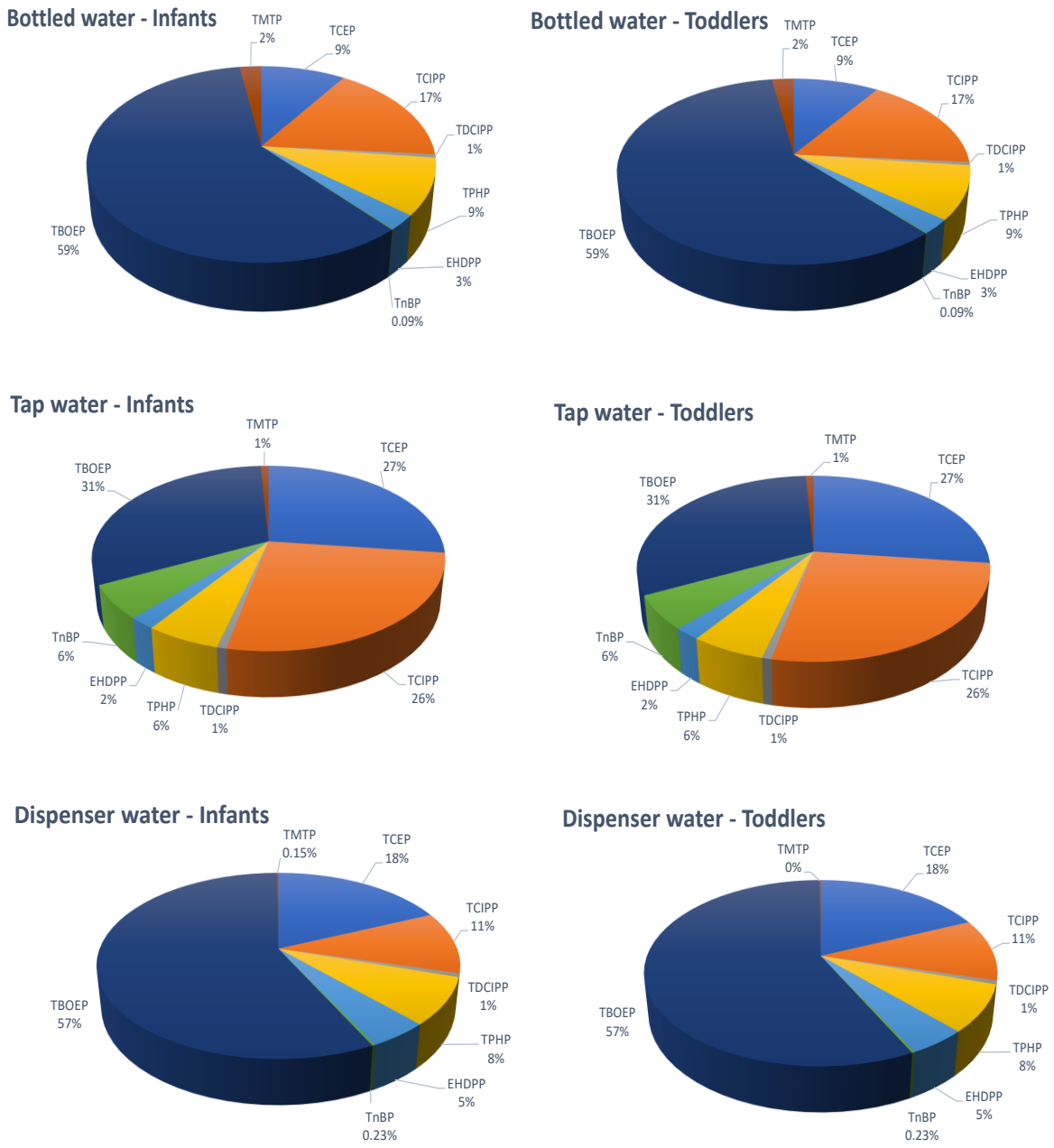


Fig. 4.4: Relative contribution of the individual OPEs to the total EDI via the ingestion (ng/kg bw/day) of the three-drinking water for infants and toddlers

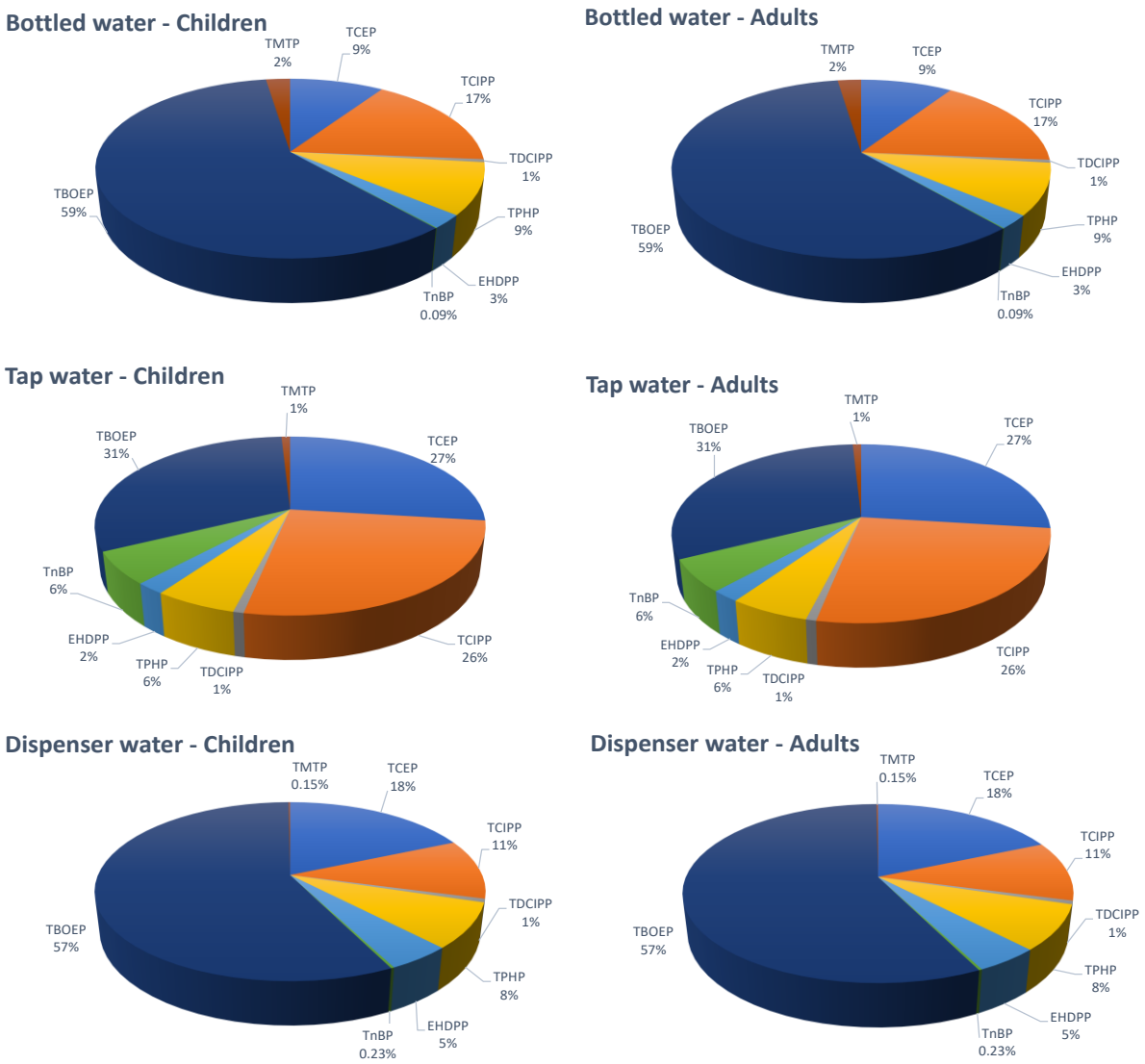


Fig. 4.5: Relative contribution of the individual OPEs to the total EDI (ng/kg bw/day) via the ingestion of the three-drinking water for children and adults

Table 4.7a: Estimated daily intake of OPEs via bottled water ingestion (ng (kg of bw)$^{-1}$ day^{-1})

OPEs	Infants		Toddlers		Children		Adults	
	Mean	95th Percentile	Mean	95th Percentile	Mean	95th Percentile	Mean	95th Percentile
TCEP	0.032	0.199	0.015	0.096	0.012	0.073	0.010	0.065
TCIPP	0.057	0.235	0.028	0.113	0.022	0.085	0.017	0.076
TDCIPP	0.002	0.019	0.001	0.009	0.001	0.007	0.001	0.006
TPHP	0.031	0.126	0.015	0.061	0.012	0.046	0.009	0.041
EHDPP	0.008	0.107	0.004	0.052	0.003	0.039	0.002	0.035
TnBP	0.000	0.001	0.000	0.0004	0.000	0.000	0.0001	0.0003
TBOEP	0.199	1.081	0.098	0.519	0.075	0.394	0.060	0.352
TMTP	0.008	0.157	0.004	0.075	0.003	0.057	0.002	0.051
∑OPEs	0.338	1.924	0.166	0.925	0.127	0.701	0.102	0.627

Table 4.7b: Estimated daily intake of OPEs via Tap water ingestion (ng (kg of bw)$^{-1}$ day^{-1})

OPEs	Infants		Toddler		Children		Adults	
	Mean	95th Percentile	Mean	95th Percentile	Mean	95th Percentile	Mean	95th Percentile
TCEP	0.159	0.938	0.078	0.451	0.060	0.342	0.048	0.305
TCIPP	0.154	0.966	0.076	0.464	0.058	0.352	0.047	0.315
TDCIPP	0.004	0.023	0.002	0.011	0.002	0.008	0.001	0.007
TPHP	0.034	0.251	0.017	0.121	0.013	0.091	0.010	0.082
EHDPP	0.012	0.136	0.006	0.065	0.005	0.050	0.004	0.044
TnBP	0.034	0.545	0.017	0.262	0.013	0.199	0.010	0.177
TBOEP	0.186	1.584	0.091	0.761	0.070	0.577	0.056	0.516
TMTP	0.005	0.058	0.002	0.028	0.002	0.021	0.002	0.019
∑OPEs (SUM)	0.589	4.50	0.289	2.164	0.222	1.640	0.178	1.466

Table 4.8: Comparison of the estimated daily intake (EDI, ng (kg of bw)$^{-1}$ day^{-1}) of OPEs via drinking water for different countries and with other pathways in the UK.

Exposure Pathway	Number of OPEs	Country	EDI toddlers		EDI children		EDI adults		Reference
			Mean	95th %ile	Mean	95th %ile	Mean	95th %ile	
Drinking water ingestion	8	United Kingdom	0.46	3.1	0.35	2.3	0.28	2.1	This study
Drinking water ingestion [a]	3	Korea	2.55	16.5	2.10	13.6	1.81	11.8	[21]
Drinking water ingestion	9	China	-	-	6.88	11.3	6.56	10.7	[14]
Drinking water ingestion [a]	5	China	-	-	4.37	37.2	4.14	35.5	[15]
Drinking water ingestion	11	China	1.65	114	0.65	44.6	0.93	64.5	[17]
Drinking water ingestion	8	China	-	-	3.22	-	3.27	-	[28]
Food ingestion	8	UK	420	1547	155	836	62.3	278	[35]
Dermal absorption	3	UK	15.5 – 36	293	-	-	4.1-25.1	36.9	[36,37]
Air inhalation	8-20	Germany, China, USA and Norway	ND-2.4	ND	ND-273	ND-916	0.41-170	ND-570	[38-41]
Dust ingestion [a]	7	UK	-	-	70	1740	1.3	28	[42]

Note: ND means not detected

[a] Median concentrations

Table 4.9. Estimated daily drinking water ingestion data (mean and – in parentheses - high-exposure scenario (ng/kg bw/day) for OPEs and their corresponding reference doses (RfDs)

Age group	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TBOEP	TnBP	TMTP	∑OPEs
Infants (1 to < 3 months)	0.19 (1.1)	0.21 (1.2)	0.01 (0.04)	0.07 (0.38)	0.02 (0.24)	0.39 (2.7)	0.03 (0.55)	0.01 (0.22)	0.93 (6.4)
Toddlers (2 to < 3 years)	0.09 (0.55)	0.10 (0.58)	0.003 (0.02)	0.03 (0.18)	0.01 (0.12)	0.19 (1.3)	0.02 (0.26)	0.01 (0.10)	0.46 (3.1)
Children (11 to < 16 years)	0.07 (0.41)	0.08 (0.44)	0.002 (0.02)	0.03 (0.14)	0.008 (0.09)	0.15 (0.97)	0.01 (0.20)	0.005 (0.08)	0.35 (2.3)
Adults (≥ 21 years)	0.06 (0.37)	0.06 (0.39)	0.002 (0.01)	0.02 (0.12)	0.006 (0.08)	0.12 (0.87)	0.011 (0.18)	0.004 (0.07)	0.28 (2.1)
RfD (ng/kg bw/day) [a]	7000	10000	20000	NA	NA	NA	10000	NA	
RfD (ng/kg bw/day) [b]	2200	8000	1500	7000	600 [d]	1500	2400	NA	
RfD (ng/kg bw/day) [c]	22000	80000	15000	70000	NA	15000	24000	NA	
RfD (ng/kg bw/day) [e]	NA	3600	NA	NA	NA	NA	NA	NA	

[a] Reference dose (RfD) values of [43]

[b] [44]

[c] [45]

[d] [46]

[e] [47]

NA = Not available.

4.6.1 Risk assessment of OPEs via drinking water

To evaluate the health risks of OPEs via drinking water in UK, the ∑EDI values for $\sum_8$OPEs for infants, toddlers, children, and adults were compared with different oral reference doses (RfDs) available in the literature. Specifically, these are: those of [44,45], those promulgated by the [43] (Table 4.9), as well as published RfDs for TCIPP [47] and EHDPP [46]. The mean and high exposure EDI values for $\sum_8$OPEs for infants (0.93 and 6.4 ng (kg of bw)$^{-1}$ day^{-1}), toddlers (0.46 and 3.1 ng (kg of bw)$^{-1}$ day^{-1}), children (0.35 and 2.3 ng (kg of bw)$^{-1}$ day^{-1}), and

adults (0.28 and 2.1 ng (kg of bw)$^{-1}$ day^{-1}) (Table 4.9) were several order of magnitude below the reference dose values provided by [43-47].

To evaluate the overall human exposure to OPEs in UK, the present study examined the combined mean and high-end human exposure to OPEs for adults and toddlers in UK drinking water with exposure data for dust ingestion for adults [42] and toddlers [48], dermal uptake for adults and toddlers [37] – while the high-end exposure estimate for dermal uptake for adults was obtained from [36], with the recent UK dietary intake exposure data [35]. The available dermal uptake exposure data for only three Cl-OPEs (TCEP, TCIPP and TDCIPP) were used for this combined exposure risk assessment as there is no available data for all other OPEs for all age groups. A further important point for future studies is that there is no UK data for OPEs exposure via air inhalation for all age groups [35]. Based on the available UK OPEs exposure data for the other exposure pathways (dust ingestion, dermal and food ingestion), the combined exposure risk for UK population was evaluated for adults and toddlers for five OPEs (TCEP, TCIPP, TDCIPP, TPHP and EHDPP). For adults, these EDIs for mean and high-end exposure via these four pathways combined were as follows: TCIPP (mean = 26, high-end: 52 = ng/kg bw/day) > EHDPP (14 and 46 ng/kg bw/day) > TPHP (10 and 44 ng/kg bw/day) > TDCIPP (6.8 and 22 ng/kg bw/day) > TCEP (4.1 and 21 ng/kg bw/day) (see appendix 3.3). However, for toddlers, the combined EDIs were: TCIPP (mean = 296, high-end = 1340 ng/kg bw/day) > EHDPP (126 and 335 ng/kg bw/day) > TPHP (123 and 309 ng/kg bw/day) > TDCIPP (24 and 123 ng/kg bw/day) > TCEP (17 and 95 ng/kg bw/day) (Table 4.10 and see appendix 4.4).

Our results for the combined exposures for adults and toddlers were still below the reference dose values ($\sum$EDIs <<< RfDs) cited in Table 4.10 and appendix 4.4 [43-47]. However, for some OPEs, ΣEDIs approached one or more of the RfD values. This may be expressed quantitatively as the hazard quotient (HQ) which represents the ratio of the ΣEDI to the RfD. There is a significant exposure risk for OPEs with HQ $\geq$ 1, a situation where the exposure

matches or exceeds the RfD value. As an illustration, Table 4.10 shows the HQ values for toddlers under the average and high-end exposure scenario, and those adults are provided in appendix 4.4 respectively. While HQ values did not exceed 1 for any of our target OPEs; for toddlers, those for EHDPP were: 0.21 (mean) and 0.56 (high-end) using the RfD value of 600 ng/kg bw/day [46]. Also for toddlers, those for TCIPP ranged from 0.03 (mean) to 0.37 (high-end) depending on which RfD value was used, while a maximum HQ value of 0.08 was obtained for TDCIPP when high-end toddler exposure was compared to an RfD of 1500 ng/kg bw/day [44] (see appendix 4.4). This shows that of our target OPEs, exposure risk to UK toddlers is greatest for EHDPP, TCIPP, and to lesser extent TDCIPP (Table 4.10), and for EHDPP and TCIPP is within an order of magnitude of one or RfD values. It should also be noted that our ΣEDIs do not include inhalation exposure, which will further erode the margin of safety between exposure and the RfD.

Table 4.10: Average and high exposure risk estimates (ng/kg bw/day) for toddlers in the UK via dust ingestion, dermal absorption, dietary intake, and water ingestion combined

Toddlers (average)	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**
Dust – [48] [a]	3.55	262	3.06	6.13	9.65
Food – [35]	12.5	19.4	20.5	117	116
Dermal – [37]	1.2	14.3			
Drinking water (this study)	0.09	0.10	0.003	0.03	0.01
SUM	**17**	**296**	**24**	**123**	**126**
RfD [43]	7000	10000	20000		
RfD [44]	2200	8000	1500	7000	600 [b]
RfD [45]	22000	80000	15000	70000	NA
RfD [47]	NA	3600	NA	NA	NA
HQ based on RfD value provided by [43]	0.0025	0.030	0.0012	-	-
HQ based on RfD value provided by [44]	0.0079	0.037	0.016	0.018	0.21 [b]
HQ based on value provided by [45]	0.00079	0.0037	0.0016	0.0018	NA
HQ based on RfD value provided by [47]	NA	0.082	NA	NA	NA
High-end exposure					
Dust – [48] [a]	14.2	1049	12.2	24.5	38.6
Food – [35]	41.6	71.5	74.2	284	296
Dermal – [36]	38.6	218	37		
Drinking water - (this study)	0.55	0.58	0.02	0.18	0.12
SUM	**95**	**1340**	**123**	**309**	**335**

HQ based on RfD value provided by [43]	0.014	0.13	0.0062	-	-
HQ based on RfD value provided by [44]	0.043	0.17	0.082	0.044	0.56 [b]
HQ based on RfD value provided by [45]	0.0043	0.017	0.0082	0.0044	-
HQ based on RfD value provided by [47]		0.37 [a]			

NA = Not available

[a] Median EDI values

[b] [46]

4.7. Conclusion

This study provides the first data on concentrations of OPEs in UK drinking water (comprising tap and bottled water). The most abundant OPEs detected in UK tap water were: TCEP (range: 0.37-7.6 ng/L; average: 3.0 ng/L), TCIPP (range: <LOQ – 9.9 ng/L; average: 2.9 ng/L), TPHP (range: <LOQ – 2.5 ng/L; average: 0.64 ng/L), and TBOEP (range: <LOD – 13 ng/L; average: 3.5 ng/L). Our data shows that tap water was the most contaminated with chlorinated OPEs (TCEP and TCIPP), aryl-OPEs (TPHP and EHDPP), and alkyl-OPEs (TBOEP). Comparison of our drinking water data with other exposure pathways to OPEs in the UK, reveals drinking water ingestion poses a lower exposure risk to OPEs than through dermal uptake, food, and dust ingestion. Estimated exposure of the UK population to $\sum_8$OPEs via drinking water was of the order: infants (mean: 0.93; high-end: 6.4 ng/kg bw/day) > toddlers (mean: 0.46; high-end: 3.1 ng/kg bw/day) > children (0.35; high-end: 2.3 ng/kg bw/day) > (0.28; high-end: 2.1 ng/kg bw/day). While estimated exposure to OPEs via drinking water fell well below reference dose values; the combined exposure of the UK population via: dermal uptake, drinking water, dust, and food ingestion revealed exposure to be within an order of magnitude of the respective RfDs for: EHDPP and TCIPP for toddlers. Overall, UK drinking water ingestion is an appreciable source of human exposure to OPEs, representing a small but significant addition to overall human exposure.

4.8 References

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CHAPTER V

Presence, source attribution, and human exposure to organophosphate esters in indoor dust from various microenvironments in Nigeria

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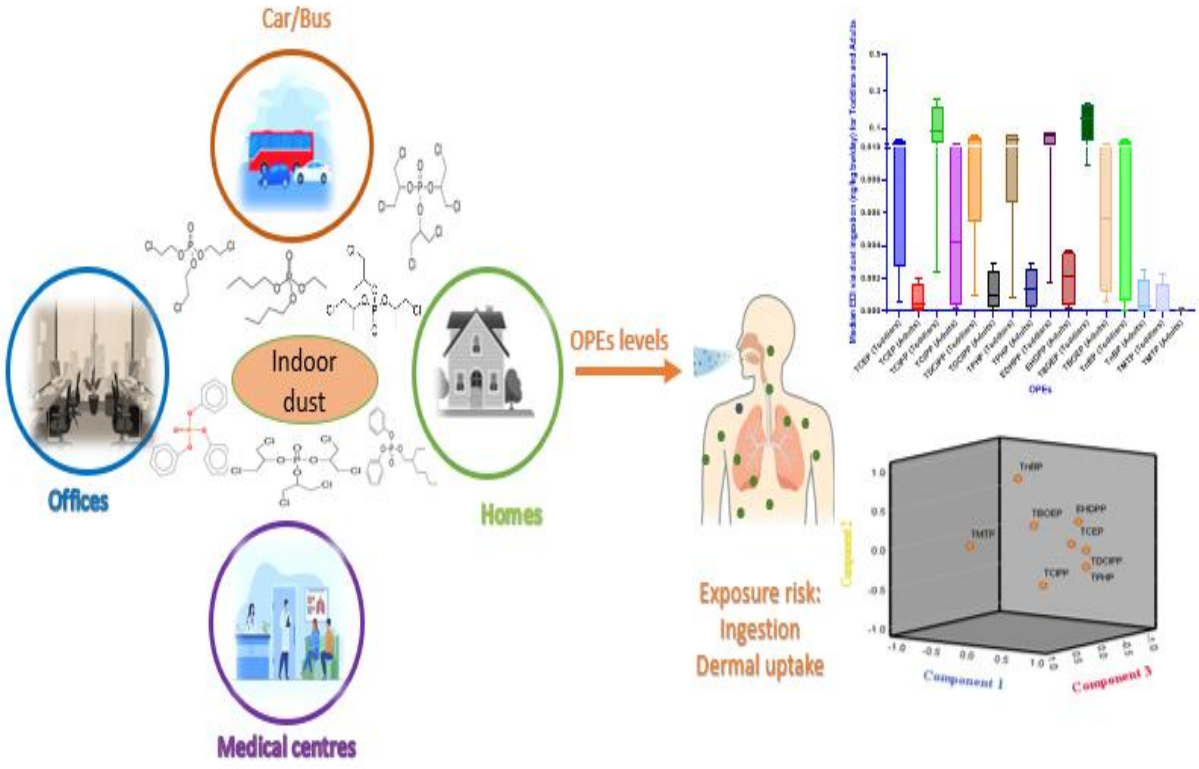
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Graphical abstract



5.1 Abstract

To date, only three studies have reported the presence of the organophosphate esters (OPEs) in the African environment. This is the first study to document the concentrations, profiles, and human exposure to eight organophosphate esters (OPEs) in indoor dust from various microenvironments in Nigeria, specifically: cars/buses (n = 10), homes (n = 20), offices (n = 20), and medical centres (n = 14). Concentrations of OPEs in these indoor dust samples were among the lowest reported internationally. Concentrations of $\sum_8$OPEs varied substantially between individual samples and the predominant OPEs were: tris(2-butoxyethyl) phosphate (TBOEP) (detection frequency (DF) = 90 - 100%), tris(1-chloro-2-propyl) phosphate (TCIPP) (DF = 100%), and 2-ethylhexyl-diphenyl phosphate (EHDPP) (DF = 100%). There were no significant differences ($p > 0.05$) between $\sum_8$OPEs concentrations in dust samples from

cars/buses (average = 295 ng/g), offices (231 ng/g), homes (277 ng/g), and medical centres (127 ng/g). Concentrations of chlorinated OPEs: tris(2-chloroethyl) phosphate (TCEP), TCIPP, and tris(1,3-dichloro-2-propyl) phosphate (TDCIPP) were significantly correlated with those of triphenyl phosphate (TPhP), EHDPP, and TBOEP. Estimated daily intakes (EDI) of target OPEs via indoor dust ingestion and dermal absorption were lower than the corresponding reference dose (RfD) values and indicated that exposure to the studied OPEs in the indoor environment does not pose a significant health risk for the general population in Nigeria, even under a high-end exposure scenario.

Keywords: Organophosphate esters, indoor dust, Africa, vehicles, homes, offices, medical centres.

5.2 Introduction

Due to concerns about the toxicity and bioaccumulation potential of brominated flame retardants (BFRs), that have led to bans and restrictions on the manufacture and new use of polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCDD); production and use of organophosphate esters (OPEs) as alternative flame retardants (FRs) has grown [1]. OPEs represent a heterogeneous class of phosphoric acid esters in which the hydrogen in the phosphate group is replaced by an alkyl, aryl, or chlorinated group [2]. As of 2016, OPEs represented the second most produced flame retardants (FRs) reaching 18% of the total global market [3], with a substantial increase reported in global consumption of OPEs from 680,000 t in 2015 to 2,800,000 t in 2018 [4-6]. As a result of their release from commercial and industrial products, OPEs have been detected in diverse indoor and outdoor environmental matrices, such as: air and dust [7-11], drinking water and sediments [5, 12-15], soil [16,17], food [18-23], as well as handwipes and wristbands [24]. Furthermore, human biomonitoring

studies have detected OPEs in human tissues or biological fluids and other non-invasive matrices [25,26].

Moreover, several toxicological studies have shown that some OPEs are neurotoxic, carcinogenic, and endocrine disruptors. For instance, tris(2-chloroethyl) phosphate (TCEP) and tris(1,3-dichloro-2-propyl) phosphate (TDCIPP) were reported to exhibit neurotoxic effects on PC12 cells [27]. TDCIPP also elicited developmental abnormalities and neurotoxicity in embryonic zebrafish [28], while TCEP has been shown to be carcinogenic to both rats and mice and classified as a Category 2 carcinogen by the European Union [29,30]. In addition, tri-n-butyl phosphate (TNBP) and triphenyl phosphate (TPhP) have been reported to be neurotoxic to zebrafish larvae and rats [31,32].

Indoor dust serves as a sink for many organic pollutants and its ingestion has been identified as a major human exposure pathway to emerging pollutants such as OPEs [11,33]. However, despite the mounting evidence of human exposure to and consequent adverse effects of OPEs, there remains scarce information on their presence in indoor environments in developing countries. To our knowledge, only three studies have determined human exposure to OPEs via indoor dust ingestion in Africa, specifically Egypt [10,34] and South Africa [9]. This study thus constitutes the first report of concentrations of OPEs in indoor dust from domestic and non-domestic microenvironments (offices, cars, medical centres, and homes) in Nigeria. The aims of the present study are to: (i) investigate the concentrations and profiles of target OPEs in indoor dust from Nigeria, (ii) compare the concentration profiles of OPEs in different microenvironments (cars, offices, medical centres, and homes), (iii) evaluate possible sources of OPEs in Nigerian indoor dust, and (iv) derive estimates of human exposure to OPEs via indoor dust in Nigeria and its potential human health implications.

5.3 Materials and Methods

5.3.1 Standards and reagents

Eight OPEs, comprising: TCEP, TCIPP, TDCIPP, TBOEP, TPHP, EHDPP, tri-n-butyl phosphate (TnBP), and tri-m-tolyl phosphate (TMTP); as well as two isotopically labelled internal (or surrogate) standards (TnBP-d_{27} and TPHP-d_{15}) and 2,3,4,6-tetrachlorobiphenyl (PCB-62) used as a recovery determination standard (RDS) (or syringe standard) were purchased from Wellington Laboratories, (Guelph, ON, Canada). The purity of all analytical standards was > 98 % except for TBOEP (> 94%). The physicochemical properties of our target OPEs are provided in appendix 5.1. HPLC-grade n-hexane (HEX, 95%), ethyl acetate (ETAC, 99.8%), dichloromethane (DCM, 99.8%), iso-octane (ISOC, 99.5%) and acetone (ACE, 99.8 %) were purchased from Fisher Scientific (Loughborough, UK) and Sigma-Aldrich (St Louis, MO, USA). Indoor dust standard reference material SRM 2585 was purchased from the US National Institute of Standards and Technology (NIST, Gaithersburg, MD, USA). Hypersep Florisil® SPE cartridges were purchased from Thermo Scientific (Rockwood, USA), and the nitrogen gas used for solvent evaporation was purchased from BOC gases, United Kingdom.

5.3.2 Sampling Methods

A total of 64 indoor dust samples were collected from offices (n = 20), cars and buses (n = 10), homes (n = 20) and medical centres (n = 14) between July 2021 to September 2021 in Ijebu-Ode in Ogun State and Lagos State in Southwest Nigeria. Surface dust from offices, homes, and medical centres were collected using paintbrushes (prewashed with hexane and dichloromethane) from elevated surfaces such as tables and shelves as well as from air conditioning and electronic control panels (TVs and radios) with which the occupants have daily contact. For cars and buses, indoor dust was collected from the interior according to a modified version of the protocol reported by [35]. At the time of sampling the daily temperature

was between 24 - 32° C and information on potential sources of OPEs in each sampled indoor environment was recorded (see appendix 5.2). Following collection, dust samples were wrapped in aluminium foil [36], transferred to individual zip lock bags, stored at -20 °C and carefully conveyed to the University of Birmingham, UK for extraction and GC-MS analysis. At the University of Birmingham, dust samples were passed through a 500 μm mesh sieve and homogenised thoroughly prior to extraction and analysis.

5.3.3 Sample extraction and clean-up

Accurately weighed aliquots (~ 100 mg) of the homogenised dust samples were extracted according to the method described by [37]. Samples were spiked with internal (surrogate) standard mixture containing 50 ng of isotopically labelled TnBP-d_{27} and TPhP-d_{15} and extracted using 4 mL of hexane: acetone (3:1 v/v) by a combination of vortexing (2 mins) and ultrasonication extraction (5 mins) in three cycles. After each extraction cycle, dust extracts were centrifuged at 3,500 rpm for 5 min and the supernatants collected and transferred into clean glass tubes. Pooled supernatants were evaporated to incipient dryness under a gentle nitrogen flow and resolubilised in 1 mL of hexane. These concentrates were fractionated into two fractions using Hypersep Florisil® cartridges conditioned with 6 mL of hexane. Extracts were quantitatively transferred to the cartridge, and eluted with 8 mL hexane (F1, discarded) followed by 10 mL ETAC (F2) which contained the target OPEs. The second fraction (F2) was evaporated to incipient dryness and resolubilised in 100 μL of 500 pg/μL of PCB-62 in isooctane as recovery determination or (syringe) standard. These final extracts were transferred into glass vials and analysed using GC-EI/MS. Details information on the instrumental analysis are presented in our previous paper (Gbadamosi et al., 2022)

5.3.4 QA/QC

Quality assurance and control checks were carried out using indoor dust standard reference material (SRM 2585). Two procedural blanks (without dust samples) and one indoor dust standard reference material (SRM 2585) were analysed for each batch of ten dust samples to evaluate the accuracy and precision of the method. In addition, five field blanks (comprising ~ 0.5 g of sodium sulfate treated as a dust sample following the same sampling method) were analysed to check for background contamination from the materials used for sampling and storage. Among the OPEs analysed, only TCEP was detected in the blanks at between 5 and 20% of the concentration detected in samples. Thus, the mean concentration of TCEP detected in the blanks from the same batch was subtracted from the raw TCEP concentration in the samples for each batch. Average recoveries of 79 ± 1.2 % and 93 ± 3.0 % were obtained for TBP-d_{27} and TPHP-d_{15} respectively (Table 5.1). OPE recoveries from anhydrous sodium sulfate spiked at 50 ng of each native target OPE range from 87 – 102.3 % with a relative standard deviation < 20% (n = 5). A 5-point calibration plot was constructed with OPE standard solutions in the concentration range 50 pg/µL – 750 pg/µL, with excellent linear response coefficients (r^2 > 0.99). Moreover, the relative standard deviations of the relative response factors (RRFs) in the five calibration standards were below 6%. For every ten samples, a 500-pg/µL OPE standard mixture was injected to check instrumental stability and calibration. Instrumental limits of detection (LODs) and limits of quantification (LOQ) were set at a signal to noise ratio of 3 and 10, respectively (Table 5.1). For target OPEs not detected in the blanks, sample LOQs were calculated based on a signal-to-noise ratio of 10:1. For TCEP which was detected in blanks, the LOQ was calculated as the three times the standard deviation of the blank value divided by the mass of dust typically used for analysis (~ 100 mg) [10]. A further quality control check was achieved via replicate analysis (n=7) of NIST SRM 2585 (organic contaminants in house dust). Results showed good accuracy and precision of the method

compared to concentrations of our target OPEs reported previously for NIST SRM 2585 [10,34,38-41] (Table 5.2).

Table 5.1: Internal standard recovery, blank concentrations, and limit of detection (LOD) and limit of quantification of OPEs

Target OPES	Internal standard	Range of IS Recovery (%) (mean ± SD, RSD %) (n=4)	Na_2SO_4 IS recovery (%) (n=5) (50 ng/µL)	Procedural Blanks (ng/g) (n=13)	LOD (pg/injection)	LOQ (pg/injection)
TnBP	d_{27}-TnBP	77.4 – 80.3 (92 ± 1.24 1.35)	93.1-102.3 (96.1±3.5)	ND	0.30	37.2
TCEP	d_{27}-TnBP	77.4 – 80.3 (92 ± 1.24 1.35)	93.1-102.3 (96.1±3.5)	0.58 ± 0.18	0.72	89.0
TCIPP	d_{27}-TnBP	77.4 – 80.3 (92 ± 1.24 1.56)	93.1-102.3 (96.1±3.5)	ND	0.95	119
TDCIPP	d_{15}-TPHP	91.0 – 97.4 (93.2 ± 3.01, 3.23)	87.0 – 92.6 (90.4±6.3)	ND	0.62	64.0
TPHP	d_{15}-TPHP	91.0 – 97.4 (93.2 ± 3.01, 3.23)	87.0 – 92.6 (90.4±6.3)	ND	0.31	32.3
EHDPP	d_{15}-TPHP	91.0 – 97.4 (93.2 ± 3.01, 3.23)	87.0 – 92.6 (90.4±6.3)	ND	0.38	39.3
TBOEP	d_{15}-TPHP	91.0 – 97.4 (93.2 ± 3.01, 3.23)	87.0 – 92.6 (90.4±6.3)	ND	9.32	968
TMTP	d_{15}-TPHP	91.0 – 97.4 (93.2 ± 3.01, 3.23)	87.0 – 92.6 (90.4±6.3)	ND	0.37	38.6

Table 5.2: Comparison of concentrations (ng/g dry weight) and standard deviation (SD) of OPEs in inorganic contaminants in-house indoor dust standard reference material® (SRM 2585) between different studies – Indicative values

OPEs	This study (n=6)	Certified values (NIST, 2018)	[39] (n=6)	[74] (n=5)	Harrad et al., 2016 (n=56)	[10] (n=5)	[41] (n=14)	He et al., 2017 (n=3)	Persson et al. (2018) (n=13)	[40] (n=3)	[34] (n=4)
	Mean ± SD, (RSD, %)	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
TCEP	923±38.5, (RSD =8.56)	925 ± 149	867 ± 88	930 ± 110	790 ± 110	720 ± 50	792 ± 127	550 ± 110	550 ± 99	1260±69	640±50
TCIPP	874±18.1 (RSD =5.89)	1120 ± 350	1043 ± 51	740 ± 60	900 ± 70	750 ± 120	944 ± 264	1000 ± 200	603 ± 110	1238±55	480±20
TDCIPP	1802±120 (RSD =12.3)	NA	1618 ± 114	2245 ± 490	1830 ± 140	1900 ± 110	1556 ± 529	1500 ± 240	1230 ± 240	2705±123	1910±20
TPHP	949±70.0 (RSD =7.37)	1190 ± 130	919 ± 43	1110 ± 100	980 ± 60	970 ± 50	1104 ± 99	870 ± 70	700 ± 130	1169±170	1260±50
EHDPP	1059±101 (RSD =9.58)	NA	812 ± 77	1219 ± 90	820 ± 60	880 ± 20	963 ± 202	1300 ± 170	741 ± 100	2223±504	ND
TBOEP	73094±9302 (RSD=12.7)	NA	ND	77152 ± 3600	ND	75000 ± 4200	73464 ± 32324	ND	ND	69023 ± 556	43900 ± 2900
TNBP	267±10.3 (RSD=3.85)	276 ± 3.6	219 ± 36	ND	180 ± 20	170 ± 20	269 ± 19	140 ± 20	185 ± 22	593 ± 24	ND
TMTP	256±27.2 (RSD=10.6)	NA	ND	ND	ND	ND	ND	ND	ND	ND	ND

ND = not determined, NA = not available

5.3.5 Data analysis

Descriptive statistics (mean, median, maximum, minimum, standard deviation, and the 95th percentile concentrations) were calculated using Microsoft 365 Excel, with IBM SPSS statistics version 28 used for: analysis of variance (ANOVA), correlational analysis (CA), principal component analysis (PCA), and hierarchical cluster analysis (HCA). The statistical distribution of the OPEs concentrations was evaluated in SPSS using the Shapiro-Wilk and Kolmogorov-Smirnov normality tests and found to be normally distributed (see appendix 5.3). PCA was performed with Kaiser-Meyer Olkin (KMO) test for sampling adequacy test and Bartlett's test of sphericity that was found to be significant ($p < 0.05$). Potential linear relationships between the variables were investigated using Pearson's rank correlation. The statistical differences between or within studied microenvironments were conducted using ANOVA. P-values lower than 0.05 ($p < 0.05$) were accepted as statistically significant. Hierarchical cluster analysis (HCA) was used for the identification and classification of variables with similar characteristics to a new group using the average linkage method. GraphPad prism was used for the box and whisker plots. Where the concentrations of a given OPE with detection frequency (DF > 50%) were below the LOQ, concentrations were assigned as half of the LOQ for that compound (<LOQ = 0.5 * LOQ). Then when the detection frequency (DF) of the target OPE was <50%, concentrations below LOQ were reported as f * LOQ, where f is the fraction of samples above LOQ. This was done to reduce the influence of non-detects on the estimated average concentrations and for other statistical analysis [10,42,43].

5.4 Estimated daily intake and exposure risk assessment

Concentrations of OPEs were used to determine human exposure via indoor dust ingestion in Nigeria for toddlers and adults using two exposure scenarios. These were: (i) average, where it is assumed that humans ingest dust contaminated at the average concentration at an average

ingestion rate of 50 and 20 mg day^{-1} for toddlers and adults respectively, and (ii) a high exposure scenario where it is assumed that humans ingest dust contaminated at the 95th percentile concentration and at a high-end ingestion rate of 200 and 50 mg day^{-1} for toddlers and adults respectively [10,44,45]. We also assumed 100% absorption of intake in the absence of experimental data for this parameter [46]. As a result of a lack of comprehensive data on time - activity patterns for the Nigerian population, we assumed that dust ingestion occurs pro rata to typical time activity patterns previously reported (i.e., for adults: 63.8% homes; 22.3% offices; 4.1 % cars; 5.1 % medical centres, and 4.7% outdoors; and for toddlers: 86.1 %, 5.1%, 4.1%, and 4.7% for homes, medical centres, cars, and outdoors [10,47,48]. The estimated daily intake (EDI) of OPEs via indoor dust ingestion and dermal uptake for toddlers and adults were calculated using equations (1) and (2) [39,40,49].

$$EDI_{ingestion} = \frac{C_{dust} x\ IngR_{dust} x AF_{gastro} x\ ITAP}{BW} \quad (1)$$

$$EDI_{dermal} = \frac{C_{dust} x\ DAS\ x\ ESSA\ x\ FA_{dermal}\ x\ ITAP}{BW} \quad (2)$$

In the algorithms above, C_{dust} is the concentration of OPEs in indoor dust (average and 95th percentile concentrations, ng/g); $IngR_{dust}$ is the indoor dust ingestion rate (average = 50 and 20 mg/day; high-end = 200 and 50 mg/day for toddlers and adults respectively) [10,46]; AF_{gastro} is the gastrointestinal absorption fraction (100% for all OPEs) [39,40,50], ITAP is the indoor time activity pattern given above and BW is the body weight (14 kg for toddlers and 80 kg for adults) [44]. DAS represents the dust adhered to skin rate which is 0.04 mg cm^{-2} and 0.01 mg cm^{-2} for toddlers and adults respectively [51,52]; ESSA is the exposed skin surface area for which the values assumed were: 2564 cm^2 and 4615 cm^2 for toddlers and adults respectively [8,49], and FA_{dermal} is the fraction of OPEs sorbed by the skin (TCIPP: 0.25; TCEP: 0.28; TDCIPP: 0.13 and 0.17 for TPHP, EHDP, TNBP and TBOEP [40,52].

5.5. Results and discussion

5.5.1 Total concentrations and profiles of OPEs in indoor dust from different microenvironments

Descriptive statistics of OPE concentrations in the four microenvironments studied are summarised in Table 5.3. Most target OPEs were detected in all microenvironments with a detection frequency (DF) of 100 %. However, TnBP was not detected in any samples from homes and its DF varies from 10 – 100 % for medical centres, offices, and cars/buses respectively. In addition, the DF of TMTP varies from 15 – 57 % in the studied microenvironments. Among the OPEs considered in this study, TBOEP displays the highest average concentrations with a DF of 100% in all four microenvironments. The range and average concentrations of TBOEP were: cars/buses (mean = 99; range: = 63 – 199 ng/g), offices (mean = 66; range = 1.4 – 257 ng/g), homes (mean = 88; range = 0.49 - 200 ng/g), and medical centres (mean = 53; range = 41 - 93 ng/g), representing between 28 - 41 % of the total OPE concentrations in the 4 microenvironments (Table 5.3; Fig. 5.1). This agrees with studies that reported elevated concentrations of TBOEP in Japanese house dust (average = 1.57×10^7 ng/g) [41] and Swedish office dust (average = 2.5×10^5 ng/g) [53]. This predominance of TBOEP may be attributed to its widespread use in floor finish and wax, paint, and glue.

Concentrations of $\sum_8$OPEs in Nigerian house dust (mean: 277; range: 24 - 956 ng/g; n = 20) are generally in line with those reported for: Egypt (average = 310 ng/g; n = 20) [10], Pakistan (average = 394 ng/g; n = 15; 138 ng/g; n = 25) [54,55], the Philippines (average: 387 ng/g; n = 34) [56], India (276 ng/g; n = 25) [55], and Colombia (374 ng/g; n = 45) [55]. In contrast, they are several orders of magnitude lower than those reported for Western countries. As observed by [10], the low concentrations of OPEs detected in house dust from Africa and some parts of Asia and South America may be attributed to factors such as: fewer fire safety regulations,

combined with the tropical nature of the climate in such regions which leads to increased ventilation of indoor environments e.g., via air-conditioning.

Table 5.3: Statistical summary of OPE concentrations (ng/g) and detection frequencies (DF, %) in indoor dust from Lagos, Nigeria

Microenvironment	Statistical Parameter	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TBOEP	TnBP	TMTP	∑OPEs
Cars/Buses (n=10)	Mean	8.2	71	18	19	37	99	26	17	295
	Median	6.3	73	13	16	37	80	24	<LOQ	250
	Standard deviation	5.0	18	19	8.6	6.8	45	7.7	30	140
	Minimum	3.8	38	6.7	12	30	63	19	<LOQ	173
	Maximum	21	103	69	42	53	199	40	83	612
	95^{th} percentile	16	96	48	32	48	176	39	70	449
	DF (%)	100	100	100	100	100	100	100	30	
Offices (n=20)	Mean	40	34	20	29	32	66	8.6	0.7	231
	Median	5.7	19	13	18	22	54	8	<LOQ	139
	SD	78	34	34	31	35	52	5	2	271
	Min.	1.9	5.1	1.8	2.6	2.6	1.4	1.4	<LOQ	17
	Max.	259	126	159	124	129	257	20	7.9	1082
	95^{th} percentile	216	97	43	77	102	111	16	4.4	573
	DF (%)	100	100	100	100	100	100	100	15	
Homes (n=20)	Mean	20	81	26	30	25	88	<LOQ	7.6	277
	Median	13	85	18	18	20	78	<LOQ	<LOQ	231
	SD	15	43	26	60	17	57	<LOQ	18	235
	Min.	3.5	12	2.6	0.015	5.8	0.49	<LOQ	<LOQ	24
	Max.	59	148	124	282	73	200	<LOQ	70	956
	95^{th} percentile	44	141	53	51	62	177	<LOQ	39	457
	DF (%)	100	100	100	95	100	90	0	30	
Medical centres (n=14)	Mean	3.5	13	6.2	5.4	23	53	14	9.1	127
	Median	3.3	13	4.7	4.6	9.7	49	13	13	110
	SD	1.1	2.7	5.4	2.8	47	13	2.7	8.8	83
	Min.	2.5	9.2	1.8	3.8	6.3	41	11	<LOQ	76

	Max.	6.7	19	24	15	184	93	20	25	386
	95^{th} percentile	5.2	17	14	9.2	81	73	18	22	220
	DF (%)	100	100	100	100	100	100	100	57	

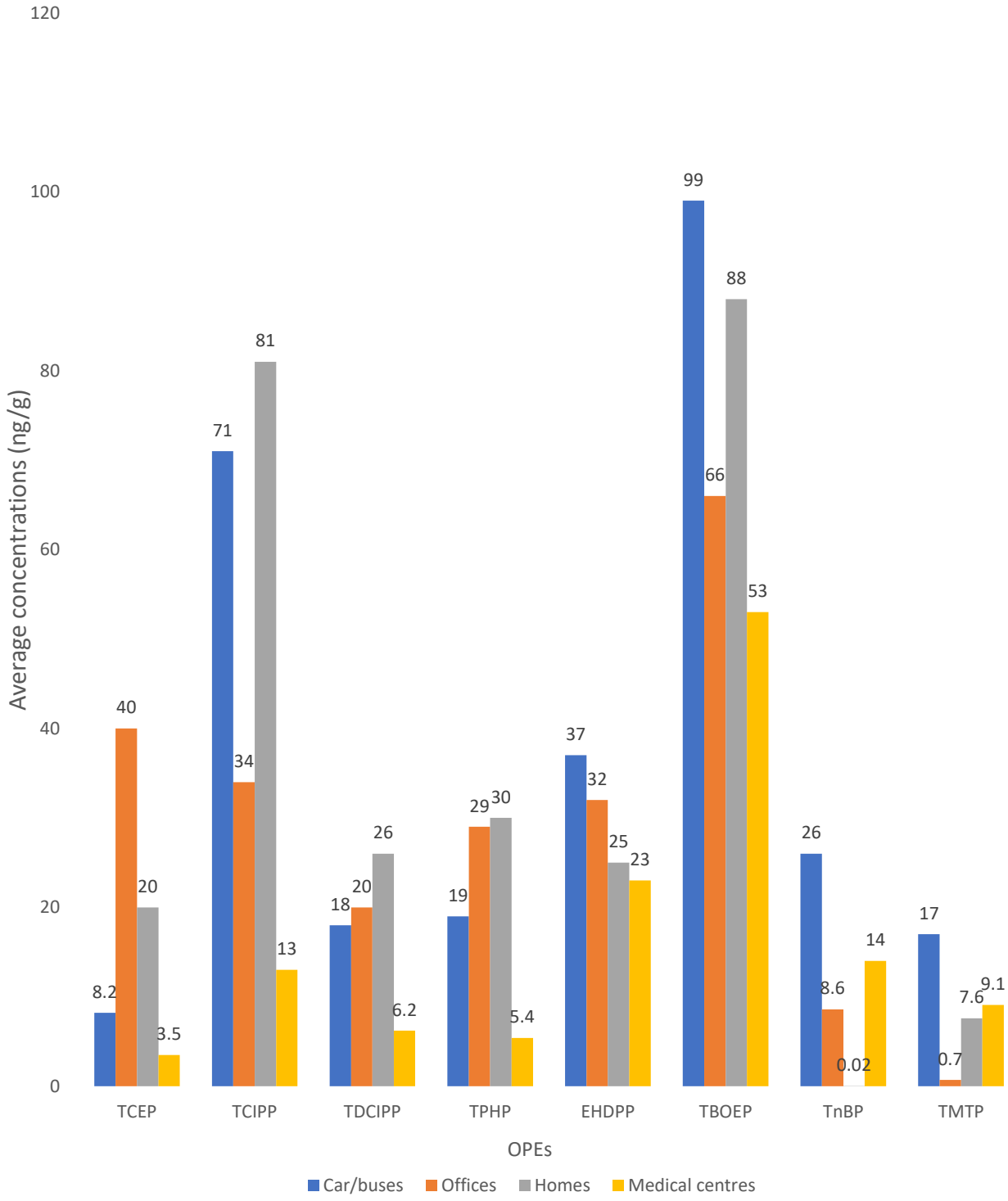


Fig. 5.1: Average concentrations (ng/g) of OPEs in dust from different indoor microenvironments in Lagos, Nigeria

5.5.2 Concentrations and profiles of OPEs in indoor dust from different microenvironments in comparison with other studies

ANOVA revealed there to be no significant differences ($p > 0.05$) between the concentrations of $\sum_8$OPEs in the four microenvironments considered in this study. The mean and range of concentrations of $\sum_8$OPEs in the microenvironments were in the order: cars (mean: 295; range: 173 – 612 ng/g) > homes (mean: 277; range: 24 – 956 ng/g) > offices (mean: 231; range: 173 – 612 ng/g) > medical centres (mean: 127; range: 76 – 386 ng/g) respectively. The highest TBOEP concentrations (mean: 99 ng/g; 63 – 199 ng/g) were obtained in car dust, followed by house dust (mean: 88 ng/g; 0.49 – 200 ng/g), office dust (66 ng/g; 1.4 – 257 ng/g) and the lowest in medical centres (mean: 53 ng/g; 41 – 93 ng/g). The three Cl-OPEs represented between 3 - 24%, 8 - 17%, 7 - 29% and 2 - 10% of the mean concentration of $\sum_8$OPEs for car/buses, offices, homes, and medical centres respectively (Table 5.3). The highest concentrations of the chlorinated OPEs: TCEP (DF=100%) (mean: 40; range: 1.9 – 269 ng/g), TCIPP (DF =100%) (mean: 34; range: 5.1 – 126 ng/g) and TDCIPP (DF =100%) (mean: 20; range: 1.8 – 159 ng/g) were found in offices, followed by car/buses, homes with the lowest seen in medical centres (Table 5.3).

The ubiquitous presence of Cl-OPEs in dust in this study, implies wide application of these compounds in various consumer and industrial products in Nigeria [10,52]. The observed high detection frequency (DF = 100%) of the Cl-OPEs in this study is similar to reports from: Egypt [10], Iraq [39], China [8,45], Canada and Turkey [34], the UK [11,58], Greece [59], Kuwait and Pakistan [54], and Spain [7]. The reported high concentrations of Cl-OPEs in house and car dust from Kuwait and attributed this to their use in polyurethane foam furniture filling and as plasticisers [54]. Similar studies conducted in Iraq and Spain found TCIPP was the most abundant OPE [39,60], while in the US, TDCIPP and TCIPP were the most abundant OPEs [61-63]. Broadly in line with our study, in Egypt, the dominant OPEs were TDCIPP and

TBOEP in house and office dust respectively [10]. In this study, the mean concentrations obtained for TPhP and EHDPP were comparable to those reported for office dust and house dust in Egypt (73 and 48 ng/g) [10] and Nepal (48 and 25.9 ng/g) [33]. There is no statistically significant difference ($p > 0.05$) between the TPhP and EHDPP concentrations observed in dust from the four microenvironments studied. However, the concentrations we detected of TPhP and EHDPP in Nigerian indoor dust were at least an order of magnitude lower than those reported for western countries (see appendix 5.4; Fig. 5.2). These higher concentrations of aryl-OPEs reported in most western countries may be due to international differences in their usage patterns [34,64,65].

Interestingly, concentrations of $\sum_5$OPEs (TCEP, TCIPP, TDCIPP, TPHP, and EHDPP) (DF = 100 %) observed in this study (averages - offices:155 ng/g; homes: 182 ng/kg; cars: 153 ng/g and medical centres: 51.1 ng/g) were the lowest reported worldwide (Fig. 5.1), although comparable to the values reported in Nepal (247 ng/g) [66] and in Egypt (401 ng/g) [10]. The average concentration of $\sum_5$OPEs in this study for medical centres (51.1 ng/g) was below those reported for hospital wards in Sweden (10,200 ng/g) [67] and public microenvironments (PMEs) in Egypt (2,118 ng/g) [10]. Concentrations of TPhP and EHDPP have been reported in different microenvironments from various countries, however, those obtained in this study were lower than those previously reported (see appendix 5.4). The highest concentrations of TPhP (30 ng/g) and EHDPP (37 ng/g) detected in this study were found in house and car dust respectively. The median concentrations of TPhP and EHDPP in dust from offices (18 and 22 ng/g), homes (18 and 20 ng/g), and cars (16 and 37 ng/kg) in this study were between 4-239 and 2 - 265 times lower than those reported in indoor dust from the same microenvironments in Egypt [10], China [8], and the UK [11]. Our mean concentrations for TnBP in: cars = 26 ng/g; offices = 8.6 ng/g; medical centres = 14 ng/g, and homes = <LOQ were below those reported in Egypt (cars: 74; offices: 27 ng/g) [10], China (offices: 57 ng/g; homes: 38 ng/g)

[8], Germany (cars: 110 ng/g; homes: 130; and offices: 220 ng/g), and US, Canada and Czech Republic (homes: 114, 63, and 51.6 ng/g) [68] (see appendix 5.4)

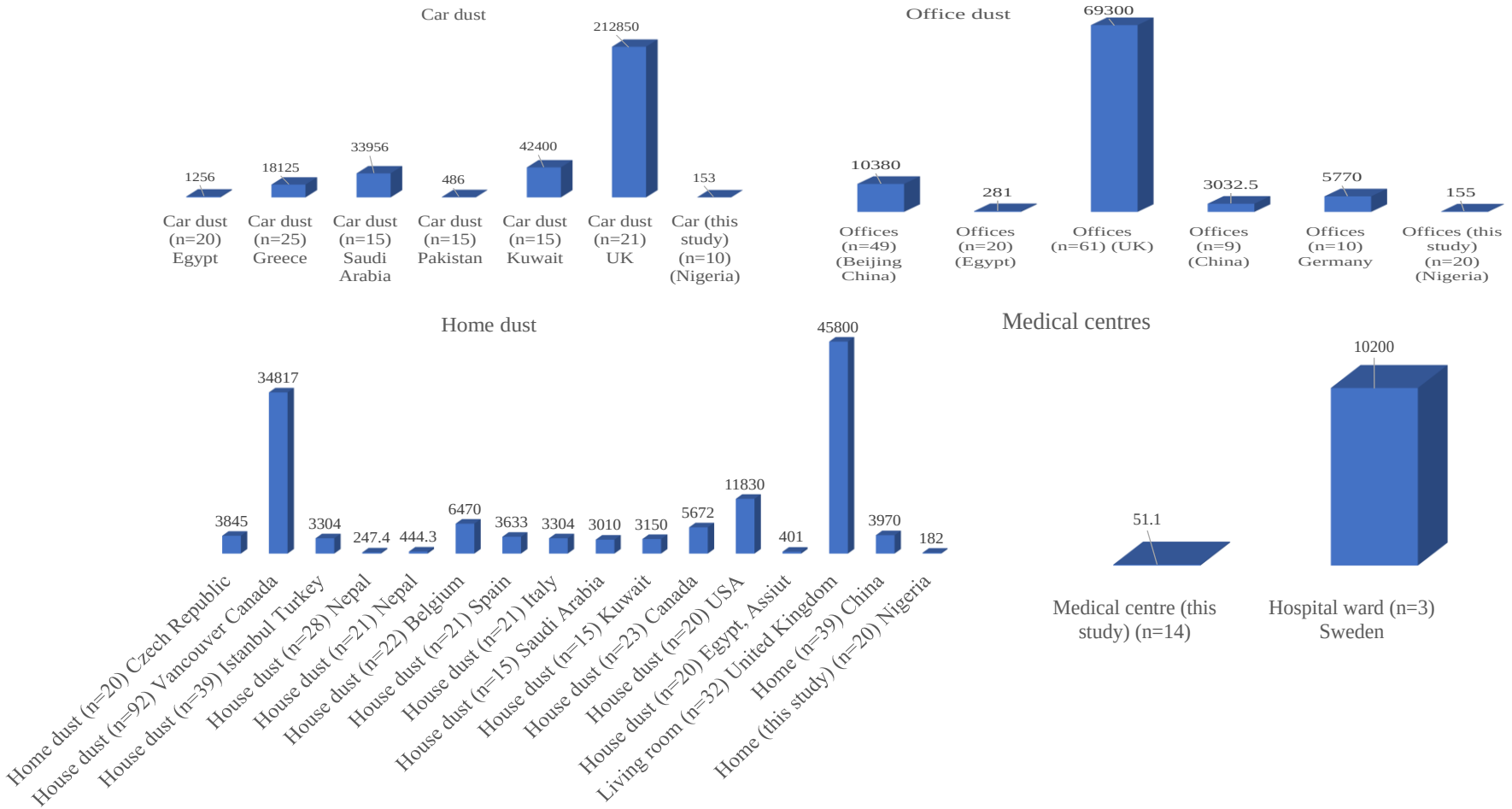


Fig. 5.2: Global comparison between average concentrations of Σ_5OPEs (ng/g) reported in indoor dust from different microenvironments
[Reported sampling years for the analysed dust were: Egypt (2012−2013) [10], UK (2011-2012) [11], China (2015) [8,69]; Czech Republic, Canada, and the USA (2013) [68]; Vancouver, Canada, and Istanbul, Turkey (2007-2008) [34], Nepal (2014, 2015) [33,66]; Belgium, Spain, and Italy (2016-2017) [40]; Saudi Arabia (2014) [57]; Kuwait and Pakistan (2011) [54]; Sweden (2003) [67]*; Greece (2018) [59]*. *[NB: For Sweden and Greece, the publication year was assumed as the sampling year]

5.5.3 Potential sources of OPEs in the studied indoor microenvironment in Nigeria

Concentrations of all OPEs were normally distributed using the Shapiro-Wilk and Kolmogorov-Smirnov tests (see appendix 5.3), thus Pearson rank correlations were performed to evaluate the possible common exposure sources and ascertain whether their presence in the consumer products from different countries are similar with this study. The results showed a significant correlation between the Cl-OPEs ($r = 0.346 – 0.586$; $p < 0.01$) (Table 5.4). In addition, TCEP showed significant correlation with TPhP, EHDPP, and TBOEP ($r = 0.403 – 0.470$; $p < 0.01$) (Table 5.4), TDCIPP showed a significant positive correlation with TPhP, EHDPP and TBOEP ($r = 0.421 – 0.791$; $p < 0.01$) while for TCIPP, the correlation was significant with TPhP ($r = 0.451$; $p < 0.01$) (Table 5.4). Moreover, TPhP and EHDPP were significantly correlated ($r = 0.453$; $p < 0.01$) as were EHDPP vs TBOEP ($r = 0.278$; $p < 0.05$) (Table 5.4). Those OPEs displaying significant positive correlations likely share a common source or sources. These findings are largely corroborated by the results of the principal component analysis (PCA) where the initial dimension reduction produced three components that explained 79% of the total variation (Table 5.5). The first principal component (PC-1) explained 48.98% of the total variation and was primarily driven in a positive direction by the three Cl-OPEs: TDCIPP (0.90), TCEP (0.75), TCIPP (0.59) and two aryl-OPEs: TPHP (0.82) and EHDPP (0.70) (Table 5.5). This supports the hypothesis that these OPEs have similar sources. The second and third principal components (PC-2 and PC-3) respectively explained 15.65% and 14.40 % of the total variance and were driven primarily by TnBP (PC-2 = 0.879) and TMTP (PC-3 = 0.855) (Table 5.5; Fig. 5.3). These two compounds have been reported to have applications distinct from those of the other OPEs measured. Hierarchical cluster analysis (HCA) was also performed on the data to further establish the similarity between concentrations of OPEs using the average linkage method. This revealed two distinctive clusters with varied degree of similarities between the variables, as shown by the dendrogram

provided in Fig. 4.4. The first cluster (Cluster-I) was comprised of: TDCIPP, TPhP, and EHDPP with major similarities with TCEP and TCIPP and a minor similarity with TBOEP through the subclusters (Fig. 5.4), that suggests similar sources of these OPEs. Cluster-II consisted of TnBP and TMTP (Fig. 5.4). Thus, the HCA findings are consistent with both our correlation analyses and PCA.

Table 5.4: Pearson correlation coefficient between concentration of target OPEs in indoor dust from Nigeria

Correlations									
		TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TBOEP	TnBP	TMTP
TCEP	Pearson Correlation	1	.346**	.586**	.470**	.439**	.403**	.057	-.043
	Sig. (2-tailed)		.005	<.001	<.001	<.001	<.001	.654	.736
TCIPP	Pearson Correlation		1	.395**	.451**	.271*	.287*	-.131	.079
	Sig. (2-tailed)			.001	<.001	.030	.021	.304	.533
TDCIPP	Pearson Correlation			1	.791**	.549**	.421**	.036	-.066
	Sig. (2-tailed)				<.001	<.001	<.001	.777	.603
TPHP	Pearson Correlation				1	.453**	.078	-.050	-.103
	Sig. (2-tailed)					<.001	.539	.696	.420
EHDPP	Pearson Correlation					1	.278*	.227	-.081
	Sig. (2-tailed)						.026	.072	.525
TBOEP	Pearson Correlation						1	.212	.092
	Sig. (2-tailed)							.092	.467
TnBP	Pearson Correlation							1	.187
	Sig. (2-tailed)								.139
TMTP	Pearson Correlation								1
	Sig. (2-tailed)								
**. Correlation is significant at the 0.01 level (2-tailed).									
*. Correlation is significant at the 0.05 level (2-tailed).									

Table 5.5: Principal component analysis (after varimax rotation) showing contribution of statistically significant variables (in bold)

Rotated Component Matrix [a]				Communalities
	Component			
	1	2	3	
TDCIPP	**.900**	.031	.002	0.810
TPHP	**.824**	-.203	-.110	0.733
TCEP	**.748**	.108	.085	0.579
EHDPP	**.698**	.360	-.132	0.635
TCIPP	**.592**	-.388	.431	0.687
TBOEP	**.455**	.366	.427	0.523
TnBP	.020	**.879**	.128	0.790
TMTP	-.154	.101	**.855**	0.765
Eigen-value	3.151	1.352	1.019	
% of variance explained	48.980	15.650	14.397	
Cumulative (%)	48.980	64.630	79.027	

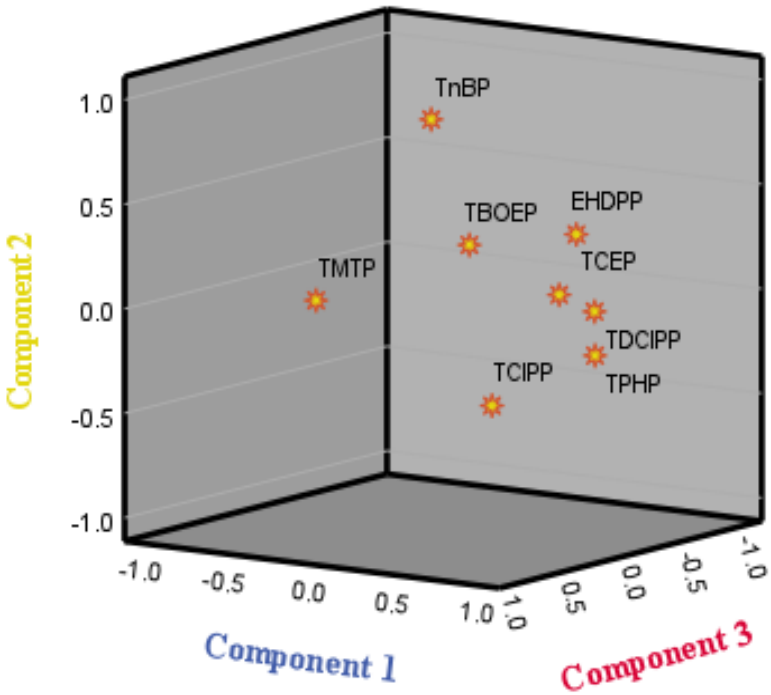


Fig. 5.3: Graphical representation of principal components PC-1 (48.98%), PC-2 (15.65%) and PC-3 (14.40 %).

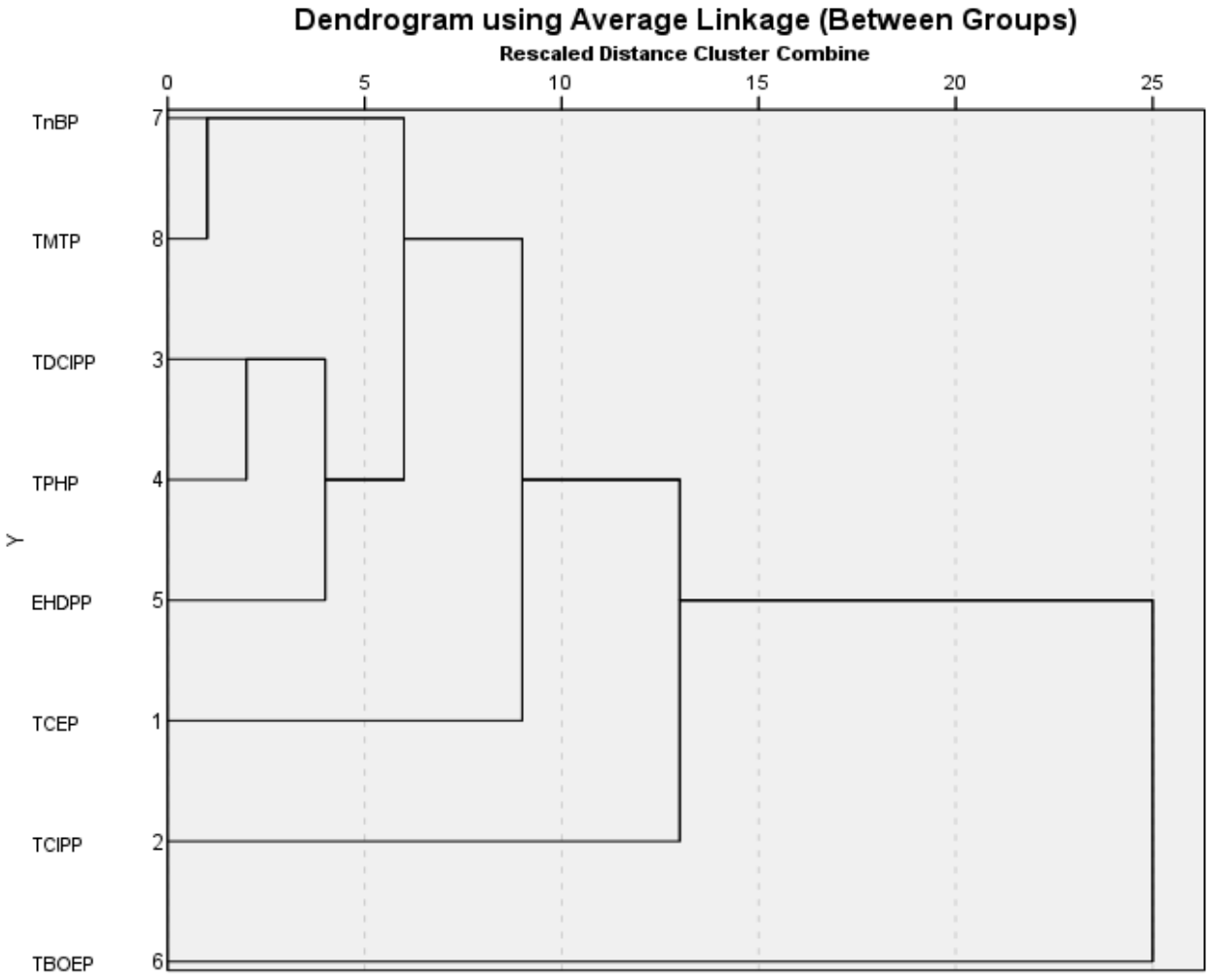


Fig. 5.4: Dendrogram showing the cluster formation of OPEs in the indoor dust

5.6 Human exposure to OPEs via indoor dust ingestion and dermal absorption

Concentrations of OPEs in indoor dust in this study were used to assess the exposure via dust ingestion and dermal absorption from dust of Nigerian toddlers and adults. Estimated daily intakes (EDIs) of our target OPEs via indoor dust ingestion and dermal absorption in Nigeria are summarised in Table 5.6. The mean and high exposure doses (based on the mean and 95th percentile concentrations respectively) are presented in Table 5.6. The same table also expresses EDIs for each OPE as a percentage of the corresponding reference dose (RfD) (provided in parentheses in Table 5.6). The results show that the median exposure doses of $\sum_8$OPEs via indoor dust ingestion and dermal absorption from the microenvironments were

(1.6 and 0.07 ng/kg bw/day) and (0.63 and 0.03 ng/kg bw/day) for toddlers and adults respectively (Table 5.6). As a result of their lower body weight, more frequent hand-to-mouth contact (Hou et al., 2016) and greater proximity to the floor; toddlers are more exposed to OPEs than adults. Specifically, the median EDI value for ΣOPEs obtained for toddlers in this study was about 21-23 times higher than that for adults via the two exposure pathways considered (Table 5.6). The median estimated EDIs for toddlers and adults in this study via indoor dust ingestion and dermal absorption were comparable to those reported in China [49,70], Nepal [66] and Egypt [71]; below the value reported in the UK [11], Germany [72], Pakistan and Kuwait [54], Saudi Arabia [57], Egypt [10], the USA, Canada, and the Czech Republic [68], Iraq [39], Canada, Turkey, and Egypt [34]; China [8,45], South Africa [9] US [73], and Norway [74]. However, the median and high-end EDIs obtained for the carcinogenic TCEP (4.3×10^{-5} and 1.6×10^{-4} ng/kg bw/day), TCIPP (2×10^{-4} and 5×10^{-4} ng/kg bw/day), and TDCIPP (6×10^{-5} and 4.5×10^{-4} ng/kg bw/day) for adults in medical centres in this study, were below the value reported in hospital wards in Sweden [67], in indoor dust from Egypt [10], China [8], and Canada [34] (see appendix). In the same vein, our median EDI value for six OPEs (TCEP, TCIPP, TDCIPP, TPHP, EHDPP and TnBP) combined for dermal absorption from dust for adults (0.02 ng/kg bw/day) was lower than the value reported for dermal absorption in Nepal (5.58 ng/kg bw/day) [66]. In this study, our median and high exposure EDIs via dust ingestion for toddlers in offices (0.50 and 9.5 ng/kg bw/day) and house dust (0.71 and 7.0 ng/kg bw/day) were significantly higher ($p < 0.05$) than those obtained for cars/buses (0.37 and 3.1 ng/kg bw/day) and medical centres (0.02 and 0.17 ng/kg bw/day) respectively (Table 5.6; see appendix 5.5). The same trends were observed for dermal absorption from dust for adults and toddlers (Table 5.6 and see appendix 5.5).

In addition, the overall mean, median, and high exposure scenario EDIs for each OPE for both toddlers and adults were compared with their respective reference doses (RfDs) obtained from

[50,75,76] (value in parenthesis in Table 5.6) to ascertain the human health risk via the two exposure pathways (Table 5.6). The results showed that TBOEP poses the greatest exposure risk of our target OPEs, with OPE risk arising from both pathways combined falling in the order: TBOEP > EHDPP > TPHP > TCIPP > TCEP > TDCIPP > TnBP for adults and toddlers (Table 5.6). There is no RfD value for TMTP currently with which the TMTP EDI value can be compared. In summary, the levels of exposure for OPEs were several orders of magnitude lower than their respective RfD values except for some compounds such as TBOEP and EHDPP where the EDI value under the high exposure scenario for toddlers via indoor dust ingestion was about 0.3% and 0.4% of their respective RfD value (Table 5.6; see appendix 5.5). Similar to what was reported for indoor dust in Greece by [59], the exposure risk obtained in this study via dust ingestion exceeded that from dermal absorption (see appendix). Our data for the sum of the median EDIs for all the microenvironments studied for dust ingestion for toddlers (1.6 ng Σ_8OPEs/kg bw/day) and dermal absorption (0.63 ng Σ_8OPEs/kg bw/day) showed that dust ingestion contributed about 72% while dermal absorption comprised 28% of the total exposure (Table 5.6). For adults, dust ingestion contributed about 70% with the remaining 30% arising from dermal absorption (see appendix 5.5). Therefore, for both toddlers and adults, dust ingestion is the main human exposure route to OPEs present in indoor dust.

Table 5.6: Estimated daily intakes (EDIs, ng/kg bw/day) of OPEs via indoor dust ingestion and dermal absorption for toddlers and adults in Nigeria (numbers in parentheses represent EDIs as a percentage of the corresponding reference dose value)

		Dust ingestion (ng/kg body weight/day)						Dermal absorption (ng/kg body weight/day)					
		Toddlers			Adults			Toddlers			Adults		
OPE	RfD (ng/kg bw/day)	Mean	Median	95th Percentile	Mean	Median	95th Percentile	Mean	Median	95th Percentile	Mean	Median	95th Percentile
TCEP	7,000 [a]	0.22 (0.003)	0.07 (0.001)	3.7 (0.05)	0.006 (<0.001)	0.003 (<0.001)	0.05 (<0.001)	0.12 (0.002)	0.04 (<0.001)	0.54 (0.008)	0.004 (<0.001)	0.002 (<0.001)	0.013 (<0.001)
TCIPP	10,000 [a]	0.48 (0.005)	0.44 (0.004)	3.7 (0.04)	0.02 (<0.001)	0.02 (<0.001)	0.09 (<0.001)	0.25 (0.003)	0.22 (0.002)	0.47 (0.005)	0.013 (<0.001)	0.013 (<0.001)	0.022 (<0.001)
TDCIPP	20,000 [a]	0.18 (0.001)	0.12 (0.001)	1.5 (0.008)	0.007 (<0.001)	0.005 (<0.001)	0.04 (<0.001)	0.05 (<0.001)	0.03 (<0.001)	0.10 (<0.001)	0.002 (<0.001)	0.001 (<0.001)	0.005 (<0.001)
TPHP	7000 [b]	0.23 (0.003)	0.15 (0.002)	1.9 (0.03)	0.008 (<0.001)	0.006 (<0.001)	0.04 (<0.001)	0.08 (0.001)	0.05 (<0.001)	0.17 (0.002)	0.003 (<0.001)	0.002 (<0.001)	0.006 (<0.001)
EHDPP	600 [c]	0.25 (0.04)	0.19 (0.03)	2.6 (0.43)	0.01 (0.002)	0.008 (0.001)	0.05 (0.008)	0.09 (0.02)	0.07 (0.01)	0.22 (0.04)	0.004 (0.001)	0.003 (0.001)	0.008 (0.001)
TBOEP	1500 [b]	0.66 (0.04)	0.56 (0.04)	4.8 (0.3)	0.03 (0.002)	0.02 (0.001)	0.13 (0.009)	0.23 (0.02)	0.19 (0.01)	0.42 (0.03)	0.011 (0.001)	0.010 (0.001)	0.021 (0.001)
TnBP	10,000 [a]	0.07 (0.001)	0.07 (0.001)	0.48 (0.005)	0.003 (<0.001)	0.003 (<0.001)	0.01 (<0.001)	0.02 (0.002)	0.02 (<0.001)	0.04 (<0.001)	0.001 (<0.001)	0.001 (<0.001)	0.002 (<0.001)
TMTP	-	0.05	0.002	0.97	0.003	0.0002	0.04	0.02	0.00	0.1	0.001	0.0001	0.005
$\sum_8$OPEs	-	2.1	1.6	19.8	0.09	0.07	0.45	0.86	0.63	2.05	0.04	0.03	0.08

[a] Reference dose (RfD) values of [75]

[b] [50]

[c] [76]

5.7 Conclusions

This is the first study to report concentrations of OPEs in indoor dust in four microenvironments (cars/buses, offices, homes, and medical centres) in Nigeria. Concentrations of OPEs detected in this study were comparable to those reported in other developing African and Asian countries and lower than the values reported in most western countries. Our findings add to the increasing evidence of indoor contamination with OPEs. Correlation, principal component, and hierarchical cluster analyses revealed similar sources for most target OPEs, but distinct sources of TnBP and TMTP. Assessment of exposure to OPEs of Nigerians via indoor dust ingestion and absorption from dermal contact with indoor dust and comparison with the corresponding health-based limit values, do not reveal any significant health risks associated with such exposure. Exposure via dust ingestion exceeds that via dermal absorption from contact with dust. However, further studies are needed to fully determine overall human exposure to OPEs of the Nigerian population via other exposure routes including air inhalation [77], dietary ingestion [23], water ingestion [12], and dermal uptake via contact with OPE-containing products like furniture [78].

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CHAPTER VI

Occurrence and Dietary Exposure to Organophosphorus Esters in foodstuffs of Nigerian origin

Paper under review:

Journal: Food Control

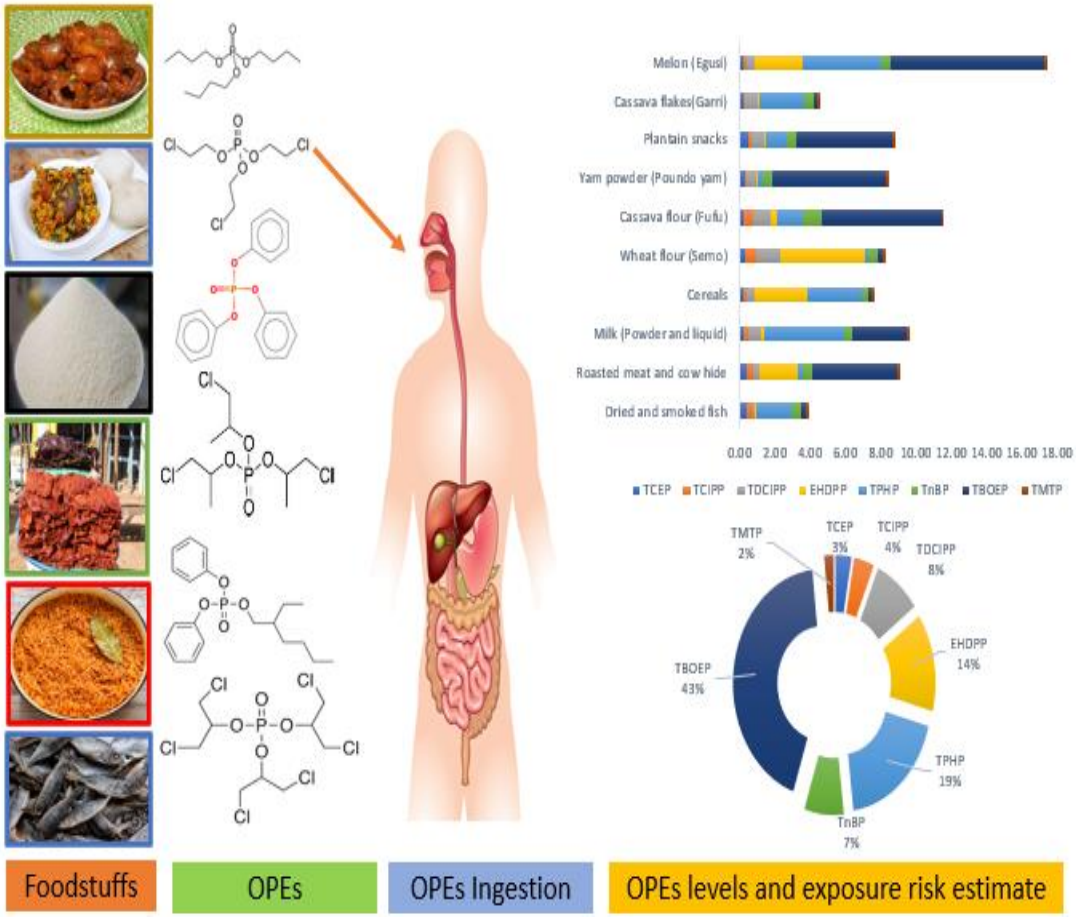
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Graphical abstract



6.1 Abstract

Despite extensive evidence of the presence of organophosphate esters (OPEs) in various environmental matrices including foodstuffs in some developed countries, there are no data on the presence of OPEs in African foodstuffs. This study provides the first data on concentrations of OPEs in foods of Nigerian origin by measuring the concentrations of eight OPEs in 85 food items either purchased in Nigeria or from major African stores in Birmingham, UK. Foodstuffs analysed were divided into ten categories. Median concentrations of $\sum_8$OPEs in melon (Egusi) (17.4 ng/g ww), cassava flour (Fufu) (11.6 ng/g ww), and milk (9.62 ng/g ww) were the highest of the food categories examined. Tris(2-butoxyethyl) phosphate (TBOEP) and triphenyl phosphate (TPHP) were the dominant OPEs. Cassava flour (Fufu) was the major contributor

to the estimated daily intakes (EDIs) of S_8OPEs, accounting for 26 and 33% of the EDI for children and adults respectively. For individual OPEs, TBOEP contributed the highest median EDI of 183 ng/kg bw/day (42% of the EDI for S_8OPEs) for children and 159 ng/kg bw/day (39%) for adults, followed by TPHP (median – children: 92.3 ng/kg bw/day (21%); adults: 90.6 ng/kg bw/day (22%)). The range of OPE concentrations in the present study were comparable to data reported from other countries and EDIs for all OPEs were well below their corresponding health-based reference doses. This study identifies diet as a substantial human exposure pathway to OPEs in Africa.

Keywords: organophosphate esters, Africa, foodstuffs, dietary intakes

6.2 Introduction

Organophosphate esters (OPEs) are chemical additives integrated into combustible materials and other consumer products to reduce the spread/risk of fire, meet flammability standards, and/or modify the properties of the material to which they are added (Castro et al., 2020; van der Veen and de Boer, 2012). Their extensive use as flame retardants, stabilisers, anti-foaming agents, or plasticisers in various consumer and industrial products such as: flexible polyurethane foam (PUF), electronics, furniture, plastics, construction materials, floor polish, and paints has led some OPEs to be catalogued as high production volume chemicals (Castro et al., 2020). In 2017, the global consumption of phosphorus-based FRs reached 797,234 tons, accounting for more than 30% of the total global consumption of FRs, compared to 20% for bromine-based FRs (McWilliams, 2018; Wang et al., 2019). Due in part to the regulation of brominated flame retardants such as polybrominated diphenyl ethers and hexabromocyclododecane, production and usage of OPEs has increased and led to their ubiquitous presence and detection in various environmental matrices and human samples

(Gbadamosi et al., 2021; Wang et al., 2019; Hou et al., 2020). Pertinently, OPEs are physically added into polymeric materials and not chemically bonded (Zhao et al., 2020); this allows their facile release and pollution of the environment as a result of volatilisation, abrasion, and leaching (Brommer and Harrad, 2015; Wei et al., 2015: Hou et al., 2020). Moreover, several toxicological, and epidemiological studies have reported serious adverse effects of OPEs that include: carcinogenicity, cardiotoxicity, neurotoxicity, genotoxicity, reproductive disorders, and dermatitis (McGee et al., 2013, Zhao et al., 2021; Wang et al., 2019). Based on the potential exposure health risks of OPEs in various products, the European Union (EU) in 2008 set regulations and criteria 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 pose major health and/or environmental hazards (Chen et al., 2021). Consequently, while over 100 countries regulate the use of certain OPEs (Blum et al., 2019; Chen et al., 2021), there is to our knowledge no regulation on the production and use of OPEs in Africa. This is of concern, given that because of the ubiquitous presence of OPEs in various environmental compartments, and their possible accumulation in biota and other fatty tissues; humans can be exposed via: ingestion of dust, water, and food, inhalation of air, and dermal absorption (Gbadamosi et al., 2021; Abdallah and Covaci, 2014; Poma et al., 2017; 2018; Leet et al., 2016 and Wang and Kannan, 2018). Contamination of foodstuffs with OPEs can occur through biomagnification in the food chain via crops, aquatic organisms/seafood, and livestock through their feed and absorption from soil and water (Zhang et al., 2016), as well as directly via migration from food packaging materials (Wang and Kannan, 2018) and contamination from food processing and storage (Poma et al., 2018; Ding et al., 2018; Gbadamosi et al., 2021). Consequently, it has been established that dietary intake is one of the main human exposure pathways to OPEs for the general population (Gbadamosi et al., 2021; Wang et al., 2022; Li et al., 2019a). However, information on the occurrence of OPEs in foodstuffs is limited to

countries such as: Australia (He et al., 2018), China (Ding et al., 2018; Zhao et al., 2019, Zhou et al., 2022; Chen et al., 2022, Zhang et al., 2016; Wang et al., 2022; He et al., 2019; Liu et al., 2019), the USA (Wang and Kannan, 2018; Han et al., 2019), Sweden and Belgium (Poma et al., 2017; 2018), the United Kingdom (Gbadamosi et al., 2022), Canada (McGoldrick et al., 2014), and the Philippines (Xu et al., 2015). While the OPEs measured varies between studies, the reported median concentration of ∑OPEs in these studies varies from 0.08 – 50 ng/g wet weight (ww) in the various foodstuffs analysed. Out of all studies of which the authors are aware, the highest median concentrations of ∑OPEs were found in rice (7.59 – 55.9 ng/g) from four provinces in China (Zhang et al., 2016), and in fat and stock (median: 63.5 and 16.7 ng/g ww) in Belgium (Poma et al., 2018). The highest concentrations of individual OPEs reported in all the foodstuffs from these studies were TDCIPP and TCIPP in fat (16.1 ng/g and 31.0 ng/g ww) (Poma et al., 2018) and EHDPP in stock and desserts (12.3 and 8.72 ng/g ww) from Belgium (Poma et al., 2018). In studies in the USA, China, Sweden, Belgium, and Australia, mean EDIs of ∑OPEs were in the range 1.9 - 601 ng/kg bw/day for the general population (Wang and Kannan, 2018; (Zhang et al., 2016; Zhao et al., 2019; Chen et al., 2021; Poma et al., 2017; 2018; He et al., 2018). However, current data and understanding on the occurrence of OPEs in foodstuffs and dietary exposure and consequent health risk is far from sufficient especially given the absence of data for Africa. Therefore the aims of the current study are: (i) to report for the first time the concentrations and distribution of eight OPEs in a wide range of Nigerian foodstuffs collected directly from local markets in Nigeria along with some collected from major African stores in Birmingham, UK that could be identified as originating from Nigeria; (ii) to investigate the likely contamination sources of OPEs in Nigerian foodstuffs; and (iii) to estimate human dietary exposure to OPEs to individuals consuming foods of Nigerian origin under different exposure scenarios.

6.3 Materials and Methods

6.3.1 Sample collection

Between June – August 2021, a total of 85 food samples were collected directly from local markets in Lagos, Nigeria (n=21) and from three major African stores in Birmingham, UK (n=64) (Table 6.1). The origin of the samples collected in the UK was established via information provided on product labelling and/or via confirmation from the store owners that the foods were from Nigeria. Collected food samples were stratified into 12 categories: cereal (rice and noodles) (n = 10), dried and smoked fish (n=26), roasted beef (Suya and Kilishi), cow hide meat (ponmo) (n = 23), milk (n = 6), fried plantain snacks (n = 3), wheat flour (Semovita) (n = 3), yam powder (Poundo yam) (n = 3), cooked cassava flour dough (Fufu) (n = 3), cassava flakes (Garri) (n = 5), and Egusi (melon) (n = 3) (Table 6.1). Some food samples such as Kilishi and Fufu were purchased in the processed and ready to eat form. Samples collected in Nigeria were collected directly from the local vendors, carefully packaged in aluminium foil, placed in a sealed zip lock bag, and shipped to the laboratory at the University of Birmingham for chemical analysis. Those collected from African stores in Birmingham were taken directly to the lab after collection. On arriving at the laboratory, edible parts of solid foods were freeze-dried and individually homogenised, then stored at -20 °C prior to extraction and analysis. Further information about the foodstuffs analysed are presented in (Table 6.1)

Table 6.1: List of analysed food samples

Food category	Collected from African stores in UK	Collected from local market from Nigeria	Total
Dried and smoked fish - Dried stock fillet, dried periwinkled, dried shawa, dried prawn, dried tilapia, smoked tilapia, dried catfish	17	9	26
Roasted meat and cow hide - (Beef floss, dried cow skin, beef jerky, roasted meat (suya), kilishi), dried snail	16	7	23

Milk (Liquid and powder) – Liquid and powder milk	6	-	6
Cereals (Rice and Indomie noodles)	5	5	10
Wheat flour (Semovita) – Honeywell Semovita	3	-	3
Cassava flour (Fufu)	3	-	3
Yam powder (Poundo yam)	3	-	3
Plantain snacks	3	-	3
Cassava flakes (Garri)	5	-	5
Melon (Egusi)	3	-	3
Total	64	21	85

6.3.2 Chemicals and reagents

Standards of the 8 OPEs measured in this study namely: tris(2-chloroethyl) phosphate (TCEP), tris(2-chloroisopropyl) phosphate (TCIPP), tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), tris(2-butoxyethyl) phosphate (TBOEP), triphenyl phosphate (TPHP), 2-ethylhexyl-diphenyl phosphate (EHDPP), tri-n-butyl phosphate (TnBP), and tri-m-tolyl phosphate (TMTP), internal (surrogate) standards (ISs) d_{27}-TnBP and d_{15}-TPHP, and 2,3,4,6-tetrachlorobiphenyl (PCB-62) used as a recovery determination (syringe) standard (RDS) were purchased from Wellington laboratories, (Guelph, ON, Canada). Hypersep Florisil® cartridges were purchased from Thermo Scientific (Rockwood, USA. All glassware, as well as the knife and weighing spoon used for sample preparation, along with Na_2SO_4 were baked at 450 °C and 600 °C overnight and rinsed before each use with dichloromethane (three times), toluene, and acetonitrile (ACN) to minimise residual organic contamination.

6.3.3 Analytical Procedures

Concentrations of target OPEs in the foodstuffs were determined via GC-MS using a previously reported method (Gbadamosi et al., 2022;2023). Briefly, for most samples ~ 1 g of each freeze-dried sample was accurately weighed in a 15 mL polypropylene (PP) tube - with smaller aliquots (ca 0.5 – 0.8 g) used for high fat matrices (i.e. >20 % lipid) to minimise matrix interferences. After adding 5 mL of ACN and 5 mL of 5 % formic acid in ACN (v/v), each

sample was spiked with 50 ng of both ISs and extracted via vortexing (1 min), sonication (15 mins), and centrifugation (3500 rpm for 5 mins) in three cycles. The pooled supernatant was then transferred into a precleaned glass tube and evaporated to ~ 2 mL under a gentle nitrogen stream. This concentrated extract was subjected to dispersive solid phase extraction via addition of 100 mg of C18 and 50 mg of primary-secondary amine sorbent powder to remove fats, sugars, and other polar pigments that may act as interferences, followed by vortexing for 1 min and centrifugation for 5 mins at 3500 rpm. The resultant supernatant was collected into a clean glass tube and evaporated to incipient dryness, resolubilised in 0.5 mL of n-hexane:ethyl acetate (ETAC) (1:1 v/v) and further cleaned by elution through a Florisil® cartridge preconditioned with 6 mL ETAC and 6 mL n-hexane. Fractionation was achieved with 12 mL of n-Hexane (F1, discarded) and 10 mL ETAC (F2, containing the target OPEs). F2 was concentrated to near dryness, and reconstituted in 200 µL iso-octane:ETAC (8:2 v/v) containing 100 pg μL^{-1} PCB-62 as RDS. The resultant cleaned extract was transferred into a clean glass tube and stored at -20 °C to allow precipitation of any residual lipids, after which the clean upper layer was transferred into an injection vial, and stored ready for analysis via gas chromatography electron ionisation mass spectrometry (GC-EIMS) in selected ion monitoring mode. Detailed information on the GC-EIMS method used is available elsewhere (Gbadamosi et al., 2022; 2023).

6.3.4 Quality Assurance (QA) and Quality Control (QC)

Due to the lack of certified reference materials for food, aliquots of Na_2SO_4 (prebaked at 450°C for 6 hrs) were used to assess blank contamination and method accuracy via analysis of aliquots spiked: (a) with ISs, and (b) with ISs and native OPE standards. In addition, the following matrix spike samples were analysed: five samples each of vegetable oil and egg samples (from the same grocery store) were spiked with ISs (50 ng of each) and each of the target OPEs (also

50 ng each) and analysed. Results from these matrix spike samples, showed good IS recoveries ranging from 62.3 ± 16.9 to 79.4 ± 7.3 % for d_{15}-TPHP and d_{12}-TBP and the average recoveries of the native OPEs varies from 73.1 – 99.5 % and 71.4 – 99.6% for vegetable oil and egg respectively (Table 6.2). Average recoveries of the ISs spiked into Na_2SO_4 ranged between 72 and 96 % (Table 6.3). Two procedural blanks comprising 1 g Na_2SO_4 treated as a sample were analysed per each batch of 10 samples (n = 9). This revealed some low-level contamination (ranging between 0.02-0.07 ng/g dw) for TCEP only (Table 6.3). Other quality control measures followed in this research are reported in our previous study of UK foodstuffs (Gbadamosi et al., 2022) The limit of detection (LOD) and the limit of quantification (LOQ) were calculated as the amounts of an analyte that yielded a signal to noise ratio of 3 and 10 respectively (Table 6.3; see appendix 6.1), while for TCEP the LOD and LOQ was calculated as 3 and 10 times the standard deviation of the blank values.

6.2: Standard recoveries (SRs) and relative standard deviation (RSD) of target OPEs measured in spiked vegetable oil and egg samples

OPEs	Vegetable oil (n=5)			Egg (n=5)		
	Standard recovery (%)	Mean	RSD (%)	Standard recovery (%)	Mean	RSD (%)
TCEP	76.4 – 114.1	93.5	17.7	60.2 – 83.2	73.7	12.0
TCIPP	72.9 – 123.5	95.5	18.8	55.6 – 89.3	75.2	16.5
TDCIPP	76.2 – 112.8	99.5	19.8	59.6 – 86.1	71.4	13.6
TnBP	63.8 – 78.6	73.1	8.1	73.9 – 116.1	85.8	20.0
EHDPP	55.9 – 111.2	91.1	23.2	75.9 - 111.2	95.1	13.9
TPHP	70.3 – 80.2	75.5	4.6	75.7 – 115.8	84.2	21.7
TBOEP	64.0 – 116.7	85.2	24.8	63.1 – 108.1	86.6	24.7
TMTP	76.8 – 119.7	98.9	17.9	87.3 – 109.9	99.6	8.8

Table 6.3: Instrumental performance, procedural blanks, and instrument detection limits (IDLs) for target OPEs

OPE	RT (min)	Calibration range (ng/µL)	Linear (R^2)	Isotope labelled IS	Relative Response factors (RRFs)	IS Recovery (%) (n=40) (50 ng/µL)	Na_2SO_4 IS Recovery (%) (n=5) (50 ng/µL)	Procedural blank (ng/g) (dw) (n=9)	Instrument detection limit (IDL) (LOD) (pg/injection)
TCEP	8.87	0.05-0.75	0.9983	d27-TnBP	0.13±0.02	74.9 – 86.2 (mean = 79.4, RSD = 7.3)	72-81	0.02-0.07	0.57
TCIPP	9.07	0.05-0.75	0.9974	d27-TnBP	0.04±0.01	74.9 – 86.2 (mean = 79.4, RSD = 7.3)	72-81	ND	1.00
TDCIPP	12.16	0.05-0.75	0.9975	d15-TPHP	0.04±0.01	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	78-96	ND	0.51
TPHP	12.75	0.05-0.75	0.9958	d15-TPHP	0.53±0.03	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	78-96	ND	1.82
EHDPP	12.99	0.05-0.75	0.9981	d15-TPHP	1.45±0.11	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	78-96	ND	1.15
TnBP	8.17	0.05-0.75	0.9987	d27-TnBP	1.11±0.11	74.9 – 86.2 (mean = 79.4, RSD = 7.3)	72-81	ND	3.95
TBOEP	12.58	0.05-0.75	0.9998	d15-TPHP	0.45±0.05	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	78-96	ND	1.93
TMTP	14.40	0.05-0.75	0.9815	d15-TPHP	0.24±0.01	51.7 – 75.2 (mean = 62.3, RSD = 16.9)	78-96	ND	1.25

R^2 = regression coefficient

6.3.5 Data analysis

Descriptive statistics, specifically: mean, median, maximum, minimum, standard deviation, and the 97.5th percentile were obtained using Microsoft 365 excel, while the multivariate statistical tests were carried out using IBM SPSS statistics version 28 and GraphPad prism 9 (version 9.5.0). Our data were not normally distributed using Shapiro-Wilk and Kolmogorov normality tests and visual inspection, as a result, nonparametric statistical test such as Mann-Whitney U test and Kruskal-Wallis H test were employed used to test for differences in concentrations of OPEs in foodstuffs (P-values lower than 0.05 ($p < 0.05$) were deemed statistically significant). Bivariate correlations (Spearman's correlation analysis) were used to investigate associations between OPEs. The data were log10 transformed prior to analysis to permit use of component analysis. 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 (Gbadamosi et al., 2018). Combined with the Spearman's correlation analysis, PCA helped identify whether common sources exist of our target OPEs in foodstuff, and if so, for which OPEs. A one-way analysis of variance (ANOVA) was used to test for differences in concentrations of OPEs in foodstuffs (P-values lower than 0.05 ($p < 0.05$) were deemed statistically significant). Where concentrations of a given OPE in a sample were <LOQ, the concentration value was assigned as half the LOQ for that OPE (< LOQ = 0.5 x LOQ).

Table 6.4: KMO and Bartlett's Test

KMO and Bartlett's Test		
Kaiser-Meyer-Olkin Measure of Sampling Adequacy.		.769
Bartlett's Test of Sphericity	Approx. Chi-Square	22.082
	Df	21
	Sig.	.002

6.4 Estimated dietary intakes and risk assessment

Estimation of human dietary intake was undertaken using the formula (Zhao et al., 2019; Gbadamosi et al., 2022):

$$EDI = \frac{\sum_{i=1}^{n} C_i \, x \, CF_1}{BW} \qquad (1)$$

Where EDI is the estimated dietary intake of a given OPE(s) (ng/kg bw/day), Ci is the median/97.5th percentile concentrations of OPEs in each food category (ng/g); CFi is the daily food consumption rate of the corresponding food category (g/day/person) obtained from previous studies in Nigeria (Sanusi et al., 2022; Orisakwe et al., 2015; Hayford 2009; Ayanda et al., 2020; Nejabat et al., 2017; Giri et al., 2021; Ijeoma et al., 2020; Patrick-Iwuanyanwu and Udowelle, 2017) (Table 6.5). EDIs were calculated for children (4 - 18 yrs) and adults (19 - 64 yrs). BW is the average body weight (kg) of the population assumed to be 20 kg and 60 kg for children and Nigerian adults respectively (Brommer and Harrad, 2015; Charles et al., 2017; Walpole et al., 2012). In this study, we assumed that the population consumes all the food analysed in this study in quantities that correspond to those that a typical Nigerian consumes, even though some of the foods were bought from African stores in UK and some in Nigeria. The median and the 97.5th percentile concentrations of each foodstuff were multiplied by the median consumption rate data under the average and the high-exposure scenarios for the same foodstuffs for humans and are listed in Table S8. The high-end exposure data was derived by multiplying the median consumption rate data with the 97.5th percentile concentrations for each food category. This is due to the fact that only median consumption rate data are available for Nigeria (Table 6.5)

Table 6.5: Median quantities of food consumed by Africa population in UK (Children and adults) (g/day)

Food category	Children (g/day)	Reference	Adults (g/day)	Reference
Fish	27.5	Sanusi et al., 2022	34.5	Orisakwe et al., 2015
Meat	15.2	Sanusi et al., 2022	182	Ayanda et al., 2020
Milk	24.2	Sanusi et al., 2022	300	Giri et al., 2021
Wheat flour (Semovita)	76.4	Sanusi et al., 2022	334	Nejabat et al., 2017
Cassava flour (Fufu)	192.2	Sanusi et al., 2022	800	Hayford et al., 2009
Yam powder	170	Sanusi et al., 2022	300	(Based on personal consumption survey)
Plantain snacks	53.9	Sanusi et al., 2022	200	Patrick-Iwuanyanwu and Udowelle, 2017
Cassava flakes (Garri)	192	Sanusi et al., 2022	800	Hayford et al., 2009
Melon (Egusi)	82.1	Sanusi et al., 2022	65	(Based on personal consumption survey
Cereal	138	Sanusi et al., 2022	331	Ijeoma et al., 2020

6.5 Results and discussion

6.5.1 Occurrence of OPEs in Nigerian foodstuffs

A statistical summary of the concentrations of OPEs in foodstuffs of Nigerian origin is presented in Table 6.6. Detection frequencies (DFs) of the chlorinated OPEs (TCEP, TCIPP, and TDCIPP) exceed those of our other target OPEs (DF = 67 – 100%) except in smoked and dried fish samples, where the DF for TDCIPP is 23%. DFs for the two aryl OPEs: TPHP and EHDPP each vary from 0 – 100%, with TMTP not detected in any food sample in this study (Table 6.6). The DFs for the alkyl-OPEs: TBOEP and TnBP, vary between 0 - 67% and 0 - 100% respectively (Table 6.6). This variation in the DFs of our target OPEs likely arises from a combination of factors, including whether the foodstuff is processed, and the use volumes, physicochemical properties, half-lives, degradation, and metabolism of the OPEs (He et al., 2018). Our frequent detection of the Cl-OPEs in food samples, confirms reports of high DFs of Cl-OPEs in various environmental compartments due to their wide application (Gbadamosi et al., 2022; Brandsma et al., 2014, Reemtsma et al., 2015). Notwithstanding their frequent detection, Cl-OPEs were present in this study at relatively low concentrations in animal-based foods which may be because their transfer from feed is inefficient (Gbadamosi et al., 2022; Zhang et al., 2022).

The highest concentrations of $\sum_8$OPEs were obtained in melon (median: 17.4; range: 14.9 – 23.6 ng/g ww), followed by cassava flour (median: 11.6; range: 8.60 – 18.5 ng/g ww), milk (median: 9.62; range 5.68 – 18.0 ng/g ww), roasted meat and cow hide (median: 9.08; 1.30 – 47.1 ng/g ww); while the least contaminated food was dried and roasted fish (median: 3.90; range: 1.61 – 28.1 ng/g ww) (Table 6.6). The elevated OPE concentrations in melon may result from uptake of OPEs from soil, as Egusi melon belongs to the genus *cucurbitae*, and previous studies have shown that plants from this genus display unusually high propensity for root

uptake from soil and translocation to fruits, of organic chemicals such as chlorinated dioxins (Hulster et al., 1994).

The values obtained in this study are comparable to those observed in our previous study of OPEs in UK foodstuffs (Gbadamosi et al., 2022). However, our detection of the highest Σ_8OPE concentrations in melon, contrasts with previous studies in the USA, China, Australia, Belgium, Sweden, and the UK, where the highest median concentrations of OPEs were reported in fish, rice/meat/cereals, vegetables, fats/oils, cereals and milk and milk products (Wang and Kannan, 2018; Zhang et al., 2016; Chen et al., 2021, Ding et al., 2018; He et al., 2018; Poma et al., 2017; 2018; Gbadamosi et al., 2022). Across all food samples, TBOEP was present at the highest median concentration (36.2 ng/g ww, 41% of Σ_8OPEs), followed by TPHP (20.0 ng/g ww, 22%), EHDPP (13.8 ng/g ww, 15%) with the lowest median concentration reported for TMPT (<0.32; <2%) (Table 6.6; Fig. 6.1). The sum of the median concentrations of the three aryl-OPEs (∑aryl-OPEs, TPHP, EHDPP, and TMTP) and the two alkyl-OPEs (∑alkyl-OPEs, TBOEP and TnBP) were respectively 35.3 ng/g ww (40% Σ_8OPEs) and 41.9 ng/g ww (47%), which exceeded significantly those of the three Cl-OPEs (∑Cl-OPEs, TCEP, TCIPP and TDCIPP; median: 12.2 ng/g ww, 14%) ($p < 0.05$). The $\sum_8$OPE concentrations in most foods in this study were within the range reported previously in other studies around the world (Wang and Kannan, 2018; Gbadamosi et al., 2022; Poma et al., 2017; 2018; Chen et al., 2021; Zhao et al., 2019; He et al., 2018). However, for milk, our concentrations (median: 9.62; 5.68 – 18.0 ng/g ww) were approximately 100 times lower than those reported for dairy products in China (median: 952, range: 33.8 – 3065 ng/g ww) (Zhang et al., 2016), but exceeded those reported in studies from: Sweden, Belgium, the USA, China, Australia, and the UK (Poma et al., 2017; 2018; Wang and Kanaan et al., 2018; Zhao et al., 2019; Wang et al., 2022; He et al., 2018; Gbadamosi et al., 2022). This variation in the distribution of OPE concentration data obtained in our study along with those from previous

studies from different countries is likely attributed to international variations in the regulation, production, and use of OPEs.

TPHP was the main OPE detected in dried and smoked fish (median: 2.02 ng/g, 52%), milk (median: 4.54 ng/g ww, 47%), cereals (median: 3.06 ng/g ww, 40%), cassava flakes (Garri) (median: 2.50 ng/g ww, 55%), and melon (median: 4.47 ng/g, ww, 26%) respectively (Table 6.6; Fig. 6.2). EHDPP was the main compound detected in wheat flour (Semo) (median: 4.77 ng/g ww, 58%) followed by cereal (median: 3.01 ng/g, ww; 39%). This is consistent with EHDPP being one of the main OPEs used in food packaging materials. Similar to observations in previous studies in the USA (Wang and Kannan, 2019), China (Ding et al., 2018, Zhang et al., 2016), and the UK (Gbadamosi et al., 2022), TBOEP was the major OPE detected in our study, contributing about 41% to the median concentration of $\sum_8$OPEs in the foodstuffs analysed. This may be because of the high bioaccumulation factor (BAF) of TBOEP (25.6) (Wang and Kannan, 2019) or its wide application in various consumer and industrial products leading to its ubiquitous presence in the environment. In contrast, the Cl-OPEs were the lowest contributors to Σ_8OPE concentrations, apart from TMTP that was not detected in any sample. The most abundant Cl-OPE in this study was TDCIPP, which was detected in: cassava flakes (median: 0.67 ng/g, ww: 15% Σ_8OPEs) and wheat flour (median: 1.39 ng/g, ww; 17%); followed by TCEP in dried and smoked fish (median: 0.40 ng/g, ww; 10%). (Table 6.6). For TnBP, the greatest contribution of 14% Σ_8OPEs occurred in dried and smoked fish (median: 0.53 ng/g, ww).

To evaluate whether transport of foodstuffs (and associated factors such as additional time spent in contact with food packaging) lead to markedly increased concentrations of OPEs; we compared concentrations of OPEs in dried and smoked fish, roasted meat, and cereals collected in African stores in the UK, with those purchased in Nigeria. Our data showed higher mean concentrations of $\sum_8$OPEs in fish purchased in the UK (n = 17; 10.3 ng/g ww) than in those

bought in Nigeria (n = 9; 5.11 ng/g ww) (Kruskal-Wallis H test, $p > 0.05$) (Table S9). For the three Cl-OPEs (TCEP, TCIPP and TDCIPP) there is no significant differences in concentrations between samples of fish bought in the UK and Nigeria (Kruskal-Wallis H test, $p > 0.05$). In contrast, concentrations of the aryl-OPEs: TPHP and EHDPP, in fish purchased in the UK (3.25 and 2.33 ng/g ww) exceeded significantly those in fish bought in Nigeria (1.20 and 0.14 ng/g ww) ($p < 0.05$) (Mann-Whitney U tests) (Table S9). However, for roasted meat and cereals, there are significantly difference ($p > 0.05$) in concentrations of TPHP and EHDPP (although higher) in the sample bought in the African stores in UK and those from Nigeria. In the same vein, a higher concentration of Cl-OPEs (but not significantly so, Kruskal-Wallis H test, $p > 0.05$) are seen in UK-purchased samples of meats and cereals (Table S9). The same trend was obtained for the alkyl-OPEs: TBOEP, where higher concentrations but not significant (Kruskal-Wallis H test, $p > 0.05$) were found in roasted meat, dried and smoked fish, and cereal collected in the UK (8.54, 2.75 and 0.24 ng/g ww) from those collected in Nigeria (3.09, 1.89 and 0.87 ng/g ww) (Table S9). TnBP was not detected in any of the samples purchased in Nigeria while the median concentrations were 0.18 and 0.55 ng/g ww in cereal and roasted meat purchased in the UK. Our results suggest that some food of Nigerian origin sold in the UK are more contaminated with aryl-OPEs and TBOEP than in equivalent foodstuffs sold in Nigeria. While our comparison is based on relatively few samples, this raises a potential concern for exposure of individuals consuming such imported foods, and more detailed investigation of this issue is recommended strongly.

Concentrations of OPEs in foodstuffs bought from major African stores in the UK were also compared with those in equivalent "typical" UK foodstuffs bought from major grocery stores and reported in a previous study (Gbadamosi et al, 2022). The median concentrations of S_8OPEs obtained in dried and smoked fish (5.91 ng/g ww) and cereal (13.0 ng/g ww) collected from African stores in the UK were comparable to those reported for dried and smoked fish

(5.58 ng/g ww) and cereal (13.8 ng/g ww) in our previous study of UK foodstuffs (Gbadamosi et al., 2022). In contrast, significantly higher (Kruskal-Wallis H test, $p>0.05$) concentrations of S_8OPEs were detected in milk of UK origin (median 17.6 ng/g) (Gbadamosi et al., 2022) than in milk from Nigeria (median: 9.62 ng/g ww) bought in the UK; while the median concentration of S_8OPEs in roasted meat (11.5 ng/g ww) from Nigeria purchased in African stores in the UK exceeded that detected in meat (median 6.30 ng/g ww) from UK supermarkets (Gbadamosi et al., 2022).

Table 6.6: Overall descriptive statistics of OPEs in Nigerian foodstuffs (ng/g, ww)

Food category and # samples purchased in Nigeria and UK	Statistical parameter	TCEP	TCIPP	TDCIPP	EHDPP	TPHP	TnBP	TBOEP	TMTP	∑OPEs
Dried and smoked fish (n=26) Nigeria (n=9), UK (n=17)	Mean	0.48	0.49	0.27	1.40	2.38	<0.53	2.38	<0.16	8.09
	Median	0.40	0.35	0.06	0.14	2.02	<0.53	0.24	<0.16	3.90
	Range	0.12-1.04	<0.13-1.35	<0.06-1.13	<0.14-7.70	<0.23-7.64	<0.53	<0.24-8.53	<0.16	1.61-28.1
	97.5th Percentile	1.02	1.13	1.09	7.54	6.79	<0.53	8.47	-	
	DF (100 %)	100	92	23	27	85	0	31	0	
Roasted meat and cow hide (n=23) Nigeria (n=7), UK (n=16)	Mean	0.52	0.40	0.59	2.33	0.97	0.52	7.23	<0.18	12.7
	Median	0.43	0.29	0.36	2.25	0.23	0.53	4.83	<0.18	9.10
	Range	0.12-1.25	0.11-1.00	<0.07-1.97	<0.14-8.71	<0.22-4.07	<0.53-0.57	<0.26-29.4	<0.18	1.63-47.1
	97.5th Percentile	1.19	0.86	1.94	7.39	3.68	0.53	25.7	-	
	DF (100 %)	100	100	70	70	39	4	44	0	
Milk (Liquid and Powder) (n=6) All in the UK	Mean	0.18	0.34	0.88	<0.16	4.64	<0.60	3.62	<0.16	10.6
	Median	0.18	0.29	0.75	<0.16	4.54	<0.60	3.03	<0.16	9.71
	Range	0.10-0.33	0.18-0.60	0.45-1.63	<0.16	3.87-5.40	<0.60	<0.27-9.20	<0.16	5.79-17.8
	97.5th Percentile	0.31	0.59	1.56	<0.16	5.39	<0.60	8.80	-	
	DF (100%)	100	100	100	0	100	0	50	0	
Cereal (n=10) Nigeria (n=5), UK (n=5)	Mean	0.19	0.31	0.66	2.92	3.39	0.31	0.55	<0.17	8.50
	Median	0.18	0.25	0.42	3.01	3.06	0.33	0.24	<0.17	7.66
	Range	0.11-0.28	0.20-0.56	<0.06-2.12	<0.16-5.93	<0.24-7.03	<0.07-0.53	<0.26-2.13	<0.17	1.27-18.7
	97.5th Percentile	0.28	0.54	1.93	5.85	6.94	0.53	1.89	<0.17	18.1
	DF (100%)	100	100	83	67	83	50	17	0	
Wheat flour (n=3) All UK	Mean	0.28	0.56	1.21	5.04	<0.25	<0.58	<0.26	<0.17	8.35
	Median	0.29	0.64	1.39	4.77	<0.25	<0.58	<0.26	<0.17	8.35

	Range	0.23-0.33	0.25-0.79	0.50-1.74	3.64-6.71	<0.25	<0.58	<0.26	<0.17	5.88-10.8
	97.5th Percentile	0.33	0.78	1.72	6.62	<0.25	<0.58	<0.26	<0.17	10.7
	DF (100%)	100	100	100	100	0	0	0	0	
Cassava flour (n=3) (Fufu) All UK	Mean	0.36	0.45	0.97	0.35	2.18	1.13	7.31	<0.21	12.9
	Median	0.26	0.48	1.04	0.32	1.49	1.09	6.75	<0.21	11.6
	Range	0.21-0.61	0.38-0.49	0.76-1.11	<0.19-0.60	0.60-4.46	<0.72-1.76	5.82-9.35	<0.21	8.89-18.6
	97.5th Percentile	0.59	0.49	1.10	0.59	4.31	1.73	9.22	<0.21	18.2
	DF (100%)	100	100	100	67	100	67	100	0	
Yam powder (n=3) (Poundo yam) All UK	Mean	0.22	0.14	0.39	<0.16	<0.23	0.40	6.04	<0.16	7.74
	Median	0.29	0.13	0.48	<0.16	<0.23	0.53	6.50	<0.16	8.48
	Range	0.04-0.34	<0.07-0.23	<0.06-0.61	<0.16	<0.23	<0.14-0.53	5.08-6.55	<0.16	5.94-8.81
	97.5th Percentile	0.34	0.23	0.61	<0.16	<0.23	0.53	6.55	<0.16	8.81
	DF (100%)	100	67	67	0	0	33	100	0	
Plantain snacks (n=3) All UK	Mean	0.41	0.29	0.90	<0.19	1.06	0.47	4.07	<0.21	7.60
	Median	0.46	0.18	0.71	<0.19	1.19	0.53	5.46	<0.21	8.93
	Range	0.27-0.51	0.17-0.51	0.59-1.39	<0.19	<0.30-1.76	<0.16-0.53	<0.32-6.49	<0.21	2.21-11.6
	97.5th Percentile	0.50	0.50	1.35	<0.19	1.73	0.53	6.44	<0.21	11.5
	DF (100%)	100	100	100	0	67	33	67	0	
Cassava flakes (Garri) (n=5) All UK	Mean	0.22	0.24	0.66	2.21	2.98	<0.53	1.01	<0.16	8.01
	Median	0.21	0.13	0.67	0.14	2.50	<0.53	0.24	<0.16	4.58
	Range	0.13-0.32	<0.13-0.47	0.64-0.68	<0.15-6.34	2.36-4.08	<0.53	<0.25-2.54	<0.16	4.35-15.1
	97.5th Percentile	0.32	0.46	0.68	6.03	4.00	<0.53	2.42	<0.16	14.6
	DF (100%)	100	67	100	33	100	0	33	0	
Melon (Egusi) (n=3) All UK	Mean	0.21	0.22	0.37	2.64	4.71	<0.48	9.84	<0.18	18.7
	Median	0.22	0.19	0.45	2.71	4.47	<0.48	8.71	<0.18	17.4
	Range	0.15-0.26	0.16-0.29	0.20-0.47	2.31-2.90	4.11-5.54	<0.48	7.33-13.5	<0.18	14.9-23.6
	97.5th Percentile	0.26	0.29	0.47	2.89	5.49	<0.48	13.2	<0.18	23.3

	DF (100%)	100	100	100	100	100	0	100	0	

* Sum of two isomers (TMTP1 and TMTP2)

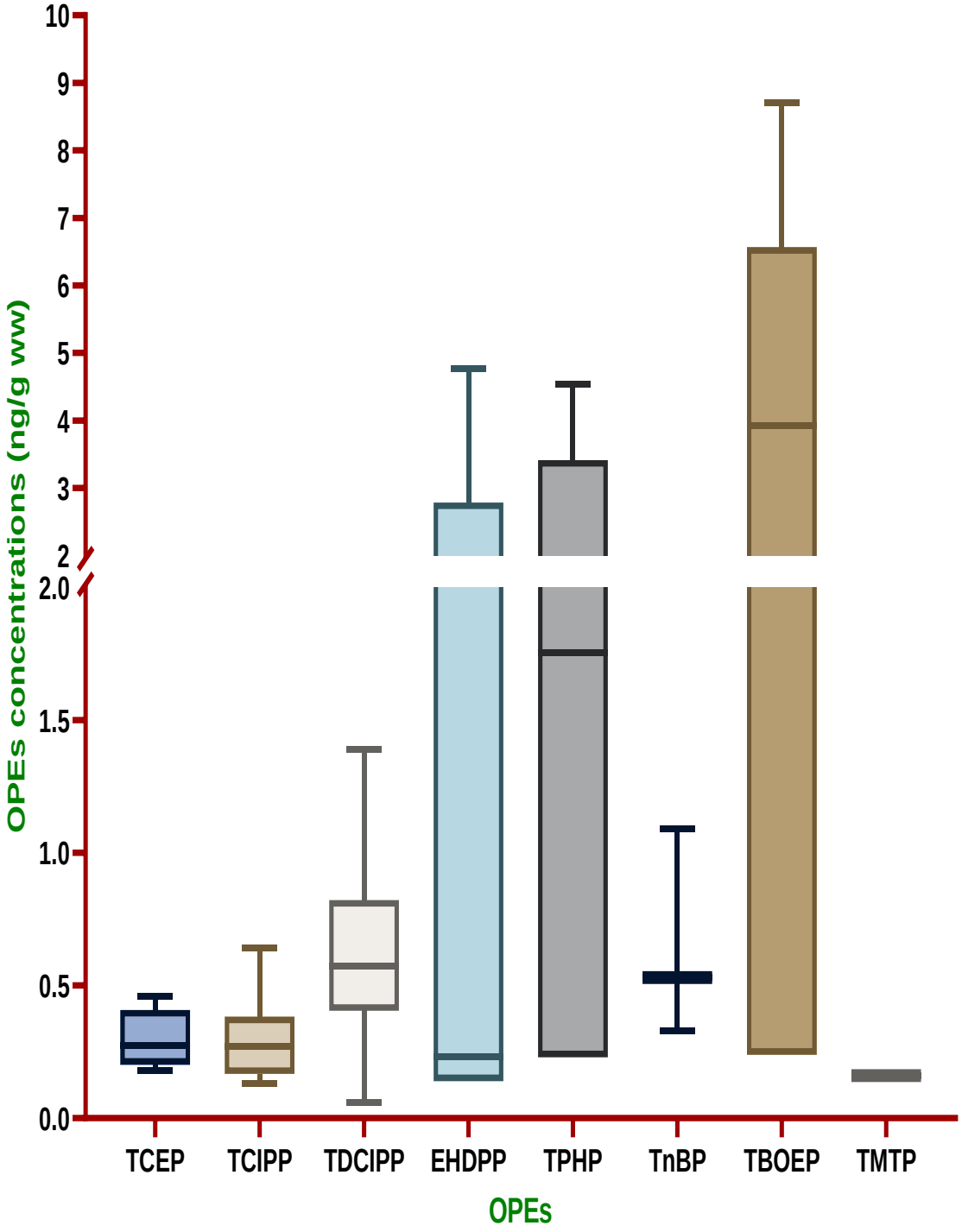


Fig. 6.1: Box and whisker-plot showing lower and upper concentrations of OPEs in African foodstuffs (ng/g ww). [The central box represents the concentrations from 25th to 75th percentile. The middle bold line is the median OPE concentrations, while the top and bottom lines of the y-error bars represent the maximum and minimum OPE concentrations]

6.6 Source identification and correlation between individual OPEs in foodstuffs of Nigerian origin

The results of a Spearman's rank correlation analysis were used to establish the relationship between the concentrations of individual OPEs in the foodstuffs (Table 6.7) after removing the outliers using the interquartile range method (IQR) and all TMTP data as this OPE was not detected in any sample. TCEP shows a significant strong negative correlation with TPHP ($r = -0.767$; $p < 0.01$), and a weak negative correlation with TDCIPP ($r = -0.164$). A weak non-significant correlation also existed between TCIPP and TDCIPP ($r = 0.207$), moderate between TCIPP and EHDPP ($r = 0.586$), weak between TCIPP and TnBP ($r = 0.312$) and weak negative correlations with TPHP ($r = -0.172$) and TBOEP ($r = -0.191$) (Table 6.7). In the same vein, weak non-significant correlation existed between TDCIPP with TBOEP and TnBP ($r = 0.119 - 0.467$). EHDPP also correlated weakly but non-significantly with TnBP and TBOEP ($r = -0.053$ to -0.249) (Table 6.7). The positive correlation between TDCIPP, TCIPP and EHDPP suggests that these chemicals share the same contamination sources in the foodstuffs, while the negative correlation between TDCIPP and TPHP implies that their sources are unrelated. This contrasts with what was obtained in some previous studies where a significant positive correlation between a number of OPEs were found in foodstuffs from the USA (Wang and Kannan, 2019), China (Chen et al., 2021a), the UK (Gbadamosi et al., 2022) and in other matrices such as house dust (Huang et al., 2020) and human milk (Chen et al., 2021b).

Principal component analysis (PCA) was also applied to further establish the possible contamination sources of the OPEs in the foodstuffs. Using PCA, the whole dataset was dimensionally reduced to three components which explained 79.0 % of the total variation, similar to what was obtained in our previous study in UK foodstuffs where the three extracted components explained 78.9% of the total variation (Gbadamosi et al., 2022). The first component (PC-1) explained 31.5% of the variance and was loaded heavily in a positive

direction by TCIPP (0.891) and TDCIPP (0.880) (Table 6.8; Fig. 6.2). The second component (PC-2) explained 23.8% of the total variation and was loaded significantly by two OPEs: TCEP (0.93) in a positive direction and TPHP in a negative direction (-0.88), while the third component explained 23.7% of the total variation and was significantly positively loaded by two OPEs: TnBP (0.81) and TBOEP (0.76) and significantly negatively loaded by EHDPP (-0.63) (Table 6.8; Fig. 6.2). The PCA results are to some extent consistent with the correlational analysis where a positive correlation was obtained between TCIPP and TDCIPP which is PC-1 and a negative correlation between TCEP and TPHP i.e., PC-2 ($p < 0.05$).

Table 6.7: Spearman's correlation between the concentrations of OPEs in foodstuffs of Nigerian origin.

Correlations								
OPEs	Spearman's	TCEP	TCIPP	TDCIPP	EHDPP	TPHP	TnBP	TBOEP
TCEP	Correlation Coefficient	1	0.182	-0.164	-0.071	-0.767**	0.234	0.119
	Sig. (2-tailed)		0.614	0.651	0.845	0.010	0.516	0.744
TCIPP	Correlation Coefficient		1	0.207	0.586	-0.172	0.312	-0.191
	Sig. (2-tailed)			0.567	0.154	0.634	0.380	0.597
TDCIPP	Correlation Coefficient			1	0.071	-0.092	0.467	0.119
	Sig. (2-tailed)				0.845	0.800	0.173	0.744
EHDPP	Correlation Coefficient				1	-0.098	-0.249	-0.053
	Sig. (2-tailed)					0.787	0.488	0.884
TPHP	Correlation Coefficient					1	-0.236	-0.051
	Sig. (2-tailed)						0.511	0.890
TnBP	Correlation Coefficient						1	0.522
	Sig. (2-tailed)							0.122
TBOEP	Correlation Coefficient							1
	Sig. (2-tailed)							

Table 6.8: Principal component scores (after varimax rotation) obtained from analysis of OPE concentrations in foods of Nigerian origin.

OPES	Component			
	1	2	3	Communalities
TCIPP	**.891**	.172	-.150	0.847
TDCIPP	**.880**	-.078	.097	0.789
TCEP	-.185	**.925**	.067	0.894
TPHP	-.274	**-.879**	.000	0.847
TnBP	.495	.067	**.808**	0.903
TBOEP	-.110	.013	**.759**	0.589
EHDPP	.521	-.024	**-.625**	0.663
Eigen-value	2.260	1.760	1.512	
% of variance explained	31.516	23.824	23.670	
Cumulative (%)	31.516	55.339	79.009	

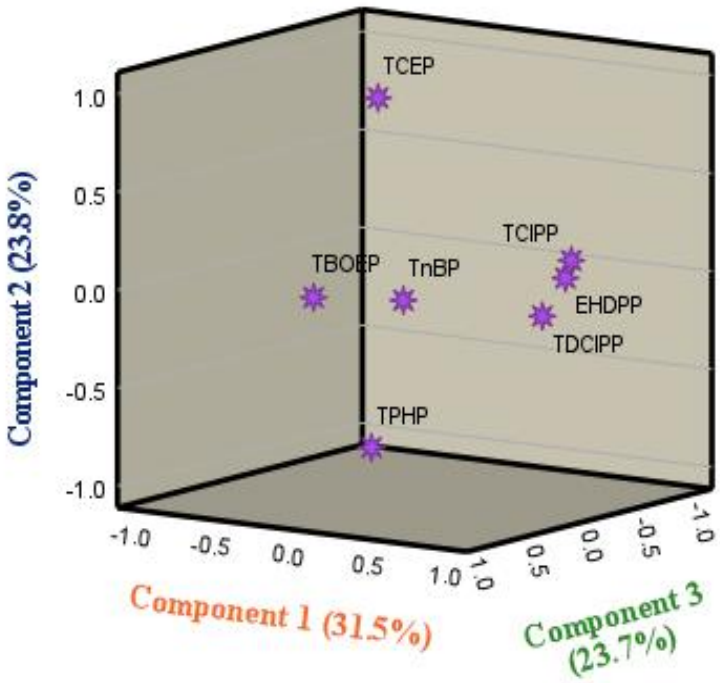


Fig. 6.2 Graphical representation of components (PC-1 = 31.5 %, PC-2 = 23.8 %, and PC-3 = 23.7 %)

6.7 Evaluation of human dietary exposure to OPEs from consumption of foods of Nigerian origin

Median and high-end EDIs for $\sum_8$OPEs based on consumption of the foods analysed in this study were respectively: 431 and 771 ng/kg bw/day for children and 405 and 798 ng/kg bw/day for adults (Table 6.9 a-b; Fig. 6.3). The median and high-end EDI for the aryl-OPEs: TPHP (children: 92.3 and 176 ng/kg bw/day; adults: 90.6 and 176 ng/kg bw/day) and EHDPP: (children: 58.2 and 159 ng/kg bw/day; adults: 52.2 and 162 ng/kg bw/day) exceed those obtained for the UK population (Gbadamosi et al., 2022). The same trend was observed for the Cl-OPEs. However, the median children EDI value for the Cl-OPEs: TCEP (12.6 ng/kg bw/day), TCIPP (13.5 ng/kg bw/day) and TDCIPP (33.8 ng/kg bw/day) in our study were comparable to those reported in US (Wang and Kannan, 2018). The exposure data obtained for OPEs in foodstuffs of Nigerian origin for children and adults fall mainly within the international range reported previously for foodstuffs from other countries/regions. Compared to previous observations whereby cereal and milk and milk products were the highest contributor to OPE exposure for adults in Belgium, China, and the UK (Poma et al., 2017, Ding et al., 2018; Gbadamosi et al., 2022); in our study, dough cassava flour (Fufu), a locally processed food was the main contributor to human dietary exposure to OPEs in this study accounting for between 23 – 33 % of Σ_8OPE EDIs for adults and children respectively (Table 6.9a-b; Fig. 6.4). However, for children, other major contributors to dietary exposure to Σ_8OPEs (median and high-end EDIs) were: yam powder (poundo yam) (72 and 75 ng/kg bw/day), melon (71.6 and 96 ng/kg bw/day), and cereals (52.9 and 125 ng/kg bw/day). For adults, the main contributors in addition to cassava flour were: cassava flakes (Garri) (52.4 and 167 ng/kg bw/day) > milk (41.2 and 74.9 ng/kg bw/day) > wheat flour (Semo) (39.3 and 50.6 ng/kg bw/day) > yam powder (poundo yam) (36.3 and 37.6 ng/kg bw/day) > cereals (36.1 and 85.5 ng/kg bw/day) > plantain snacks (25.3 and 32.4 ng/kg bw/day) > roasted meat and cow

hide (23.6 and 108 ng/kg bw/day) > melon (16.2 and 21.7 ng/kg bw/day) > dried and smoked fish (1.92 and 13.2 ng/kg bw/day) (Table 6.9a-b, Fig. 6.3).

With respect to individual OPEs, the main contributor to Σ_8OPE concentrations was TBOEP, which accounted for 39% Σ_8OPEs for adults and 42% for children, followed by TPHP (22% adults – 21 % children), EHDPP (13 – 21 %), TDCIPP (7 – 9 %), TnBP (5 - 8%), TCIPP (3 – 4 %), TCEP (3%), and TMTP (1 – 2 %) (Table 6.9a-b; Fig. 6.3). This is similar to the situation for UK foodstuffs where TBOEP was the major contributor to Σ_8OPE exposure for all four of the age groups considered (Gbadamosi et al., 2022) and also consistent with assessment of the dietary exposure of the US population where TBOEP was the principal contributor to ΣOPEs exposure at ~30% for each age group studied (Wang and Kannan, 2018). In line with our previous study of UK dietary exposure (Gbadamosi et al, 2022), much of the contribution of TBOEP to overall dietary exposure originated from consumption of cassava flour, yam powder, melon, and plantain snacks rather than uniformly across all foodstuffs. Among the Cl-OPEs, TDCIPP makes the highest contribution to Σ_8OPE exposure (33.8 – 36.9 ng/kg bw/day, 8 – 9 %) for adults and children respectively (Table 6.9 a-b, Fig. 6.3).

Our mean exposure EDIs obtained for five OPEs namely TCEP, TCIPP, TDCIPP, TPHP, and TBOEP for children (335 ng/kg bw/day) were between 3 - 13 times higher than the value reported for children in UK foodstuffs (111 and ng/kg bw/day) (Gbadamosi et al., 2022), in Eastern China (39.1 ng/kg bw/day) (Ding et al., 2018) and for children in New York (26.6 ng/kg bw/day) (Wang and Kannan, 2018) (see appendix 6.3). The high exposure EDI value for children (567 ng/kg bw/day) was comparable to the value reported for children in UK (664 ng/kg/bw/day) under high-exposure scenario (Gbadamosi et al., 2022) (see appendix 6.3). More so, the mean and high-exposure data for the five OPEs for adults (314 and 590 ng/kg bw/day) in this study were below those reported for male (378 and 618 ng/kg bw/day) and

female (427 and 664 ng/kg bw/day) adults in China (Zhang et al., 2016), in USA (mean EDI =16.6 ng/kg bw/day) (Wang and Kannan, 2018), in UK (42.5 and 213 ng/kg bw/day) (Gbadamosi et al., 2022), in Belgium (mean: 77.5 ng/kg bw/day) (Poma et al., 2018), and in China (9.10-34.4 and 21.3-309 ng/kg bw/day) (Zhao et al., 2019; Sala et al., 2022; Wang et al., 2022) (see appendix 6.3).

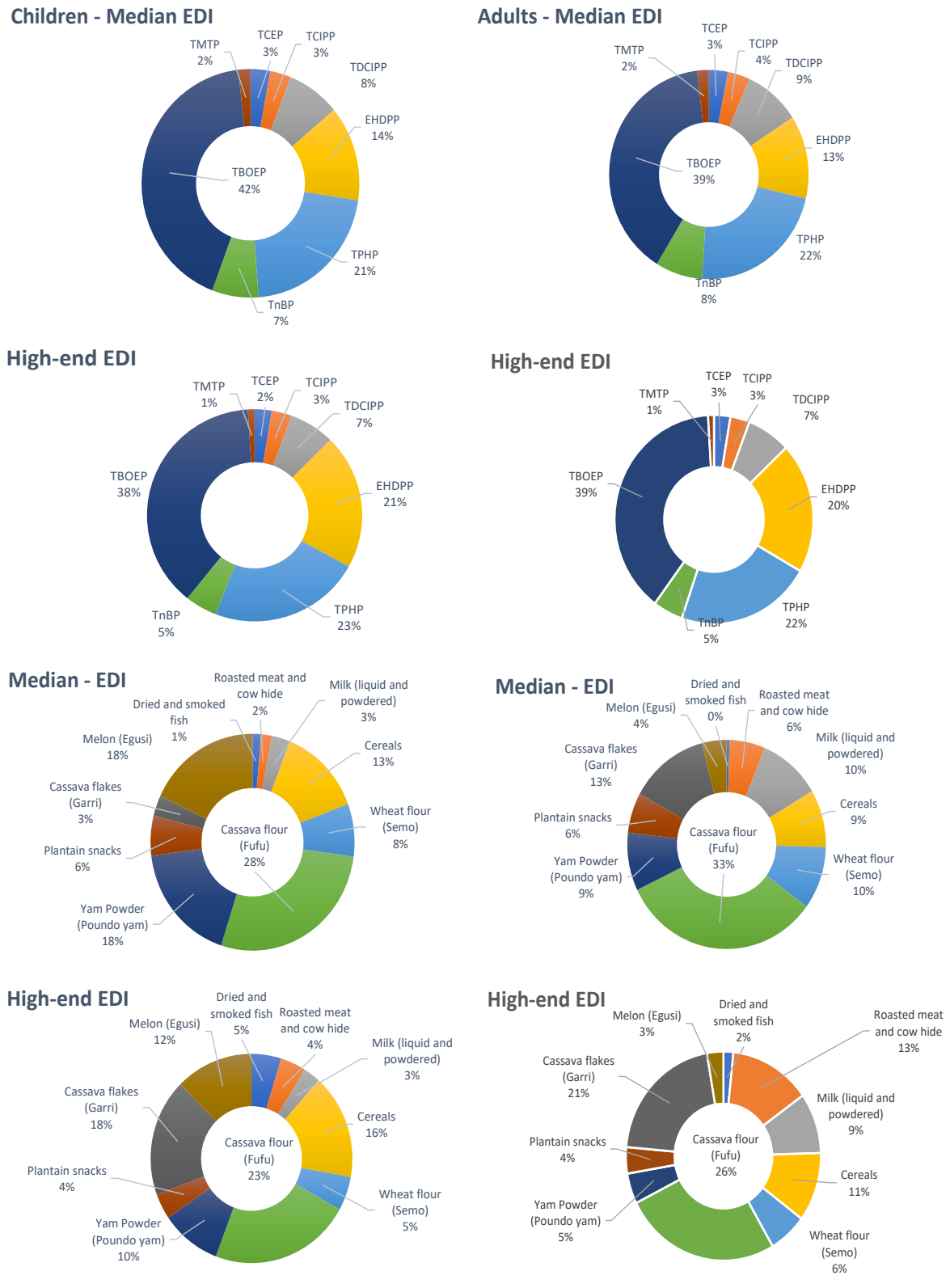


Fig. 6.3: Median and high-end exposure percent contributions of individual OPEs and different foodstuffs to Σ_8OPE EDIs for children and adults

Table 6.9a: Estimated Daily Dietary Intakes (EDI, ng/kg bw/day) of Organophosphate Esters in Various foodstuffs for Children Consuming Foods analysed in this Study (high-exposure data are in parentheses)

OPE/Foodstuff	Dried and smoked fish	Roasted meat and cow hide	Milk (liquid and powdered)	Cereals	Wheat flour (Semo)	Cassava flour (Fufu)	Yam Powder (Poundo yam)	Plantain snacks	Cassava flakes (Garri)	Melon (Egusi)	∑OPE	% Contribution to the ∑OPEs in ∑foodstuffs
TCEP	0.55 (1.41)	0.33 (0.91)	0.21 (0.38)	1.25 (1.93)	1.13 (1.25)	2.47 (5.65)	2.48 (2.87)	1.25 (1.36)	2.04 (3.05)	0.92 (1.07)	12.6 (19.9)	3 (3)
TCIPP	0.48 (1.55)	0.22 (0.65)	0.35 (0.71)	1.74 (3.72)	2.45 (2.99)	4.61 (4.72)	1.11 (1.93)	0.47 (1.33)	1.25 (4.39)	0.80 (1.18)	13.5 (23.2)	3 (3)
TDCIPP	0.08 (1.49)	0.27 (1.48)	0.91 (1.88)	2.91 (13.3)	5.29 (6.58)	10.0 (10.6)	4.12 (5.15)	1.92 (3.65)	6.45 (6.57)	1.83 (1.93)	33.8 (52.6)	8 (7)
EHDPP	0.19 (10.4)	1.71 (5.62)	0.17 (0.17)	20.8 (40.4)	18.2 (25.3)	3.04 (5.65)	1.19 (1.19)	0.38 (0.38)	1.34 (57.9)	11.1 (11.9)	58.2 (159)	13 (21)
TPHP	2.78 (9.30)	0.17 (2.80)	5.49 (6.52)	21.2 (48.0)	0.88 (0.88)	14.3 (41.4)	1.96 (1.96)	3.22 (4.66)	24.0 (38.4)	18.4 (22.5)	92.3 (176)	21 (23)
TnBP	0.73 (0.73)	0.40 (0.40)	0.64 (0.64)	2.25 (3.67)	2.02 (2.02)	10.5 (16.6)	4.51 (4.51)	1.43 (1.43)	5.09 (5.09)	2.18 (2.18)	29.7 (37.2)	7 (5)
TBOEP	0.33 (11.7)	3.67 (19.5)	3.67 (10.6)	1.66 (13.1)	0.92 (0.92)	64.8 (89.0)	55.3 (55.6)	14.7 (17.4)	2.30 (23.3)	35.8 (54.3)	183 (295)	42 (38)
TMTP	0.22 (0.22)	0.12 (0.12)	0.19 (0.19)	1.11 (1.11)	0.61 (0.61)	1.54 (1.54)	1.36 (1.36)	0.43 (0.43)	1.54 (1.54)	0.66 (0.66)	7.77 (7.77)	2 (1)
∑OPEs (ng/kg bw/day)	5.36 (36.7)	6.90 (31.5)	11.6 (21.1)	52.9 (125)	31.5 (40.5)	111 (175)	72.0 (75.0)	23.8 (30.6)	12.4 (140)	71.6 (96)	**431 (771)**	100

Table 6.9b: Estimated Daily Dietary Intakes (EDI, ng/kg bw/day) of Organophosphate Esters in Various foodstuffs for Adults Consuming Foods analysed in this Study (high-exposure data are in parentheses)

OPE/Foodstuff	Dried and smoked fish	Roasted meat and cow hide	Milk (liquid and powdered)	Cereals	Wheat flour (Semo)	Cassava flour (Fufu)	Yam Powder (Poundo yam)	Plantain snacks	Cassava flakes (Garri)	Melon (Egusi)	∑OPEs	% Contribution to the ∑OPEs in ∑foodstuffs
TCEP	0.20 (0.50)	1.13 (3.11)	0.75 (1.35)	0.85 (1.32)	1.41 (1.57)	2.95 (6.73)	1.25 (1.45)	1.32 (1.44)	2.43 (3.63)	0.21 (0.24)	12.5 (21.3)	3 (3)
TCIPP	0.17 (0.56)	0.76 (2.24)	1.24 (2.53)	1.18 (2.54)	3.06 (3.74)	5.48 (5.62)	0.56 (0.98)	0.50 (1.41)	1.49 (5.23)	0.18 (0.27)	14.6 (25.1)	4 (3)
TDCIPP	0.03 (0.54)	0.94 (5.05)	3.23 (6.67)	1.99 (9.09)	6.61 (8.22)	11.9 (12.6)	2.08 (2.60)	2.04 (3.87)	7.68 (7.82)	0.41 (0.44)	36.9 (56.9)	9 (7)
EHDPP	0.07 (3.71)	5.84 (19.2)	0.60 (0.60)	14.2 (27.6)	22.7 (31.6)	3.62 (6.72)	0.60 (0.60)	0.40 (0.40)	1.60 (68.9)	2.52 (2.69)	52.2 (162)	13 (20)
TPHP	0.99 (3.34)	0.60 (9.57)	19.4 (23.1)	14.4 (32.7)	1.10 (1.10)	17.0 (49.2)	0.99 (0.99)	3.41 (4.95)	28.5 (45.7)	4.15 (5.10)	90.6 (178)	22 (22)
TnBP	0.26 (0.26)	1.38 (1.38)	2.27 (2.27)	1.54 (2.50)	2.53 (2.53)	12.5 (19.7)	2.27 (2.27)	1.51 (1.51)	6.06 (6.06)	0.49 (0.49)	30.8 (39.0)	8 (5)
TBOEP	0.12 (4.18)	12.6 (66.8)	13.0 (37.7)	1.13 (8.93)	1.15 (1.15)	77.2 (105)	27.9 (28.1)	15.6 (18.4)	2.74 (27.7)	8.09 (12.3)	159 (311)	39 (39)
TMTP	0.08 (0.08)	0.42 (0.42)	0.69 (0.69)	0.76 (0.76)	0.76 (0.76)	1.83 (1.83)	0.69 (0.69)	0.46 (0.46)	1.83 (1.83)	0.15 (0.15)	7.65 (7.65)	2 (1)
∑OPEs	1.92 (13.2)	23.6 (108)	41.2 (74.9)	36.1 (85.5)	39.3 (50.6)	132 (208)	36.3 (37.6)	25.3 (32.4)	52.4 (167)	16.2 (21.7)	405 (798)	100%

6.7.1 Dietary risk assessment to OPEs in the selected foodstuffs from Nigeria

EDIs for adults and children in this study exceed those obtained based on consumption of non-Nigerian foodstuffs sold in the UK (Gbadamosi et al., 2022) and are more comparable to those obtained in China (Zhang et al., 2016). Table 6.10 compares the EDIs obtained in this study with reference dose (RfD) values from five different sources for our target OPEs. In all instances, EDI values were several orders of magnitude below RfD values (Table 6.10).

Table 6.10: Comparison of the median estimated daily intakes (EDIs) for children and adults for all OPEs with their respective reference doses (RfDs) (values in parentheses are high-end EDIs)

	TCEP	TCIPP	TDCIPP	EHDPP	TPHP	TnBP	TBOEP	TMTP	∑OPEs
EDI for Children	12.6 (19.9)	13.5 (23.2)	33.8 (52.6)	58.2 (159)	92.3 (176)	29.7 (37.2)	183 (295)	7.77 (7.77)	431 (771)
EDI for Adults	12.5 (21.3)	14.6 (25.1)	36.9 (56.9)	52.2 (162)	90.6 (176)	30.8 (39.0)	159 (311)	7.65 (7.65)	405 (798)
RfD (USEPA, 2017)	7000	10000	20000	NA	NA	10000	NA	NA	
RfD (Ali et al., 2012)	22000	80000	15000	NA	70000	24000	15000	NA	
RfD (Van den Eede et al., 2011)	2200	8000	1500	NA	7000	2400	15000	NA	
RfD (Zhao et al., 2019)	NA	NA	NA	600	NA	NA	NA	NA	
RfD (Saito et al., 2007)	NA	3600	NA	NA	NA	NA	NA	NA	

6.8 Conclusion

The present study reports the levels and profiles of eight OPEs in 85 foodstuffs of Nigerian origin, of which some were purchased in Nigeria and others bought from major African stores in Birmingham, UK. TBOEP, TPHP, and EHDPP were the predominant OPEs found in the foodstuffs analysed, with highest Σ_8OPE concentrations found in melon (Egusi), cassava flour (Fufu), and milk (liquid and powder). The sum of the total concentrations of the three aryl-OPEs: TPHP, EHDPP, and TMTP significantly exceeds those of the three Cl-OPEs: (TCEP, TCIPP, and TDCIPP). Locally processed foods such as cassava flour, plantain snacks, melon, yam powder, roasted meat, and cow hide were more contaminated with TBOEP and TPHP than other foods studied. Our results revealed significantly higher concentrations of aryl-OPEs in dried and smoked fish bought from African stores in the UK than in similar samples purchased in Nigeria ($p < 0.05$). Cassava flour dough (Fufu) was the major foodstuff contributing to dietary intake of OPEs, comprising 26% Σ_8OPEs for children and 33% for adults. EDI values for OPEs were several orders of magnitude below the current reference dose values, suggesting low risks from these chemicals via consumption of foods of Nigerian origin. Nonetheless, EDIs obtained in this study exceed those for the UK population generally, and more detailed measurement of dietary exposure of Africans is recommended.

6.9 References

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CHAPTER VII

SUMMARY AND CONCLUSIONS

Rapidly increased use of OPEs globally in recent times as alternative FRs and their ubiquitous presence in all environmental compartments (food, soil, air, water etc) will increase human exposure with attendant health implications. Despite the health effects of the OPEs, information on the worldwide presence in foodstuffs remains scant. Despite the wide publication and availability of a considerable amount of information on OPEs and their health risks, recent research priorities have focused on the occurrence of OPEs in dust, indoor and outdoor air, surface and ground waters, sediment, while data on food samples are limited except a few studies in Australia, USA, Sweden, Belgium, and China which report their presence in some selected food samples. 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. Thus, a periodical monitoring of the presence of OPEs in foodstuffs from the countries where they have been reported in other matrices, dust and air especially in Western Europe, North America and China and in other countries where their presence has not been evaluated, need an urgent attention so as to be able to have a comprehensive assessment of human exposure to these chemicals.

The main objectives of this study were to investigate the magnitude and pathways of human dietary exposure to organophosphate esters (OPEs) using GC-EIMS. In this study, eight OPEs were measured in UK foodstuffs, UK drinking water, Nigeria indoor dust, and foodstuffs from African origin.

7.1 Major findings in each chapter

Chapter two: Organophosphate Esters in UK Diet; Exposure and Risk Assessment

- ❖ We investigate 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.

The 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. Our study also finds out that TBOEP is the major contributor to EDIs for Σ_8OPEs (24 – 37%) for all foods and age groups. Baby food contributed 39% of $\sum_8$OPEs 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. More so, 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. Furthermore, 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. Among our target OPEs, TBOEP, EHDPP, and TPHP posed the highest risk. Our study therefore confirms that – in line with other industrialised countries - food ingestion is a substantial pathway of human exposure to OPEs in the UK.

Chapter three: **Concentrations of organophosphate esters in drinking water from the United Kingdom: Implications for human exposure**

- We reported the concentrations of eight OPEs in 52 samples of drinking water collected in the UK with the primary objective to assess the significance of water ingestion as a pathway of exposure of the UK population.
- To the best of our knowledge, this is the first study of the occurrence of OPEs in UK drinking water and as such will form a valuable baseline against which efforts to minimize this occurrence may be evaluated.

Results obtained showed that daily intakes of $\sum_8$OPEs via tap water ingestion for the four age groups was between 41 - 44 % higher than those for bottled water. Our data shows that tap water was the most contaminated with chlorinated OPEs (TCEP and TCIPP), aryl-OPEs (TPHP and EHDPP), and alkyl-OPEs (TBOEP). Comparison of our drinking water data with other exposure pathways to OPEs in the UK, reveals drinking water ingestion poses a lower exposure risk to OPEs than through dermal uptake, food, and dust ingestion. The overall UK population's exposure to OPEs via drinking water for all age groups were below the reported values for other exposure pathways but nonetheless represents an appreciable human exposure pathway, especially for infants, toddlers, and children.

Chapter four: **Presence, source attribution, and human exposure to organophosphate esters in indoor dust from various microenvironments in Nigeria**

- We investigate the concentrations and profiles of target OPEs in indoor dust from Nigeria,

- ❖ We compare the concentrations profiles of OPEs in the different microenvironment (cars, offices, medical centres, and residential homes)
- ❖ We identify and apportion the possible sources of the OPEs in the indoor dust from the selected microenvironment in Nigeria
- ❖ We estimate the magnitude of human exposure risks to OPEs via indoor dust ingestion in Nigeria.

Among the OPEs considered, TBOEP have the highest average concentrations with a DF of 100% in all four microenvironments representing between 28 - 41 % of the total OPE concentrations in the 4 microenvironments. The highest concentrations of the chlorinated OPEs: TCEP, TCIPP and TDCIPP were found in offices, followed by car/buses, homes with the lowest seen in medical centres. We no statistically significant difference ($p > 0.05$) between the TPhP and EHDPP concentrations observed in dust from the four microenvironments studied. Our median EDI value for ΣOPEs obtained for toddlers in this study was about 21-23 times higher than that for adults via the two exposure pathways considered. As a result of their lower body weight, more frequent hand-to-mouth contact (Hou et al., 2016) and greater proximity to the floor; toddlers are more exposed to OPEs than adults. Exposure via dust ingestion exceeds that via dermal absorption from contact with dust.

Chapter five: Occurrence and Dietary Exposure to Organophosphorus Esters in foodstuffs from African origin

- ❖ We report for the first time the levels and distribution of eight OPEs in a wide range of African foodstuffs collected directly from local African market in Nigeria and those collected from major African stores in Birmingham, UK with the labelled confirming the origin from Nigeria and from the store owners

- ❖ We investigate the likely contamination sources of OPEs in African foodstuffs
- ❖ We estimate human dietary exposure to the compounds within the African population using different exposure scenarios to assess the related exposure risk

  However, current data and understanding on the occurrence of OPEs in foodstuffs and dietary exposure and consequent health risk is far from sufficient especially when there is no single data from any Africa countries.

The highest median concentrations of ∑OPEs were obtained in Melon followed by cassava flour (Fufu) milk, roasted meat and cow hide and the least contaminated food was dried and roasted fish. The sum of the median concentrations of the three aryl-OPEs (∑aryl-OPEs, TPHP, EHDPP and TMTP) and two alkyl-OPEs (∑alkyl-OPEs, TBOEP and TnBP) were significantly higher than those of the three Cl-OPEs (∑Cl-OPEs, TCEP, TCIPP and TDCIPP) (Wilcoxon signed rank test, $p < 0.05$). We therefore conclude that there is more contamination from alkyl-OPEs and aryl-OPEs than the Cl-OPEs. We obtained that Cassava flour (Fufu) contributed the highest human exposure to OPEs via dietary intake among the various foodstuffs accounting for between 26 – 33 % to the total doses for adults and children respectively.

7.2 Conclusion

A comprehensive review of the relevant literature was undertaken, that reveals human exposure to OPEs to be ubiquitous and to occur via a variety of pathways. While inhalation exposure and especially exposure via indoor dust ingestion are relatively well-characterised, exposure via the diet and drinking water were highlighted as potentially important omissions. Furthermore, a dearth of data for Africa was highlighted. This thesis thus measured the exposure of the UK population via the diet and drinking water as well as providing insights into the exposure of the Nigerian population via the diet and indoor dust ingestion. Findings confirm diet and to a lesser extent drinking water to be important in the UK and the combined

exposure with the available data for indoor dust ingestion and dermal uptake in UK showed a marginal health risk for some OPEs for toddlers and children. Moreover, exposure to OPEs in Nigeria was - although lower than in developed countries - non-negligible. Currently, exposures to OPEs in both the UK and Nigeria are within health-based limit values, but continued surveillance of exposure is recommended, as evidence of OPE toxicity continues to emerge. This study further confirmed that diet is a substantial human exposure pathway to OPEs in UK and Nigeria and a more detailed measurement of dietary exposure to OPEs in Africans and other regions where there is no dietary data and more importantly with other exposure pathways is recommended for overall human exposure assessment.

7.3. Research gaps and future perspectives

This thesis adds to the existing data on the occurrence, magnitude, and pathways of dietary exposures to organophosphate esters commonly used as flame retardants and plasticizers in various consumer products. Findings from our review reveals that relatively small studies have evaluated the magnitude of the dietary exposure to OPEs and that food ingestion is a substantial and important human exposure pathway to the compounds. More so, literature reveals that food contamination with OPEs are majorly from the industrial processing and food packaging materials especially for food such as grains, fat and oils, and dairy products. Due to this, periodic monitoring of processed foodstuffs and other animal-derived and plant derived food become necessary in future studies. In addition to the parent OPEs, there should be further extensive studies on the OPE metabolites in foodstuffs. This becomes necessary as few studies have indicated that OPE derivatives could potentially co-exist with their parent compound in environmental matrices. More importantly, some studies have stated that compared to their parent OPE triesters, such metabolites/degradation products are more biologically active with respect to several toxicological endpoints. 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.

On the drinking water as a result of the ubiquitous presence of OPEs in the aquatic ecosystem could leads to their persistent in the various matrices and which results in production of more toxic OPEs metabolites through hydrolysis, photodegradation and biotransformation process. Conclusively, comprehensive studies are needed to fully determine the overall human exposure to OPEs via other exposure routes including air inhalation, dietary ingestion, water ingestion and dermal exposure in UK and Nigeria as there exist no data on air inhalation in UK and no data for dermal uptake and other exposure pathways in Nigeria.

SUPPLEMENTARY MATERIALS PROVIDED AS APPENDIX

Appendix for chapter three:

Appendix 3.1: List of analysed food samples and average moisture contents (%)

Name of the food samples	Sample Code	Food group	Classification	Average Water content (%)
Free range egg (n=5)	EGG-1	EGG	Animal-derived food	67
Fat spread (n=5)	Fat-O	Fat and oils	Plant-derived food	ND
Cooking oils (n=6)	Fat-O	Fat and oils	Plant-derived food	ND
Pasta (n=8)	PAST	Cereal and cereal products	Industrially-processed food	4.7
Rice (n=10)	RCE	Cereal and cereal products	Industrially-processed food	8.6
Noodles (n=5)	NDLE	Cereal and cereal products	Industrially-processed food	4.3
Pizza (n=7)	PIZZ	Cereal and cereal products	Industrially-processed food	46
White bread (n=6)	WTB	Cereal and cereal products	Industrially-processed food	23
Brown bread (n=5)	BBD	Cereal and cereal products	Industrially-processed food	34
Burger bread (n=5)	BUB	Cereal and cereal products	Industrially-processed food	32
Bacon Rasher (n=5)	BCR	Savoury snacks	Industrially-processed food	1.9
Onion ring (n=6)	ORI	Savoury snacks	Industrially-processed food	3.1
Corn Chips/flakes (n=10)	CHIPS	Savoury snacks	Industrially-processed food	11-13
Mini Pretzel (n=7)	MIN	Savoury snacks	Industrially-processed food	1.3
Yorkshire puddings (n=10)	YORK	Pastries	Industrially-processed food	2.1
Croissants (n=10)	CRS	Pastries	Industrially-processed food	28
Cakes (n=7)	MUF	Pastries	Industrially-processed food	14-18
Biscuits (n=15)	BIS	Pastries	Industrially-processed food	1.7-2.3
Milk (n=24)	MLK	Milk and milk products	Animal-derived food	67-89

Ice cream (n=30)	MLK	Milk and milk products	Animal-derived food	72-88
Desserts (n=5)	MLK	Milk and milk products	Animal-derived food	76
Cheese (n=6)	MLK	Milk and milk products	Animal-derived food	42
Yogurts (n=10)	MLK	Milk and milk products	Animal-derived food	80-87
Formula milk (n=9)	BBF	Baby food	Animal-derived food	1.7-2.3
Cod (n=7)	COD	Fish	Animal-derived food	74-80
Trout (n=5)	TRT	Fish	Animal-derived food	68
Tilapia (n=5)	TLA	Fish	Animal-derived food	80
Salmon (n=5)	SAL	Fish	Animal-derived food	55-62
Tuna (n=5)	TUN	Fish	Animal-derived food	74
Prawn (n=5)	PRA	Fish	Animal-derived food	69-85
Mackerel (n=5)	MAC	Fish	Animal-derived food	50
Basa (n=5)	BAS	Fish	Animal-derived food	68-78
Lamb (n=5)	LAMB	Meat	Animal-derived food	63-65
Beef (n=10)	BEEF	Meat	Animal-derived food	61-74
Pork (n=5)	PORK	Meat	Animal-derived food	63-68
Chicken (n=5)	CHIC	Meat	Animal-derived food	72-75
Turkey (n=5)	Turk	Meat	Animal-derived food	65
Sweetcorn (n=5)	SWTC	Vegetable	Plant-derived food	87
Mixed vegetables (n=3)	MIX	Vegetable	Plant-derived food	81-82
Broccoli (n=3)	BRO	Vegetable	Plant-derived food	79-80
Vegetable Medley and Carrot (n=3)	MED	Vegetable	Plant-derived food	83
Lettuce (n=3)	LET	Vegetable	Plant-derived food	81-82
Mixed pepper (n=3)	PEP	Vegetable	Plant-derived food	79-81

Mushroom (n=3)	MUSH	Vegetable	Plant-derived food	78
Salad (n=3)	SAL	Vegetable	Plant-derived food	78
Spinach (n=3)	SPIN	Vegetable	Plant-derived food	78
Orange juice (n=5)	ORS	Non-alcoholic beverages	Plant-derived food	90-93
Apple juice (n=5)	APP	Non-alcoholic beverages	Plant-derived food	89-92
Pineapple/Banana juice (n=3)	BAN	Non-alcoholic beverages	Plant-derived food	90-94
Strawberry juice (n=3)	STRAW	Non-alcoholic beverages	Plant-derived food	90-94
Coke (n=2)	COKE	Non-alcoholic beverages	Plant-derived food	93-95
Cucumber (n=3)	CUM	Fruits	Plant-derived food	89-94
Apple (n=3)	APL	Fruits	Plant-derived food	92-93
Banana (n=3)	BNA	Fruits	Plant-derived food	89-93
Strawberry/Grapes mix (n=3)	GRA	Fruits	Plant-derived food	89-93
Oranges (n=3)	ORN	Fruits	Plant-derived food	90-94
Melon/Mangoes mix (n=3)	MEL	Fruits	Plant-derived food	88-90
Sweets (n=5)	SWT	Sweet, sugar and chocolate confectioneries	Industrially-processed food	1.6-2.1
Sugar (n=8)	SG	Sweet, sugar and chocolate confectioneries	Industrially-processed food	ND
Chocolate (n=5)	CHOCO	Sweet, sugar and chocolate confectioneries	Industrially-processed food	1.4
Salted peanuts (n=8)	PEA	Nuts	Industrially-processed food	1.6
Dried Mashed Potato (n=14)	POT	Potatoes	Plant-derived food	67-78

ND = Not determined

Appendix 3.2: **GC retention times and ions monitored**

OPE	Abbreviation	Retention time (min)	Quantification ion (m/z)	Qualifier ion (m/z)
Deuterated IS	d_{27}-TnBP	8.06	103	167
Tri-*n*-butyl phosphate	TnBP	8.17	99	155, 211
Tris(2-chloroethyl) phosphate	TCEP	8.87	249	251
Tri(3-chloropropyl) phosphate	TCIPP	9.07	277	279
Deuterated IS	d_{15}-TPHP	12.69	342	339
Tris(1,3-dichloro-2-propyl) phosphate	TDCIPP	12.16	380.9	382.9
Triphenyl phosphate	TPHP	12.75	326.1	325.1
2-ethylhexyl diphenyl phosphate	EHDPP	12.99	251	250
Tris(2-butoxyethyl) phosphate	TBOEP	12.58	124	199
Tri-m-tolyl phosphate	TMTP	14.4020	368	367
RDS	2,3,4,6-Tetrachlorobiphenyl (PCB-62)	10.09	291.9	293.9

Appendix 3.3. Limits of quantification (LOQs) for the different food groups analysed (ng/g ww).

OPEs	Cereals/Cereal products	Pastries	Savoury snacks	Milk and milk products	Baby Food	Eggs and egg products	Fish	Fats/oils	Meat and meat products	Vegetables	Non-alcoholic beverages	Fruits	Sugar/ sweets	Nuts	Potatoes
TCEP	0.23	0.09	0.10	0.18	0.10	0.18	0.09	0.22	0.20	0.23	0.24	0.25	0.09	0.12	0.18
TCIPP	0.26	0.10	0.13	0.20	0.11	0.20	0.10	0.24	0.22	0.26	0.26	0.28	0.07	0.24	0.20
TDCIPP	0.16	0.07	0.08	0.14	0.07	0.14	0.07	0.17	0.15	0.18	0.18	0.19	0.07	0.17	0.14
TPHP	0.23	0.10	0.10	0.19	0.10	0.19	0.10	0.23	0.21	0.24	0.25	0.26	0.10	0.23	0.19
EHDPP	0.26	0.10	0.10	0.19	0.10	0.20	0.10	0.24	0.22	0.25	0.26	0.27	0.10	0.24	0.20

TnBP	0.21	0.08	0.12	0.16	0.09	0.16	0.08	0.20	0.18	0.21	0.21	0.22	0.08	0.19	0.16
TBOEP	0.66	0.26	0.32	0.50	0.27	0.50	0.26	0.61	0.56	0.64	0.66	0.69	0.25	0.60	0.50
TMTP*	1.18	0.48	0.41	0.93	0.50	0.94	0.48	1.15	1.04	1.20	0.41	0.58	0.48	0.56	0.54

*Sum of two isomers

Appendix 3.4: Average Daily UK food consumption rate data for toddlers, children, adults, and elderly (g/day) for each foodstuff obtained from (National Diet and Nutrition Survey (NDNS) report Published by Public Health England and the Food Standards Agency (2014)

Food groups	Toddlers' food consumption rate (g/day)	Children food consumption rate (g/day	Adults' food consumption rate (g/day	Elderly food consumption rate (g/day	Foodstuff for which concentration is available	Comments
Cereal & cereal products	11.6	28.8	27.5	16.8	Pasta	based on 58 g/day of pasta, rice, pizza, and other miscellaneous cereals assuming equal consumption of all 5 groups and using average concentration for each of these 4 groups
Cereal & cereal products	11.6	28.8	27.5	16.8	Rice	based on 58 g/day of pasta, rice, pizza, and other miscellaneous cereals assuming equal consumption of all 5 groups and using average concentration for each of these 4 groups
Cereal & cereal products	11.6	28.8	27.5	16.8	Pizza	based on 58 g/day of Pasta, rice, pizza, and other miscellaneous cereals assuming equal consumption of all 5 groups and using average concentration for each of these 4 groups

Cereal & cereal products	11.6	28.8	27.5	16.8	Other cereals	based on 58 g/day of Pasta, rice, pizza, and other miscellaneous cereals assuming equal consumption of all 5 groups and using average concentration for each of these 4 groups
Cereal & cereal products	32	65	65	61	white bread	based on 32 g/day of white bread assuming equal consumption of both groups in this category and using average concentration
Cereal & cereal products	28	41	43	47	Brown bread	based on 28 g/day of brown bread assuming equal consumption of both groups in this category and using average concentration
Cereal & cereal products	11.6	23	22	13.5	Noodles	based on 58 g/day of Pasta, rice, pizza and other miscellaneous cereals assuming equal consumption of all 5 groups and using average concentration for each of these 4 groups
Cereal & cereal products	14	34	31	34	Burger bread	based on 14 g/day of other bread assuming equal consumption of both groups in this category and using average concentration
Pastries	9	17	18	20.5	Croissants	based on 18 g/day of buns, cakes, pastries, and fruit pies assuming equal consumption of all 2 groups and using average concentration for each of these 2 groups
Pastries	9	17	18	20.5	Cakes	based on 18 g/day of buns, cakes, pastries, and fruit pies assuming equal consumption of all 4 groups and using average concentration for each of these 4 groups
Pastries	42	48	51	69	Puddings	based on 42 g/day of puddings assuming equal consumption of both groups in this category and using average concentration

Pastries	15	26	22	19	Biscuits	based on 15 g/day of biscuits assuming equal consumption of both groups in this category and using average concentration
Savoury snacks	2.25	4.75	3.75	2.5	Mini pretzel	based on 18 g/day of buns, cakes, pastries, and fruit pies assuming equal consumption of all 4 groups and using average concentration for each of these 4 groups
Savoury snacks	2.25	4.75	3.75	2.5	Corn chips	based on 18 g/day of buns, cakes, pastries, and fruit pies assuming equal consumption of all 4 groups and using average concentration for each of these 4 groups
Savoury snacks	2.25	4.75	3.75	2.5	Bacon Rasher	based on 9 g/day of 2 Savoury snacks assuming equal consumption of all 2 groups and using average concentration for each of these 2 groups
Savoury snacks	2.25	4.75	3.75	2.5	Onion ring	based on 9 g/day of 2 Savoury snacks assuming equal consumption of all 2 groups and using average concentration for each of these 2 groups
Milk and milk products	192	154	129	165	Semi skimmed	based on 192 g/day of semi skimmed milk assuming equal consumption of both groups in this category and using average concentration
Milk and milk products	335	110	114	141	Skimmed	based on 335 g/day of skimmed milk assuming equal consumption of both groups in this category and using average concentration
Milk and milk products	280	152	121	188	Whole	based on 280 g/day of whole milk assuming equal consumption of both groups in this category and using average concentration
Milk and milk products	51.25	20.75	12.25	12.25	Evaporated milk	based on 205 g/day of 3 other milks and cream groups assuming equal consumption of all 4 groups

						and using average concentration for each of these 4 groups
Milk and milk products	51.25	20.75	12.25	12.25	Banana milk	based on 205 g/day of 3 other milks and cream groups assuming equal consumption of all 4 groups and using average concentration for each of these 4 groups
Milk and milk products	51.25	20.75	12.25	12.25	Chocolate milk	based on 205 g/day of 3 other milks and cream groups assuming equal consumption of all 4 groups and using average concentration for each of these 4 groups
Milk and milk products	21	31	27	31	Ice cream	based on 21 g/day of ice cream assuming equal consumption of both groups in this category and using average concentration
Milk and milk products	51.25	20.75	12.25	12.25	Fresh cream and spray cream	based on 205 g/day of 3 other milks and cream groups assuming equal consumption of all 4 groups and using average concentration for each of these 4 groups
Milk and milk products	10	18	20	19	Cheddar cheese	based on 10 g/day of cottage cheese assuming equal consumption of both groups in this category and using average concentration
Milk and milk products	26	37	30	25	Cottage Cheese	based on 26 g/day of cottage cheese assuming equal consumption of both groups in this category and using average concentration
Milk and milk products	29	27	36.5	38	Desserts	based on 58 g/day of two yoghurt, fromage frais and other dairy desserts assuming equal consumption of all 2 groups and using average concentration for each of these 2 groups
Milk and milk products	29	27	36.5	38	Yoghurts	based on 58 g/day of yoghurt, fromage frais and other dairy desserts assuming equal consumption

						of all 3 groups and using average concentration for each of these 3 groups
Baby Food	280	-	-	-	Baby milk (SMA, Little baby & Aptamil)	(**Assume value for whole milk**), based on 280 g/day of whole milk assuming equal consumption of both groups in this category and using average concentration
Egg and egg products	23	35	41	33	Egg and egg products	based on 23 g/day of egg and egg dishes assuming equal consumption of both groups in this category and using average concentration
Fish	4.2	7.4	10.2	10.4	Cod	assuming 21 g/day of other white fish, shellfish, fish dishes and canned tuna assuming equal consumption of all 5 groups in this category and using average concentration
Fish	4.2	7.4	10.2	10.4	tilapia	assuming 21 g/day of other white fish, shellfish, fish dishes and canned tuna assuming equal consumption of all 5 groups in this category and using average concentration
Fish	4.2	7.4	10.2	10.4	tuna	assuming 21 g/day of other white fish, shellfish, fish dishes and canned tuna assuming equal consumption of all 5 groups in this category and using average concentration
Fish	4.2	7.4	10.2	10.4	prawns	assuming 21 g/day of other white fish, shellfish, fish dishes and canned tuna assuming equal consumption of all 5 groups in this category and using average concentration
Fish	4.2	7.4	10.2	10.4	basa	assuming 21 g/day of other white fish, shellfish, fish dishes and canned tuna assuming equal consumption of all 5 groups in this category and using average concentration

Fish	7	10.8	16	14	salmon	based on 21 g/day for 3 oily fish assuming equal consumption of all the 3 groups in this category and using average concentration
Fish	7	10.8	16	14	mackerel	based on 21 g/day for 3 oily fish assuming equal consumption of all the 3 groups in this category and using average concentration
Fish	7	10.8	16	14	trout	based on 21 g/day for 3 oily fish assuming equal consumption of all the 3 groups in this category and using average concentration
Fat and oils	6	9	10	13	Fat spread	based on 6 g/day of reduced fat spread assuming equal consumption of both groups in this category and using average concentration
Fat and oils	5	8	10	14	Butter	based on 5 g/day of butter assuming equal consumption of both groups in this category and using average concentration
Fat and oils	0.5	1	1.5	1.5	Cooking oils	based on 1 g/day of margarine and other fat and oils assuming equal consumption of all 2 groups in this category and using average concentration
Meat and meat products	34	60	76	65	Lamb	based on 34 g/day of lamb and dishes assuming equal consumption of both groups in this category and using average concentration
Meat and meat products	39	79	96	91	Beef	based on 39 g/day of beef and veal dishes assuming equal consumption of all 2 groups in this category and using average concentration
Meat and meat products	27	36	55	38	Pork	based on 27 g/day of pork dishes assuming equal consumption of both groups in this category and using average concentration

Meat and meat products	12.5	34.5	45.5	34.5	Chicken	based on 25 g/day of chicken, turkey, and dishes assuming equal consumption of all 2 groups in this category and using average concentration
Meat and meat products	12.5	34.5	45.5	34.5	Turkey	based on 25 g/day of chicken, turkey, and dishes assuming equal consumption of all 2 groups in this category and using average concentration
Vegetable	6.86	10.9	14.4	15.4	Sweetcorn	based on 48 g/day of 7 vegetable (not raw) including dishes assuming equal consumption of all 9 groups in this category and using average concentration
Vegetable	6.86	10.9	14.4	15.4	Broccoli	based on 48 g/day of 7 vegetable (not raw) including dishes assuming equal consumption of all 9 groups in this category and using average concentration
Vegetable	6.86	10.9	14.4	15.4	Carrot	based on 48 g/day of 7 vegetable (not raw) including dishes assuming equal consumption of all 9 groups in this category and using average concentration
Vegetable	6.86	10.9	14.4	15.4	Mixed pepper	based on 48 g/day of 7 vegetable (not raw) including dishes assuming equal consumption of all 9 groups in this category and using average concentration
Vegetable	6.86	10.9	14.4	15.4	Mushrooms	based on 48 g/day of 7 vegetable (not raw) including dishes assuming equal consumption of all 9 groups in this category and using average concentration
Vegetable	11	15.5	28.5	29	Lettuce	based on 22 g/day of two salads assuming equal consumption of all 3 groups in this category and using average concentration

Vegetable	6.86	10.9	14.4	15.4	Spinach	based on 48 g/day of 7 vegetable (not raw) including dishes assuming equal consumption of all 9 groups in this category and using average concentration
Vegetable	11	15.5	28.5	29	Salad	based on 22 g/day of two salads assuming equal consumption of all 3 groups in this category and using average concentration
Vegetable	6.86	10.9	14.4	15.4	Mixed vegetable	based on 48 g/day of 7 vegetable (not raw) including dishes assuming equal consumption of all 9 groups in this category and using average concentration
Non-alcoholic beverages	114	170	132	133	Orange, banana, apple, and strawberry juice	based on 114 g/day of fruit juice assuming equal consumption of both groups in this category and using average concentration
Fruits	106	84	120	143	Apple, banana, strawberry, oranges, mango/melon	based on 106 g/day of fruit assuming equal consumption of both groups in this category and using average concentration
Sweet, sugar and chocolate confectioneries	9	22	20	15	Chocolate	based on 9 g/day of chocolate confectioneries assuming equal consumption of both groups in this category and using average concentration
Sweet, sugar and chocolate confectioneries	13	20	12	11	Sweet	based on 7 g/day of sugars, including table sugar, preserves and sweet spreads assuming equal consumption of all 3 groups in this category and using average concentration
Sweet, sugar and chocolate confectioneries	7	10	17	20	Sugar	based on 13 g/day of sugar confectioneries assuming equal consumption of both groups in this category and using average concentration

Nut	9	11	14	11	Nuts (all nuts)	based on 9 g/day of nuts and seeds assuming equal consumption of all 2 groups in this category and using average concentration
Potato	32	58	69	79	Potato (all)	based on 32 g/day of potato salads and dishes assuming equal consumption of all 2 groups in this category and using average concentration

Appendix 3.5: Statistical summary of concentrations of OPEs in various food groups (ng/g ww) and detection frequencies (DF)

Food groups (number of samples analysed)	Statistical Parameters	TCEP	TCIPP	TPHP	TDCIPP	EHDPP	TBOEP	TnBP	TMTP *	∑OPEs
Cereal and cereal products (n=46)	Mean [a]	0.17	0.31	1.28	0.43	3.71	9.32	<0.11	<0.59	15.9
	Median [b]	0.12	0.29	1.18	0.41	3.96	7.18	<0.11	<0.59	13.8
	SD [c]	0.09	0.20	1.18	0.24	1.89	9.71	0.15	0.83	14.3
	Min [d]	0.05	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.44	0.66	5.02	0.80	7.32	22.7	<0.21	<1.18	38.3
	97.5th percentile [f]	0.37	0.61	4.69	0.79	6.99	22.34	-	-	-
	DF [g] (%)	100	89	69	69	83	14	0	0	-
Pastries (n=42)	Mean [a]	0.30	0.13	0.05	0.15	4.28	<0.13	<0.04	<0.24	5.32
	Median [b]	0.27	0.13	0.05	0.08	4.39	<0.13	<0.04	<0.24	5.33
	SD [c]	0.17	0.07	-	0.15	2.07	-	-	-	-
	Min [d]	0.11	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.28
	Max [e]	0.64	0.22	0.10	0.37	8.04	<0.26	0.08	<0.48	10.2
	97.5th percentile [f]	0.62	0.21	-	0.35	7.40	-	-	-	-
	DF [g] (%)	100	13	2	17	88	0	0	0	
Savoury Snacks (n = 28)	Mean [a]	0.32	1.46	0.22	0.09	0.79	0.16	0.50	<0.21	3.73
	Median [b]	0.24	0.66	0.20	0.08	0.66	0.16	0.68	<0.21	2.88

	SD [c]	0.21	1.50	0.17	0.01	0.45	-	0.36	-	-
	Min [d]	0.11	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.72	5.47	0.54	0.09	1.50	<0.32	0.86	<0.41	9.91
	97.5th percentile [f]	0.69	4.63	0.50	-	1.46	-	0.86	-	-
	DF [g] (%)	100	77	23	14	50	0	27	0	
Milk and milk products (n = 75)	Mean [a]	0.22	0.41	3.00	0.55	3.76	6.81	<0.06	3.60	18.4
	Median [b]	0.15	0.37	2.42	0.40	3.62	8.54	<0.06	2.04	17.6
	SD [c]	0.18	0.28	2.03	0.47	2.34	6.40	-	3.34	-
	Min [d]	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.91	1.62	7.96	2.99	8.23	17.94	0.11	9.82	49.6
	97.5th percentile [f]	0.71	1.03	6.94	1.47	7.84	16.53	-	9.71	-
	DF [g] (%)	75	97	77	89	79	17	0	8	-
Baby food (n = 9)	Mean [a]	0.12	0.18	3.14	0.18	2.93	<0.14	<0.05	<0.25	6.98
	Median [b]	0.12	0.17	3.16	0.18	2.75	<0.14	<0.05	<0.25	6.81
	SD [c]	0.01	0.06	0.73	0.05	0.81	-	-	-	-
	Min [d]	0.12	0.13	2.26	<LOQ	1.95	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.13	0.27	4.34	0.28	4.15	<0.27	<0.09	<0.50	10.0
	97.5th percentile [f]	0.12	0.27	4.24	0.26	4.13	-	-	-	-
	DF [g] (%)	100	100	100	89	100	0	0	0	
Egg and Egg products (n = 5)	Mean [a]	0.44	<0.10	<0.10	<0.07	<0.10	<0.25	<0.08	<0.47	1.61
	Median [b]	0.50	<0.10	<0.10	<0.07	<0.10	<0.25	<0.08	<0.47	1.66
	SD [c]	0.19	-	-	-	-	-	-	-	-
	Min [d]	0.14	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.64	0.20	<0.19	0.14	<0.20	<0.50	<0.16	<0.94	2.97
	97.5th percentile [f]	0.63	-	-	-	-	-	-	-	-
	DF [g] (%)	100	0	0	0	0	0	0	0	
Fish (n = 42)	Mean [a]	0.24	1.05	2.53	1.41	0.40	0.13	<0.04	0.65	6.44
	Median [b]	0.18	0.74	2.73	0.91	0.26	0.13	<0.04	0.60	5.58

	SD [c]	0.14	1.03	2.20	1.53	0.31	0.18	0.06	0.38	5.83
	Min [d]	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.69	5.07	6.65	5.99	0.97	0.26	<0.08	1.49	21.2
	97.5th percentile [f]	0.52	3.57	6.46	5.73	0.95	0.25	-	1.34	-
	DF [g] (%)	95	98	88	57	60	45	0	17	-
Fat and oils (n = 11)	Mean [a]	0.50	0.52	0.78	0.93	3.67	0.31	0.10	0.58	7.38
	Median [b]	0.45	0.43	0.79	0.79	4.05	0.31	0.10	0.58	7.49
	SD [c]	0.29	0.45	0.32	0.39	2.03	0.43	0.14	0.81	4.87
	Min [d]	0.15	0.12	0.11	0.45	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	1.00	1.61	1.33	1.63	5.56	<0.61	<0.20	<1.15	13.1
	97.5th percentile [f]	0.97	1.45	1.26	1.62	5.51	-	-	-	-
	DF [g] (%)	100	100	100	100	50	0	0	0	-
Meat and meat products (n = 30)	Mean [a]	0.26	1.70	3.35	0.67	3.70	<0.28	<0.09	0.69	10.7
	Median [b]	0.24	0.76	2.71	0.81	0.81	<0.28	<0.09	0.61	6.30
	SD [c]	0.14	2.12	2.10	0.59	4.67	-	-	0.38	10.5
	Min [d]	0.12	0.07	0.11	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.51	7.24	9.40	1.72	12.9	<0.56	<0.18	1.49	34.0
	97.5th percentile [f]	0.51	6.47	7.83	1.59	12.68	-	-	1.36	-
	DF [g] (%)	100	100	100	25	75	0	0	25	-
Vegetables (n = 29)	Mean [a]	0.13	0.15	0.84	0.26	0.58	7.20	0.95	1.14	11.2
	Median [b]	0.12	0.14	0.71	0.26	0.54	4.39	0.21	1.20	7.58
	SD [c]	0.02	0.05	0.45	0.14	0.32	6.96	1.87	0.14	9.96
	Min [d]	0.12	0.06	0.34	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.20	0.25	2.26	0.62	1.00	19.8	6.05	1.20	31.4
	97.5th percentile [f]	0.19	0.24	1.78	0.54	0.97	19.1	5.46	1.20	-
	DF [g] (%)	100	100	100	93	10	62	21	10	-
Non-alcoholic beverages (n=18)	Mean [a]	0.20	0.17	0.47	0.35	0.43	3.60	<0.11	<0.21	5.54
	Median [b]	0.24	0.15	0.50	0.39	0.38	0.66	<0.11	<0.21	2.62

	SD [c]	0.05	0.08	0.22	0.14	0.23	4.90	-	-	-
	Min [d]	0.24	0.04	0.23	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.24	0.30	1.02	0.54	0.69	15.7	<0.21	<0.41	19.1
	97.5th percentile [f]	0.24	0.29	0.87	0.53	0.67	13.8	-	-	-
	DF [g] (%)	100	100	100	97	27	33	0	0	441.0
Fruits (FRT) (n = 18)	Mean [a]	0.28	0.40	0.70	0.44	0.16	3.23	<0.11	<0.29	5.61
	Median [b]	0.22	0.27	0.61	0.44	0.13	1.10	<0.11	<0.29	3.17
	SD [c]	0.14	0.30	0.38	0.22	0.07	3.05	-	-	-
	Min [d]	0.22	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.66	1.06	1.55	0.96	0.37	8.12	<0.22	<0.58	13.5
	97.5th percentile [f]	0.64	1.05	1.35	0.84	0.32	8.07	-	-	-
	DF [g] (%)	100	89	89	100	22	50	0	0	-
Sweet, sugar and chocolate confectioneries (SSC) (n = 18)	Mean [a]	0.28	0.23	1.95	1.04	1.76	1.09	<0.04	0.72	7.10
	Median [b]	0.22	0.25	0.51	0.62	0.68	1.12	<0.04	0.62	4.07
	SD [c]	0.16	0.07	2.68	1.20	1.98	0.61	-	0.48	-
	Min [d]	0.13	0.08	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.60	0.30	7.20	3.40	5.69	1.85	<0.08	1.57	20.7
	97.5th percentile [f]	0.57	0.30	6.99	3.22	5.36	1.84	-	1.47	-
	DF [g] (%)	100	100	80	70	90	90	0	40	-
Nuts (n=8)	Mean [a]	0.30	0.16	2.65	0.46	0.24	<0.30	<0.10	<0.28	4.49
	Median [b]	0.24	0.18	0.23	0.45	0.24	<0.30	<0.10	<0.28	2.02
	SD [c]	0.11	0.04	4.19	0.19	0.02	-	-	-	-
	Min [d]	0.23	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
	Max [e]	0.42	0.19	7.49	0.65	0.26	<0.60	<0.19	<0.56	10.4
	97.5th percentile [f]	0.41	0.19	7.13	0.64	0.26	-	-	-	-
	DF [g] (%)	100	67	33	100	33	0	0	0	-
Potato (n=14)	Mean [a]	0.16	0.26	0.56	0.24	0.69	<0.25	<0.08	<0.27	2.52

	Median [b]	0.15	0.27	0.54	0.27	0.27	<0.25	<0.08	<0.27	2.10
	SD [c]	0.04	0.03	0.42	0.12	0.89	-	-	-	-
	Min [d]	<LOQ	0.22	<LOQ	0.09	0.21	<LOQ	<LOQ	<LOQ	0.84
	Max [e]	0.21	0.30	0.97	0.34	2.02	<0.50	<0.16	<0.54	5.04
	97.5^{th} percentile [f]	0.21	0.30	0.96	0.34	1.89	-	-	-	-
	DF [g] (%)	75	100	75	100	100	0	0	0	-

[*] Sum of two isomers (TMTP1 and TMTP2)

[a] mean: mean concentration

[b] median: median concentration

[c] SD: standard deviation

[d] Min: Minimum concentration

[e] Max: Maximum concentration

[f] 97.5^{th} percentile concentration

[g] DF (%): Detection frequency

Appendix 3.6: Summary of concentrations of OPEs reported in foodstuffs

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
Present study	United Kingdom	Cereal and cereal products	0.08 (<LOD-0.16)	0.16 (0.01-0.64)	0.27 (<LOD - 0.66)	0.44 (<LOD - 0.80)	1.35 (<LOD -5.02)	3.85 (<LOD - 7.32)	-	13.9 (<LOD - 22.7)	0.47 (<LOD -0.94)	-
		Pastries	0.63 (<LOD -0.86)	0.27 (0.02-0.72)	1.26 (<LOD - 5.47)	0.15 (<LOD - 0.37)	0.21 (0.00-0.54)	2.62 (<LOD - 8.04)	-	0.13 (<LOD - 0.26)	0.18 (<LOD -0.35)	-
		Milk and milk products	0.08 (<LOD -0.16)	0.22 (0.02-0.91)	0.40 (<LOD - 1.62)	0.55 (<LOD - 2.99)	3.00 (0.00-7.96)	3.75 (<LOD - 8.23)	-	9.07 (<LOD - 17.94)	8.33 (<LOD -15.5)	-
		Baby food	0.05 (<LOD -0.09)	0.08 (0.04-0.12)	0.16 (0.05-0.27)	0.16 (<LOD - 0.28)	3.14 (2.26-4.34)	2.93 (1.95-4.15)	-	0.14 (<LOD - 0.27)	0.25 (<LOD -0.50)	-
		Egg and egg products	0.08 (<LOD -0.16)	0.44 (0.14-0.64)	0.10 (<LOD - 0.20)	0.07 (<LOD - 0.14)	0.10 (<LOD -0.19)	0.10 (<LOD - 0.20)	-	0.25 (<LOD - 0.50)	0.47 (<LOD -0.94)	-
		Fish	0.04 (<LOD -0.08)	0.22 (<LOD - 0.69)	1.11 (0.00-5.07)	1.51 (<LOD - 5.99)	2.53 (<LOD -6.65)	0.43 (<LOD - 0.97)	-	0.13 (<LOD - 0.26)	0.91 (<LOD-1.84)	-
		Fat and oils	0.16 (<LOD-0.31)	0.50 (0.15-1.00)	0.52 (0.12-1.61)	0.93 (0.45-1.63)	0.77 (<LOD-1.33)	3.16 (<LOD-5.56)	-	0.31 (<LOD-0.61)	0.52 (<LOD-1.04)	-
		Meat and meat products	0.09 (<LOD-0.18)	0.24 (<LOD-0.51)	1.77 (<LOD-7.24)	0.86 (<LOD-1.72)	3.35 (<LOD-9.40)	3.47 (<LOD-12.9)	-	0.28 (<LOD-0.56)	1.12 (<LOD-2.25)	-
		Vegetables	1.74 (<LOD-6.05)	0.09 (0.02-0.20)	0.13 (0.03-0.25)	0.26 (<LOD-0.51)	0.76 (0.34-2.26)	0.24 (<LOD-0.48)	-	10.1 (<LOD-19.8)	0.69 (<LOD-1.35)	-
		Non-alcoholic beverages	0.11 (<LOD-0.21)	0.09 (0.05-0.18)	0.16 (<LOD-0.30)	0.36 (0.10-0.54)	0.49 (<LOD-1.02)	0.36 (<LOD-0.69)	-	10.7 (<LOD-20.7)	0.62 (<LOD-1.24)	-

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
		Fruits	0.11 (<LOD-0.22)	0.17 (0.01-0.66)	0.38 (0.09-1.06)	0.44 (0.15-0.96)	0.77 (<LOD-1.55)	0.22 (<LOD-0.37)	-	7.81 (<LOD-18.5)	1.00 (<LOD-1.67)	-
		Sweet and Sugar	0.04 (<LOD-0.08)	0.27 (0.11-0.60)	0.23 (0.07-0.30)	1.45 (0.06-3.40)	2.14 (<LOD -7.20)	1.75 (<LOD-5.69)	-	1.06 (<LOD-1.85)	0.97 (<LOD-1.92)	-
		Nuts	0.10 (<LOD-0.19)	0.17 (0.04-0.51)	0.15 (0.08-0.45)	0.46 (0.27-1.37)	3.75 (<LOD-7.49)	0.11 (<LOD-0.23)	-	0.30 (<LOD-0.60)	3.69 (<LOD-7.38)	-
		Potatoes	0.10 (<LOD-0.19)	0.08 (0.03-0.12)	0.21 (0.16-0.30)	0.24 (0.09-0.34)	0.62 (<LOD-0.97)	1.01 (<LOD-2.02)	-	0.25 (<LOD-0.60)	0.42 (<LOD-0.83)	
Chen et al., 2021	China	Aquatic food	0.135 (0.027-0.342)	0.798 (0.438-3.08)	0.982 (<LOD-25.5)	0.508 (<LOD-1.114)	0.318 (0.034-5.51)	4.62 (0.009-18.9)	0.182 (0.006-18.5)	0.145 (0.008-1.63)	-	-
		Meat	0.147 (<LOD-0.515)	0.982 (0.366-3.00)	1.75 (0.065-6.15)	0.558 (0.121-1.43)	0.453 (0.082-1.63)	4.61 (<LOD-35.5)	0.178 (<LOD-5.56)	0.136 (0.003-3.53)	-	-
		Egg	0.05 (<LOD-0.545)	1.05 (0.22-4.13)	1.27 (0.107-6.94)	0.406 (0.076-6.72)	0.237 (0.046-20.9)	2.3 (0.014-26.2)	0.073 (<LOD-5.77)	0.105 (<LOD-0.733)	-	-
		Milk	0.089 (0.015-0.54)	0.237 (0.107-0.909)	0.664 (0.116-1.844)	0.292 (<LOD-0.971)	0.109 (0.023-4.719)	0.84 (<LOD-16.6)	0.129 (<LOD-4.45)	0.178 (<LOD-1.87)	-	-
		Total samples	0.105 (<LOD-0.545)	0.093 (<LOD-1.28)	0.977 (<LOD-25.5)	0.414 (<LOD-6.72)	0.274 (0.023-20.9)	1.63 (<LOD-35.5)	0.14 (<LOD-18.5)	0.136 (<LOD-3.53)	-	-
Poma et al., 2018	Belgium	Fat & Oil	6.62 (5.27-18.7)	2.57 (1.28-11.01)	38.87 (30.99-109.87)	20.18 (16.09-57.04)	2.14 (1.56-5.52)	7.57 (3.16-17.11)	6.45 (5.14-18.24)	-	-	-

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
		Eggs	0.12 (0.03-0.25)	0.03 (0.01-0.08)	0.15 (0.06-0.4)	0.05	0.12 (0.08-0.17)	0.05 (0.03-0.12)	0.15 (0.05-0.25)	-	-	-
		Fish	0.52 (0.12-4.64)	0.13 (0.02-1.48)	0.76 (0.1-6.11)	0.5 (0.17-3.28)	0.42 (0.14-7.35)	0.59 (0.05-4.75)	0.22 (0.06-1.9)	-	-	-
		Crustaceans	0.06	0.04	0.22 (0.05-0.9)	0.22	0.26	0.17 (0.04-0.69)	0.08 (0-0.2)	-	-	-
		Mussels	0.35 (0.3-0.39)	0.04 (0.01-0.09)	0.75 (0.52-1.08)	0.04	6.29 (4.28-7.82)	0.25 (0.03-0.69)	0.11 (0.04-0.26)	-	-	-
		Baby Food	1.54	0.4 (0.17-4.06)	2.41 (1.84-11.54)	1.71 (1.08-6.58)	1.63 (0.79-11.44)	4.1 (0.59-22.28)	0.41 (0.35-1.36)	-	-	-
		Grain	0.93 (0.27-2.41)	0.61 (0.04-2.82)	3.65 (0.26-15.55)	0.16	26.14 (0.11-45.19)	5.00 (0.46-12.25)	0.38 (0.17-0.85)	-	-	-
		Potatoes	0.54 (0.23-1.04)	0.38 (0.55-0.88)	1.23 (0.31-3.32)	1.01 (0.18-2)	0.85 (0.55-1.29)	2.19 (1-3.15)	0.84 (0.33-1.23)	-	-	-
		Meat	0.33 (0.15-1.38)	0.2 (0.07-0.97)	0.29 (0.14-1.2)	0.8	1.52 (0.44-14.03)	0.72 (0.11-2.97)	0.35 (0-1.34)	-	-	-
		Vegetable	0.12 (0.01-0.24)	0.01	0.02	0.01	2.01 (1.83-2.18)	0.01	0.01	-	-	-
		Stocks	0.5	0.72 (0.22-1.97)	1.17 (0.78-2.36)	0.89 (0.21-2.53)	1.48 (1.17-2.41)	12.46 (7.5-17.76)	1.56 (0.26-3.61)	-	-	-

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
		Milk	0.51	0.23	0.8	0.21	1.2	0.4 (0.12-1.14)	0.25 (0.03-1.69)	-	-	-
		Desserts	0.49	0.22	0.76	0.37 (0.21-0.70)	1.91 1.15-3.43	7.23 (0.46-12.51)	0.5 (0.1-0.8)	-	-	-
		Cheese	0.75 (0.46-3.25)	0.71 (0.11-2.78)	1.53 (0.22-8.44)	3.09 (1-13.08)	10.93 (0.19-45.3)	1.33 (0.71-6.12)	1.72 (0.21-3.70)	-	-	-
Han et al., 2019	US	Meat	2.2 (ND-10.6)	-	5.9 (1.3-15.8)	-	1.9 (ND-5.6)	-	-	-	-	-
		Fish	-	-	4.8 (ND-10.5)	-	7.4	-	-	-	-	-
Zhang et al., 2016	China	Beverages	-	304 (23.0-1007)	136 (6.56-451)	37.2 (ND-231)	125 (ND-1545)	-	482 (ND-2241)	81.5 (ND-1545)	-	-
		Dairy Products	-	202 (ND-887)	121 (ND-983)	296 (ND-1857)	196 (ND-726)	-	183 (ND-620)	45.5 (ND-286)	-	-
		Grains	-	2.97 (0.11-12.2)	0.38 (0.02-0.86)	0.76 (0.10-4.22)	0.02 (0.02-0.05)	-	3.91 (0.48-13.0)	0.04 (ND-0.11)	-	-
		Vegetables	-	4.16 (ND-17.7)	0.55 (ND-1.98)	0.65 (ND-5.91)	0.94 (ND-8.59)	-	12.7 (ND-62.4)	0.34 (ND-3.54)	-	-
		Meat	-	0.74 (ND-3.63)	0.13 (ND-0.68)	0.01 (ND-0.03)	0.11 (ND-0.41)	-	3.07 (ND-17.4)	0.07 (ND-0.34)	-	-
		Fruits	-	1.10	0.22 (0.12-0.37)	5.05 (0.02-24.6)	0.32	-	3.00	0.05	-	-

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
				(0.34-1.68)			(0.06-1.14)		(-0.84-10.1)	(0.01-0.11)		
		Rice (Sichuan)	-	25.9 (ND-89.7)	12.6 (ND-59.9)	1.84 (0.04-8.54)	14.3 (0.11-95.0)	-	10.8 (0.19-36.8)	8.95 (0.13-33.6)	-	-
He et al., 2019	China	Fish	487 (37.0-2380)	63.1 (17.1-159)	90.9 (6.55-323)	74.5 (ND-381)	16.4 (3.49-59.6)	-	-	22.7 (ND-112)	-	47.7 (11.5-181)
		Pig	109 (24.7-217)	53.0 (11.1-116)	60.0 (17.3-86.4)	80.1 (16.0-163)	17.2 (2.64-36.4)	-	-	18.0 (3.49-38.8=9)	-	115 (4.59-315)
		Chicken	234 (30.2-1260)	38.2 (9.31-135)	39.9 (7.84-96.8)	28.3 (8.82-110)	20.0 (3.76-92.1)	-	-	23.6 (ND-119)	-	173 (8.00-1090)
		Cattle	168 (49.7-461)	47.8 (15.3-123)	56.2 (16.7-152)	34.7 (ND-117)	15.2 (3.82-44.4)	-	-	26.4 (9.56-62.6)	-	36.8 (10.8-97.0)
		Vegetables	9.95 (2.66-39.9)	2.80 (1.54-3.26)	1.73 (ND-3.37)	1.41 (ND-5.86)	0.73 (ND-2.21)	-	-	1.52 (0.62-4.45)	-	7.93 (0.81-20.8)
Liu et al., 2018	China	Plecostomus	11.7	13.5	<0.004	<0.046	42.3	<0.006	14.6	7.06	-	-
		Tilapia	42.6	<0.010	<0.004	<0.046	16.3	<0.006	62.8	8.10	-	-
		Mud carp	91.3	<0.010	23.5	<0.046	<0.013	<0.006	78.2	4.69	-	-
		Catfish	22.4	6.33	<0.004	<0.046	20.3	6.95	56.3	9.46	-	-

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
Poma et al., 2017	Uppsala Sweden	Cereal	-	0.25 (<0.50)	1.23 (0.40-2.80)	0.38 (<0.50-0.89)	0.34 (<0.50-0.67)	4.17 (<3.0-9.25)	-	-	-	-
		Pastries	-	0.25 (<0.50)	0.81 (0.70-0.91)	0.25 (<0.50)	0.75 (<0.50-1.24)	9.25 (8.44-10.06)	-	-	-	-
		Meat	-	0.10 (<0.20)	0.08 (<0.15)	0.18 (<0.20-0.52)	0.46 (<0.20-1.54)	0.64 (<1.0-1.22)	-	-	-	-
		Fish	-	0.10 (<0.20)	0.08 (<0.15)	0.29 (<0.20-1.05)	0.63 (<0.20-1.56)	2.46 (<1.0-5.80)	-	-	-	-
		Dairy fluid	-	0.13 (<0.10-0.22)	0.06 (<0.10-0.15)	0.18 (<0.10-0.50)	0.08 (<0.10-0.20)	0.43 (<0.70-1.0)	-	-	-	-
		Dairy solid	-	0.15 (<0.3)	0.10 (<0.20)	0.15 (<0.30)	0.15 (<0.3)	1.00 (<2.00)	-	-	-	-
		Eggs	-	0.08 (<0.15-0.20)	0.13 (<0.15-0.23)	0.18 (<0.15-0.39)	0.08 (<0.15-0.20)	0.91 (0.58-1.26)	-	-	-	-
		Fats/oil	-	1.00 (<2.00)	0.75 (<1.5)	1.00 (<2.0)	4.74 (1.36-12.37)	5.08 (<6.0-7.61)	-	-	-	-
		Vegetable	-	0.41 (0.32-0.51)	0.18 (<0.05-0.33)	0.37 (<0.05-1.06)	0.07 (<0.05-0.13)	0.28 (<0.2-0.39)	-	-	-	-
		Fruits	-	0.09 (<0.15-0.26)	0.11 (<0.15-0.24)	0.29 (<0.15-0.57)	0.08 (<0.15)	0.47 (<0.7-0.95)	-	-	-	-
		Potatoes	-	0.11	0.17	0.29 (0.18-0.49)	0.18	0.35 (<0.70)	-	-	-	-

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
				(<0.15-0.26)	(<0.15-0.29)		(<0.15-0.48)					
		Sugar/ Sweets	-	0.23 (<0.45)	0.20 (<0.40)	0.74 (<0.5-1.23)	0.25 (<0.50)	3.71 (<3.0-5.92)	-	-	-	-
		Beverages	-	0.23 (<0.45)	0.20) (<0.40)	0.86 (0.64-1.07)	0.25 (<0.50)	1.50 (<3.0)				
He et al., 2018	Australia	Cereal	0.14-3.1	<MDL-1.5	<MDL-2.2	<MDL-0.38	<MDL-0.62	<MDL-1.1	<MDL-<MDL	<MDL-0.54	-	-
		Fruits	<MDL-0.48	<MDL-0.17	<MDL-5.3	<MDL-0.39	<MDL-<MDL	<MDL-<MDL	<MDL-4.1	<MDL-0.84	-	-
		Vegetable	<MDL-0.82	<MDL-0.18	0.72-3.9	<MDL-0.075	<MDL-1.0	<MDL-<MDL	<MDL-<MDL	<MDL-0.20	-	-
		Dairy products	<MDL-2.6	<MDL-0.16	<MDL-2.3	<MDL-<MDL	<MDL-<MDL	<MDL-<MDL	<MDL-<MDL	<MDL-0.45	-	-
		Meat	0.065-0.94	<MDL-0.35	<MDL0.52	<MDL-<MDL	<MDL-0.16	<MDL-<MDL	<MDL-<MDL	<MDL-0.062	-	-
		Fish and seafood	0.17-1.5	<MDL-0.13	0.40-1.8	<MDL—0.055	<MDL-0.57	<MDL-<MDL	<MDL-<MDL	<MDL-0.16	-	-
		Egg	0.14-0.21	<MDL-0.50	<MDL-0.73	<MDL-<MDL	<MDL-<MDL	<MDL-<MDL	<MDL-<MDL	<MDL-<MDL	-	-
		Beverages	<MDL-<MDL	<MDL-<MDL	<MDL-0.60	<MDL-0.31	<MDL-<MDL	<MDL-<MDL	<MDL-<MDL	<MDL-0.21	-	-
		Tea	<MDL-<MDL	<MDL-0.17	<MDL-3.0	<MDL-<MDL	<MDL-0.070	<MDL-<MDL	<MDL-<MDL	<MDL-0.10	-	-

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
Xu et al., 2015	China	Prawn	<0.68	<0.43	0.71	<0.65	<0.17	<0.17	<1.02	-	-	<0.61
		Lean Pork	1.26	<0.63	<0.85	<0.95	<0.25	0.30	<1.5	-	-	<0.9
		Smoked salmon	1.37	1.09	1.23	<1.26	0.72	<0.33	<1.98	-	-	<1.19
		Bacon	<1.72	<1.08	<1.47	<1.64	0.82	<0.43	<2.58	-	-	<1.55
		Mussel	<0.84	<0.53	<0.72	<0.8	0.44	1.11	<1.26	-	-	<0.76
		Canned tuna	<1	<0.63	<0.85	<0.95	<0.25	<0.25	<1.5	-	-	<0.9
		Chicken thigh	<1	<0.6	<0.85	<0.95	0.26	<0.25	<1.5	-	-	<0.9
		Free range chicken egg	<0.96	<0.6	<0.82	<0.91	0.27	<0.24	<1.44	-	-	<0.86
Zhao et al., 2019	China	Cereal	0.10 (<0.02-0.3)	2.47 (<0.03-18.5)	0.01 (<0.02)	-	0.11 (<0.10-0.4)	0.76 (<0.16-5.0)	0.1015 (<0.03)	0.05 (<0.02-0.1)	-	0.005 (<0.01)
		Vegetables	0.13 (<0.02-0.5)	0.015 (<0.03)	0.01 (<0.02)	-	0.08 (0.10-0.5)	0.08 (<0.16)	0.15 (<0.03)	0.04 (<0.02-0.2)	-	0.005 (<0.01)
		Meat	0.04 (0.02-0.1)	0.015 (<0.03)	0.01 (< 0.02)	-	0.68 (< 0.10-3.2)	0.10 (<0.16-0.2)	0.015 (<0.03)	0.02 (<0.02-0.1)	-	0.005 (<0.01)
		Poultry	0.04 (<0.02-0.2)	0.015 (<0.03)	0.01 (< 0.02)	-	0.14 (<0.10-0.3)	0.08 (<0.16)	0.015 (<0.03)	0.04 (<0.02-0.1)	-	0.005 (<0.01)

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
		Aquatic products	0.31 (<0.02-1.0)	0.015 (<0.03)	0.01 (<0.02)	-	0.09 (<0.10-0.3)	0.08 (<0.16)	0.015 (<0.03)	0.02 (<0.02-0.1)	-	0.005 (<0.01)
		Eggs	0.28 (<0.02-1.5)	0.015 (<0.03)	0.01 (<0.02)	-	0.26 (<0.10-3.0)	4.06 (<0.16-71.8)	0.015 (<0.03)	0.06 (<0.02-0.3)	-	0.005 (<0.01)
		Milk	0.10 (<0.02-0.2)	0.015 (<0.03)	0.01 (<0.02)	-	0.14 (<0.10-0.3)	0.08 (<0.16)	0.015 (<0.03)	0.05 (<0.02-0.1)	-	0.005 (<0.01)
		Fruits	0.14 (<0.02-0.6)	0.015 (<0.03)	0.01 (<0.02)	-	0.20 (<0.10-1.4)	0.08 (<0.16)	0.71 (<0.03-6.5)	0.05 (<0.02-0.1)	-	0.07 (<0.01-0.7)
		Sweet	0.07 (<0.02-0.2)	0.39 (<0.03-1.1)	5.06 (<0.02-13.1)	-	0.15 (<0.10-0.3)	4.54 (<0.16-26.3)	0.015 (<0.03)	0.02 (<0.02-0.1)	-	0.04 (<0.01-0.1)
		Dairy	$(\sum_{9} OPEs = 1.4)^{a}$		-	-	-	-	-	-	-	-
Ding et al., 2018	China	Cereals	$(\sum_{10} OPEs = 5.7 \pm 2.3)^{b}$		-	-	-	-	-	-	-	-
		Chicken	$(\sum_{10} OPEs = 4.1 \pm 1.5)^{b}$		-	-	-	-	-	-	-	-
		Pork	$(\sum_{10} OPEs = 3.8 \pm 2.5)^{b}$		-	-	-	-	-	-	-	-

Reference	Country	Food category	Mean concentration (Range) (ng.g^{-1} w.w.)									
			TnBP	**TCEP**	**TCIPP**	**TDCIPP**	**TPHP**	**EHDPP**	**TEHP**	**TBOEP**	**TMTP**	**TNPP**
		Milk & Egg	$(\sum_{10} OPEs = 2.4 \pm 0.2)^{b}$		-	-	-	-	-	-	-	-
		Tofu	$(\sum_{10} OPEs = 2.5 \pm 0.4)^{b}$		-	-	-	-	-	-	-	-
Giulivo et al., 2017	Italy	Fish	$(\sum_{14} OPEs = 50.6 - 650)^{d}$		-	-	-	-	-	-	-	
	Greece	Fish	$(\sum_{14} OPEs = 34.1 - 55.5)^{d}$	-	-	-	-	-	-	-	-	-
	Croatia	Fish	$(\sum_{14} OPEs = 14.4 - 196)^{d}$	-	-	-	-	-	-	-	--	-

[a] $\sum_{9} OPEs$ includes TCEP, TCIPP, TDCPP, TBP, TBOEP, TEHP, TMPP, TPHP and EHDPP

[b] $\sum_{10} OPEs$ includes TMP, TCEP, TEPm TCIPP, TDCIPP, TPHP, TNBP, TBOEP, TMPP and TEHP respectively

[d] $\sum_{14} OPEs$ includes DCP, EHDP, IDPP, TBP, THP, TPHP, TPPO, TBOEP, TCEP, TCIPP, TDCIPP, TEHP, IPPP and TMCP respectively.

Appendix 3.7a: Mean and High-end EDIs of OPEs (ng/kg bw/day) for various food groups for toddlers

OPEs	CRL	PASTRIES	SAVS	MLK	BBF	EGG	FSH	FAT-O	MPT	VEG	NAB	FRT	SWG	NUT	POT	∑Food groups
TCEP	0.23	0.49	0.06	1.80	2.83	0.85	0.10	0.16	0.54	0.09	1.94	2.49	0.22	0.22	0.43	12.5
TCIPP	0.43	0.13	0.21	3.84	4.22	0.19	0.45	0.17	3.54	0.10	1.61	3.49	0.19	0.12	0.70	19.4
TPHP	1.49	0.08	0.02	18.8	73.3	0.18	0.95	0.25	5.63	0.53	4.48	6.17	1.57	1.99	1.49	117
TDCIPP	0.52	0.05	0.01	4.77	4.29	0.13	0.53	0.30	0.66	0.16	3.29	3.92	0.84	0.34	0.65	20.5
EHDPP	4.55	5.53	0.09	21.3	68.3	0.19	0.38	0.72	5.84	0.11	4.12	1.44	1.42	0.18	1.85	116
TBOEP	4.08	0.20	0.03	24.9	3.15	0.48	0.06	0.10	0.58	3.49	34.2	28.5	0.88	0.23	0.67	102
TnBP	0.15	0.06	0.04	0.67	1.05	0.15	0.02	0.03	0.19	0.33	1.00	0.97	0.03	0.07	0.21	4.97
TMTP	0.84	0.38	0.04	11.8	5.8	0.90	0.14	0.18	1.27	0.40	1.95	2.56	0.45	0.21	0.72	27.6
∑OPEs	12.3	6.92	0.50	87.9	163	3.07	2.63	1.91	18.3	5.21	52.6	49.5	5.60	3.36	6.72	419
High-end Exposure Scenario																
OPEs	**CRL**	**PASTRIES**	**SAVS**	**MLK**	**BBF**	**EGG**	**FSH**	**FAT-O**	**MPT**	**VEG**	**NAB**	**FRT**	**SWG**	**NUT**	**POT**	**∑Food groups**
TCEP	0.62	1.90	0.12	10.3	2.87	2.14	0.45	0.58	1.54	0.18	5.52	12.9	0.58	0.51	1.42	41.6
TCIPP	0.93	0.54	0.45	18.7	6.30	0.67	2.24	0.82	10.1	0.19	6.76	21.1	0.39	0.24	2.02	71.5
TPHP	3.74	0.41	0.06	89.6	99.0	0.63	3.45	0.93	17.5	1.00	20.1	27.3	5.27	8.91	6.57	284
TDCIPP	1.26	0.29	0.02	24.7	6.12	0.47	2.11	0.99	2.14	0.35	12.3	17.0	3.25	0.81	2.34	74.2
EHDPP	10.3	19.8	0.16	109	96.40	0.67	1.97	2.32	15.3	0.29	15.5	6.53	4.12	0.32	12.9	296
TBOEP	8.86	1.06	0.08	131	6.14	1.67	0.32	0.48	2.25	8.36	312	163	1.99	0.73	3.33	641
TnBP	0.52	0.33	0.08	4.27	2.05	0.53	0.10	0.16	0.72	0.84	4.17	4.33	0.10	0.23	1.07	19.5
TMTP	2.91	1.96	0.11	66.2	11.40	3.13	0.74	0.91	4.59	1.08	9.20	11.4	1.29	0.68	3.60	119
∑OPEs	29.1	26.3	1.08	454	230	9.91	11.4	7.19	54.1	12.3	386	264	17.0	12.4	33.3	1547

Where: CRL = cereal and cereal products, MLK = Milk and milk products, BBF = Baby food, FSH = Fish, FAT-O = Fat and Oils, MPT = Meat and meat products, VEG = Vegetables, NAB = Non-alcoholic beverages, FRT = Fruits, SWG = Sweet and sugar, NUT = Nuts, POT = Potatoes, EGG = Eggs

NB: The estimation of high-end intakes were derived from food consumption figures in Table S9a-d, by assuming that a high-end consumer of each food groups consumes the average quantities of contaminated food + 2 × standard deviations (SD) of the 97.5 percentile concentration of the contaminated food (Tao et al., 2017)

Appendix 3.7b: Mean and High-end EDIs of OPEs (ng/kg bw/day) for various food groups for children

OPEs	CRL	PASTRIES	SAVS	MLK	EGG	FSH	FAT-O	MPT	VEG	NAB	FRT	SWG	NUT	POT	∑Food groups
TCEP	0.08	0.42	0.08	0.60	0.78	0.10	0.15	0.63	0.08	1.74	1.18	0.24	0.16	0.46	6.70
TCIPP	0.15	0.11	0.27	1.28	0.18	0.44	0.16	4.14	0.09	1.44	1.66	0.20	0.09	0.76	11.0
TPHP	0.52	0.07	0.03	6.28	0.17	0.94	0.23	6.60	0.49	4.01	2.93	1.69	1.46	1.62	27.0
TDCIPP	0.18	0.05	0.01	1.60	0.12	0.52	0.28	0.77	0.15	2.94	1.87	0.90	0.25	0.71	10.4
EHDPP	1.61	4.77	0.12	7.13	0.18	0.38	0.67	6.84	0.10	3.68	0.68	1.53	0.13	2.01	29.8
TBOEP	1.44	0.18	0.04	8.34	0.44	0.06	0.09	0.68	3.21	26.1	13.6	0.94	0.17	0.73	56.0
TnBP	0.05	0.05	0.06	0.22	0.14	0.02	0.03	0.22	0.30	0.47	0.46	0.03	0.05	0.23	2.33
TMTP	0.30	0.32	0.05	3.95	0.82	0.14	0.17	1.49	0.37	1.74	1.22	0.49	0.15	0.78	12.0
∑OPEs	4.33	5.97	0.66	29.4	2.83	2.60	1.78	21.4	4.79	42.1	23.6	6.02	2.46	7.30	155
High-end Exposure Scenario															
TCEP	0.17	1.27	0.11	3.12	2.54	0.54	0.53	1.66	0.15	5.21	7.18	0.66	0.43	1.43	25.0
TCIPP	0.26	0.36	0.43	5.65	0.79	2.70	0.75	10.9	0.16	6.38	11.7	0.44	0.20	2.04	42.8
TPHP	1.03	0.27	0.05	27.0	0.75	4.15	0.85	18.9	0.84	19.0	15.1	6.05	7.49	6.63	108
TDCIPP	0.35	0.19	0.02	7.46	0.55	2.54	0.90	2.32	0.30	11.6	9.46	3.73	0.68	2.36	42.5
EHDPP	2.85	13.3	0.16	32.9	0.79	2.37	2.12	16.5	0.24	14.6	3.63	4.73	0.27	13.0	107
TBOEP	2.64	0.71	0.08	39.6	1.97	0.39	0.44	2.43	7.01	294	90.4	2.29	0.61	3.36	446
TnBP	0.14	0.22	0.08	1.29	0.63	0.12	0.14	0.78	0.71	4.44	2.40	0.12	0.19	1.08	12.34
TMTP	0.81	1.32	0.10	18.0	3.71	0.90	0.83	4.96	0.91	8.70	6.33	1.49	0.57	3.63	52.3
∑OPEs	8.25	17.6	1.03	135	11.7	13.7	6.56	58.5	10.3	364	146	19.5	10.4	33.5	836

Appendix 3.7c: Mean and High-end EDIs of OPEs (ng/kg bw/day) for various food groups for adults

OPEs	CRL	PAST	SAVS	MLK	EGG	FSH	FAT-O	MPT	VEG	NAB	FRT	SWG	NUT	POT	∑Food groups
TCEP	0.29	0.12	0.02	0.15	0.26	0.04	0.05	0.23	0.03	0.39	0.48	0.06	0.06	0.16	2.34
TCIPP	0.54	0.03	0.06	0.32	0.06	0.18	0.05	1.54	0.04	0.32	0.68	0.05	0.03	0.26	4.16
TPHP	1.89	0.02	0.01	1.55	0.06	0.38	0.08	2.46	0.20	0.89	1.20	0.45	0.53	0.55	10.3
TDCIPP	0.65	0.01	0.00	0.39	0.04	0.21	0.10	0.29	0.06	0.65	0.76	0.24	0.09	0.24	3.73
EHDPP	5.76	1.38	0.03	1.76	0.06	0.15	0.23	2.55	0.04	0.82	0.28	0.41	0.05	0.68	14.2
TBOEP	5.18	0.05	0.01	2.05	0.15	0.02	0.03	0.25	1.35	6.79	5.54	0.25	0.06	0.25	22.0
TnBP	0.19	0.02	0.01	0.05	0.05	0.01	0.01	0.08	0.13	0.20	0.19	0.01	0.02	0.08	1.05
TMTP	1.06	0.09	0.01	0.97	0.28	0.06	0.06	0.56	0.15	0.39	0.50	0.13	0.06	0.27	4.59
∑OPEs	15.6	1.72	0.15	7.24	0.96	1.05	0.61	7.96	2.00	10.5	9.63	1.60	0.90	2.49	62.3
High-end Exposure Scenario															
TCEP	0.58	0.38	0.03	0.78	1.05	0.38	0.17	0.57	0.08	1.23	2.98	0.15	0.18	0.51	9.07
TCIPP	0.88	0.11	0.10	1.41	0.33	1.88	0.25	3.78	0.09	1.51	4.87	0.10	0.08	0.72	16.1
TPHP	3.54	0.08	0.01	6.73	0.31	2.89	0.28	6.53	0.45	4.49	6.30	1.40	3.06	2.35	38.4
TDCIPP	1.19	0.06	0.01	1.86	0.23	1.77	0.30	0.80	0.16	2.74	3.93	0.86	0.28	0.84	15.0
EHDPP	9.74	3.99	0.04	8.19	0.33	1.65	0.70	5.71	0.13	3.47	1.51	1.09	0.11	4.62	41.3
TBOEP	9.03	0.21	0.02	9.85	0.81	0.27	0.14	0.84	3.76	69.8	37.6	0.53	0.25	1.19	134
TnBP	0.49	0.07	0.02	0.23	0.26	0.08	0.05	0.27	0.38	1.05	1.00	0.03	0.08	0.38	4.39
TMTP	2.75	0.40	0.02	4.97	1.53	0.62	0.27	1.72	0.49	2.06	2.63	0.34	0.23	1.29	19.3
∑OPEs	28.20	5.30	0.25	34.0	4.85	9.54	2.16	20.2	5.54	86.4	60.8	4.50	4.27	11.9	278

Appendix 3.7d: Mean and High-end EDIs of OPEs (ng/kg bw/day) for various food groups for elderly

OPEs	CRL	PAST	MLK	BBF	EGG	FSH	FAT-O	MPT	VEG	NAB	FRT	SWG	NUT	POT	∑Food groups
TCEP	0.09	0.20	0.02	0.26	0.29	0.05	0.09	0.27	0.05	0.54	0.81	0.08	0.07	0.25	3.07
TCIPP	0.17	0.05	0.06	0.55	0.07	0.24	0.10	1.79	0.06	0.45	1.13	0.07	0.04	0.42	5.20
TPHP	0.61	0.03	0.01	2.69	0.06	0.51	0.15	2.85	0.30	1.25	2.00	0.60	0.58	0.88	12.5
TDCIPP	0.21	0.02	0.00	0.68	0.05	0.28	0.18	0.33	0.09	0.92	1.27	0.32	0.10	0.39	4.84
EHDPP	1.86	2.28	0.02	3.06	0.07	0.21	0.43	2.95	0.06	1.15	0.47	0.54	0.05	1.09	14.2
TBOEP	1.67	0.08	0.01	3.58	0.17	0.03	0.06	0.29	1.99	9.58	9.24	0.33	0.07	0.40	27.5
TnBP	0.06	0.03	0.01	0.10	0.05	0.01	0.02	0.09	0.19	0.28	0.31	0.01	0.02	0.13	1.31
TMTP	0.34	0.15	0.01	1.69	0.31	0.08	0.11	0.64	0.23	0.55	0.83	0.17	0.06	0.43	5.60
∑OPEs	5.01	2.84	0.14	12.6	1.07	1.41	1.14	9.21	2.97	14.7	16.1	2.12	0.99	3.99	74.3
High-end Exposure Scenario															
TCEP	0.27	0.74	0.03	1.49	1.01	0.31	0.33	0.77	0.11	1.52	4.78	0.21	0.21	0.89	12.7
TCIPP	0.41	0.21	0.11	2.70	0.32	1.55	0.48	5.05	0.12	1.86	7.80	0.14	0.10	1.27	22.1
TPHP	1.61	0.16	0.01	12.9	0.30	2.38	0.54	8.72	0.64	5.54	10.1	1.95	3.56	4.13	52.5
TDCIPP	0.56	0.11	0.01	3.56	0.22	1.46	0.57	1.02	0.23	3.38	6.30	1.20	0.32	1.47	20.4
EHDPP	4.57	7.68	0.04	15.7	0.32	1.36	1.35	7.63	0.19	4.28	2.42	1.53	0.13	8.13	55.3
TBOEP	4.24	0.41	0.02	18.9	0.79	0.22	0.28	1.12	5.34	86.0	60.2	0.74	0.29	2.10	181
TnBP	0.23	0.13	0.02	0.62	0.25	0.07	0.09	0.36	0.54	1.30	1.60	0.04	0.09	0.67	6.01
TMTP	1.29	0.76	0.02	9.54	1.48	0.51	0.52	2.29	0.69	2.53	4.22	0.48	0.27	2.26	26.9
∑OPEs	13.2	10.2	0.26	65.4	4.69	7.86	4.16	27.0	7.86	106	97.4	6.29	4.97	20.9	377

Appendix 3.8: Comparison of the dietary EDI with that obtained from other exposure pathways

Exposure Pathways	Ref	Population	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TnBP	∑OPEs
Food ingestion (This study)	This study (Food)	Adults	2.34	4.16	3.73	10.3	14.2	1.05	35.8
Food ingestion (This study)	This study (Food)	Children	6.7	11	10.4	27	29.8	2.33	87.2
Food ingestion (This study)	This study (Food)	Toddlers	12.5	19.4	20.5	117	116	4.97	290
Food ingestion (This study)	This study (Food)	Elderly	3.07	5.20	4.84	12.5	14.2	1.31	41.1
Dust ingestion	Dust (Brommer and Harrad, 2015)	Children	1.7	43	4	7	14	0.08	69.8
	Yadav et al., 2017	Children	0.063	0.234	0.088	0.285	0.307	0.089	1.066
	Yadav et al., 2019	Children	0.07002	0.10574	0.00237	0.06706	0.1025	0.07165	0.41934
	Abdallah and Covaci, 2014	Toddlers	3.2	4.7	7.5	7.5	2.4	1.3	26.6
	Cao et al., 2019	Toddlers	3.9	7.1	0.65	2.7	1.4	0.15	15.9
	He et al., 2015	Toddlers	13.7	2.71	0.47	0.53	1.32	0.28	19.0
	Al-Omran et al., 2021	Toddlers	3.91	7.22	2.32	1.08	0.605	0.236	15.371
	Stubbings et al., 2018	Toddlers	1.2	2.8	4.7	5	4.6	0.94	19.24
	Abdallah and Covaci, 2014	Adults	1.3	1.9	3	3	1	0.5	10.7
	Cao et al., 2019	Adults	1.1	1.3	0.13	0.31	0.14	0.02	3
	He et al., 2015	Adults	0.61	0.39	0.05	0.35	0.1	0.04	1.54
	Yadav et al., 2017	Adults	0.007	0.025	0.009	0.031	0.033	0.01	0.115
	Yadav et al., 2019	Adults	0.0075	0.01133	0.00025	0.00719	0.01098	0.00768	0.04493
	Al-Omran et al., 2021	Adults	0.2	0.369	0.118	0.0552	0.0309	0.0121	0.7852
	Xu et al., 2016	Adults	3.902	3.412	0.422	4.9	0.363	0.094	13.093
	Stubbings et al., 2018	Adults	0.099	0.24	0.4	0.43	0.39	0.081	1.64
Air inhalation	Yadav et al., 2017	Children	0.238	0.441	0.047	0.167	0.294	0.15	1.337
	Cao et al., 2019	Toddlers	0.076	1.6		0.049	0.0088	0.087	1.8208
	Zhou et al., 2017	Toddlers	8.00E-02	1.1	0.16	0.002		0.26	1.602

	Cao et al., 2019	Adults	0.1	0.86		0.001	0.02	0.042	1.023
	Yadav et al., 2017	Adults	0.062	0.115	0.012	0.044	0.077	0.039	0.349
	Zhou et al., 2017	Adults	0.09	3.6	0.16	0.004		0.59	4.444
Dermal Uptake	Yadav et al., 2017	Children	0.886	3.29	1.243	4.015	4.32	1.25	15.004
	Cao et al., 2019	Toddlers	1.9	3	0.14	1	0.54	0.58	7.16
	Zhou et al., 2017	Toddlers	0.87	6.1	1.2	1.7		0.26	10.13
	Abdallah and Harrad 2022	Toddlers	1.2	14.3					15.5
	Yadav et al., 2017	Adults	0.329	1.223	0.462	1.492	1.606	0.464	5.576
	Cao et al., 2019	Adults	0.47	0.51	0.027	0.11	0.049	0.0072	1.1732
	Zhou et al., 2017	Adults	0.08	0.59	0.12	0.16		0.03	0.98
	Abdallah and Harrad 2022	Adults	1.7	20.4	3				25.1
Drinking water ingestion	Lee et al., 2016	Children	0.23	1.01					1.24
	Lee et al., 2016	Toddlers	0.28	1.22					1.5
	Lee et al., 2016	Adults	0.2	0.87					1.07
	Liu et al., 2019	Male	2.29	2.07					4.36
	Liu et al., 2019	Female	1.97	1.78					3.75

Appendix 3.9a: The combined average and high exposure risk estimates (ng/kg bw/day) for adults in UK via dust ingestion, dietary intake (this study) and dermal uptake

Average exposure scenario (Adults)								
OPEs/Reference	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TBOEP	TnBP	TMTP
Dust (Brommer and Harrad, 2015)	0.03	0.92	0.07	0.13	0.09	2.306	0.01	
This study (Food)	2.34	4.16	3.73	10.3	14.2	22	1.05	4.59
Abdallah and Harrad, 2022	1.7	20.4	3					
Sum	4.07	25.5	6.80	10.4	14.3	24.3	1.06	4.59
RfD (USEPA, 2017)	7000	10000	20000				10000	
RfD (Van den Eede et al., 2011)	2200	8000	1500	7000	600 [a]	1500	2400	
RfD (Ali et al., 2012)	22000	80000	15000	70000		15000	24000	
RfD (Saito et al., 2007)	-	3600	-	-	-	-	-	-
HQ (USEPA, 2017)	$6x10^{-4}$	$2.5x10^{-3}$	$3x10^{-4}$	-	-	-	$1x10^{-4}$	-
HQ (Van den Eede et al., 2011)	$1.9x10^{-3}$	$3.2x10^{-3}$	$4.5x10^{-3}$	$1.5x10^{-3}$	$2.38x10^{-2}$ [a]	$1.62x10^{-2}$	$4x10^{-4}$	-
HQ (Ali et al., 2012)	$2x10^{-4}$	$3x10^{-4}$	$5x10^{-4}$	$1x10^{-4}$	-	$1.5x10^{-3}$	$4x10^{-5}$	-
HQ (Saito et al., 2007)	-	$7.08x10^{-3}$	-	-	-	-	-	-
High Exposure scenario (Adults)								
Dust (Brommer and Harrad, 2015)	1.3	13	3.1	5.6	5.1	5.764	0.02	
This study (Food)	9.07	16.1	15	38.4	41.3	134	4.39	19.3
Abdallah et al., 2016	10	22.6	4.3					
Sum	**20.4**	**51.7**	**22.4**	**44**	**46.4**	**140**	**4.41**	**19.3**
HQ (USEPA, 2017)	$3x10^{-3}$	$5x10^{-3}$	$1x10^{-3}$	-	-	-	$4x10^{-4}$	-
HQ (Van den Eede et al., 2011)	$9x10^{-3}$	$6x10^{-3}$	$1.5x10^{-2}$	$6x10^{-3}$	$7.7x10^{-2}$ [a]	$9.3x10^{-2}$	$2x10^{-3}$	-
HQ (Ali et al., 2012)	$9x10^{-4}$	$6x10^{-4}$	$1.5x10^{-3}$	$6x10^{-4}$	-	$9.3x10^{-3}$	$2x10^{-4}$	#DIV/0!
HQ (Saito et al., 2007)	-	$1.44x10^{-2}$	-	-	-	-	-	-

Appendix 3.9b: The combined average and high exposure risk estimates (ng/kg bw/day) for children in UK via dust ingestion and dietary intake (this study)

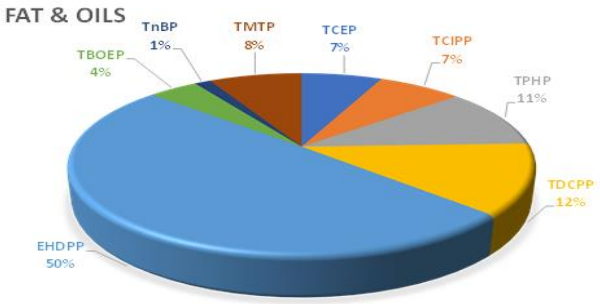
Average-exposure scenario (children)								
OPEs/Reference	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TBOEP	TnBP	TMTP
Dust (Brommer and Harrad, 2015)	1.7	43	4	7	14	-	0.08	-
This study (Food)	6.7	11	10.4	27	29.8	56	2.33	12
Sum	8.4	54	14.4	34	43.8	56	2.41	12
HQ (USEPA, 2017)	$1.2x10^{-3}$	$5.4x10^{-3}$	$7x10^{-4}$	-	-	-	$2x10^{-4}$	-
HQ (Van den Eede et al., 2011)	$3.8x10^{-3}$	$6.8x10^{-3}$	$9.6x10^{-3}$	$4.9x10^{-3}$	$7.3x10^{-2}$ [a]	$3.73x10^{-2}$	$1x10^{-3}$	-
HQ (Ali et al., 2012)	$3.8x10^{-4}$	$6.8x10^{-4}$	$9.6x10^{-4}$	$4.9x10^{-4}$	-	$3.73x10^{-3}$	$1x10^{-4}$	-
HQ (Saito et al., 2007)		$1.5x10^{-2}$						
High- exposure scenario (children)								
Dust (Brommer and Harrad, 2015)	45	740	170	360	420	-	1.3	-
This study (Food)	25	42.8	42.5	108	107	446	12.3	52.3
Sum	**70**	**783**	**213**	**468**	**527**	**446**	**13.6**	**52.3**
HQ (USEPA, 2017)	$1x10^{-2}$	$7.8x10^{-2}$	$1.1x10^{-2}$	-	-	-	$1x10^{-3}$	-
HQ (Van den Eede et al., 2011)	$3.2x10^{-2}$	$9.8x10^{-2}$	**0.142**	$6.7x10^{-2}$	**0.878** [a]	**0.297**	$6x10^{-3}$	#DIV/0!
HQ (Ali et al., 2012)	$3.2x10^{-3}$	$9.8x10^{-3}$	$1.42x1^{-2}$	$6.7x10^{-3}$	-	**$2.97x10^{-2}$**	$6x10^{-4}$	#DIV/0!
HQ (Saito et al., 2007)		**0.217**						

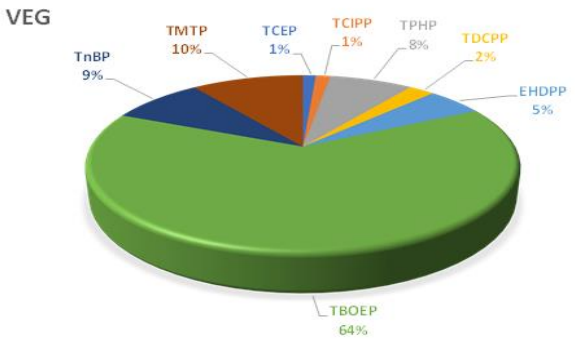
Appendix 3.9c: The combined average and high exposure risk estimates (ng/kg bw/day) for toddlers in UK via dust ingestion and dietary intake (this study)

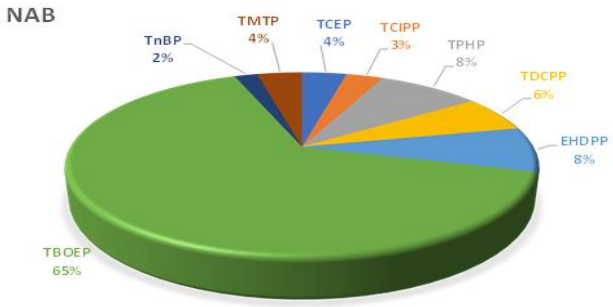
Average-exposure scenario (toddlers)								
OPEs/Reference	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TBOEP	TnBP	TMTP
Kademoglou et al., 2017 (houses dust)	3.549	262.382	3.057	6.134	9.654	32.805	1.065	
This study (Food)	12.5	19.4	20.5	117	116	102	4.97	27.6
Abdallah and Harrad, 2022	1.2	14.3						
Sum	**17.2**	**296**	**23.6**	**123**	**126**	**135**	**6.04**	**27.6**
HQ (USEPA, 2017)	$2x10^{-3}$	$3x10^{-2}$	$1x10^{-3}$	-	-	-	$1x10^{-3}$	-
HQ (Van den Eede et al., 2011)	$8x10^{-3}$	$3.7x10^{-2}$	$1.6x10^{-2}$	$1.8x10^{-2}$	**0.209** [a]	$9x10^{-2}$	$3x10^{-3}$	-
HQ (Ali et al., 2012)	$8x10^{-4}$	$3.7x10^{-3}$	$1.6x10^{-3}$	$1.8x10^{-3}$	-	$9x10^{-3}$	$3x10^{-4}$	-
HQ (Saito et al., 2007)	-	$8.2x10^{-2}$	-	-	-	-	-	-
High exposure scenario (toddlers)								
Kademoglou et al., 2017 (∑10OPEs) (houses)	14.195	1049.528	12.228	24.537	38.618	131.22	4.26	
This study (Food)	41.6	71.5	74.2	284	296	641	19.5	119
Abdallah and Harrad, 2016	38.6	218	37					
Sum	**94.4**	**1339**	**123**	**309**	**335**	**772**	**23.8**	**119**
RfD (Ali et al., 2012)	22000	80000	15000	70000		15000	24000	
HQ (USEPA, 2017)	$1.3x10^{-2}$	**0.134**	$6x10^{-3}$	-	-	-	$2x10^{-3}$	-
HQ (Van den Eede et al., 2011)	$4.3x10^{-2}$	**0.167**	$8.2x10^{-2}$	$4.4x10^{-2}$	**0.56** [a]	**0.52**	$1x10^{-2}$	-
HQ (Ali et al., 2012)	$4.3x10^{-3}$	$1.67x10^{-2}$	$8.2x10^{-3}$	$4.4x10^{-3}$	-	$5.1x10^{-2}$	$1x10^{-3}$	-
HQ (Saito et al., 2007)	-	**0.371**	-	-	-	-	-	-

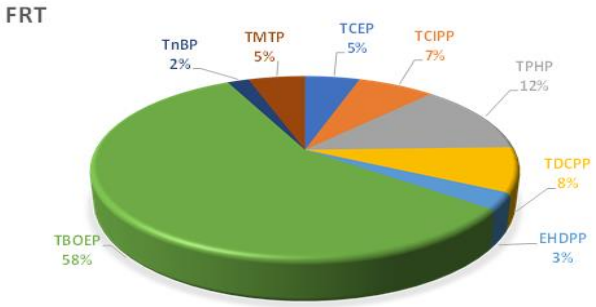
[a] Zhao et al. (2019), NB: The highlighted values represent the HQ of OPEs with greater exposure risk.

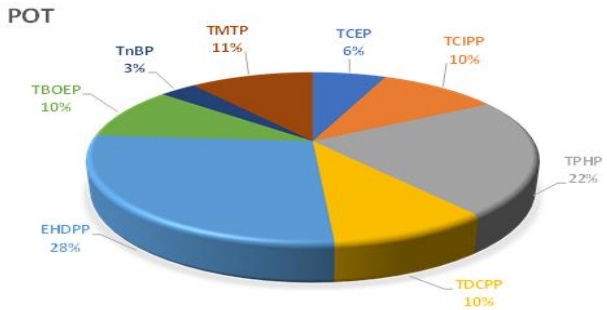
Appendix 3.10: Contributions (%ΣOPEs) of OPEs in plant-derived food groups

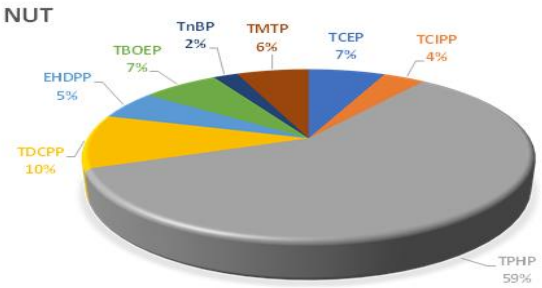

FAT & OILS
TnBP 1%
TMTP 8%
TCEP 7%
TCIPP 7%
TPHP 11%
TDCPP 12%
EHDPP 50%
TBOEP 4%


VEG
TnBP 9%
TMTP 10%
TCEP 1%
TCIPP 1%
TPHP 8%
TDCPP 2%
EHDPP 5%
TBOEP 64%


NAB
TnBP 2%
TMTP 4%
TCEP 4%
TCIPP 3%
TPHP 8%
TDCPP 6%
EHDPP 8%
TBOEP 65%


FRT
TnBP 2%
TMTP 5%
TCEP 5%
TCIPP 7%
TPHP 12%
TDCPP 8%
EHDPP 3%
TBOEP 58%


POT
TnBP 3%
TMTP 11%
TCEP 6%
TCIPP 10%
TPHP 22%
TDCPP 10%
EHDPP 28%
TBOEP 10%


NUT
TnBP 2%
TMTP 6%
TCEP 7%
TCIPP 4%
TPHP 59%
TDCPP 10%
EHDPP 5%
TBOEP 7%

Appendix for chapter four

Appendix 4.1: Names, abbreviations, formulas, and physicochemical properties of the target OPEs in the present study

OPEs classification	Name	Abbreviation (Chemical formula)	CAS#	MW	P (mmHg at 25°C)	S (mg/L at 25°C)	BP (°C)	Log K_{OW}	Log K_{OC}	Log K_{OA}	BAF
Chlorinated-OPEs	Tris(2-chloroethyl) phosphate	TCEP ($C_6H_{12}Cl_3O_4P$)	115-96-8	285.49	0.0613	**7000**	351	1.63	2.47	7.42	0.425
	Tris(2-chloroisopropyl) Phosphate	TCIPP ($C_9H_{18}Cl_3O_4P$)	13674-84-5	327.57	$5.64x10^{-5}$	**1200**	>270	2.89	3.10	8.20	3.27
	Tris(1,3-dichloro-2-propyl) Phosphate	TDCIPP ($C_9H_{15}Cl_6O_4P$)	13674-87-8	430.89	$2.98x10^{-7}$	7	237	3.65	3.96	10.6	21.4
Aryl-OPEs	Triphenyl phosphate	TPHP ($C_{18}H_{15}O_4P$)	115-86-6	326.28	$1.12x10^{-5}$	1.9	370	4.59	3.71	8.45	113.3
	2-Ethylhexyl diphenyl Phosphate	EHDPP ($C_{20}H_{27}O_4P$)	1241-94-7	362.40	$5x10^{-5}$	1.9	421	6.30	4.20	8.92	855.2
	Tri-m-tolyl phosphate	TMTP ($C_{21}H_{21}O_4P$)	56-04-2	368.4	$7.8x10^{-7}$	-	260	6.34	$4.1x10^{4}$	-	-
Alkyl-OPEs	Tris(2-butoxyethyl) phosphate	TBOEP ($C_{18}H_{39}O_7P$)	78-51-3	398.48	$1.23x10^{-6}$	**$1.20x10^{3}$**	414	3.65	5.66	13.0	25.56
	Tri-n-butyl phosphate	TNBP ($C_{12}H_{27}O_4P$)	126-73-8	266.31	$3.49x10^{-3}$	7.35	289	4.00	3.27	9.21	39.81

Where: S = solubility (mg/L) in water at 25°C; P = vapor pressure (mmHg) at 25°C; log K_{ow} = n-octanol: water partition coefficient; KOC=Organic carbon-water partition coefficient; KOA=Octanol-Air partition coefficient; BAF: bioaccumulation factor and, MW = molecular weight. The data are compiled from databases (Chemspider, 2021) and Pantelaki and Voutsa (2019).

Appendix 4.2: EDIs via drinking water ingestion (for tap and bottled) for Infants, Toddlers, Children, and Adults (ng (kg of bw)$^{-1}$ day^{-1})

Drinking water type	Infant ng (kg of bw)$^{-1}$ day^{-1})	Toddler ng (kg of bw)$^{-1}$ day^{-1})	Children ng (kg of bw)$^{-1}$ day^{-1})	Adults (ng (kg of bw)$^{-1}$ day^{-1})
Tap water (mean)	0.59	0.29	0.22	0.18
Tap water (95th Percentile)	4.5	2.16	1.64	1.47
Bottled water (mean)	0.34	0.17	0.13	0.10
Bottled water (95th Percentile)	1.92	0.93	0.70	0.63
Mean	**0.93**	**0.46**	**0.35**	**0.28**
95th percentile	**6.42**	**3.1**	**2.34**	**2.1**

Appendix 4.3: Average estimated daily intakes of OPEs (ng (kg of bw)$^{-1}$ day^{-1}) in the UK drinking water samples for the four age groups

Water type	Infants	Toddlers	Children	Adults
Tap water	0.59 (4.5)	0.29 (2.2)	0.22 (1.6)	0.18 (1.5)
Bottled water	0.34 (1.9)	0.17 (0.93)	0.13 (0.70)	0.10 (0.63)
∑EDI	0.93 (6.4)	0.46 (3.1)	0.35 (2.3)	0.28 (2.1)

Appendix 4.4: Average and high exposure risk estimates (ng/kg bw/day) for adults in the UK via dust ingestion, dermal absorption, dietary intake, and water ingestion combined

Adults (Average)	TCEP	TCIPP	TDCIPP	TPHP	EHDPP
Dust - (Brommer and Harrad, 2015)	0.03	0.92	0.07	0.13	0.09

Food – (Gbadamosi et al., 2022)	2.34	4.16	3.73	10.3	14.2
Drinking water - (this study)	0.057	0.064	0.002	0.02	0.006
Dermal – (Abdallah and Harrad, 2022)	1.7	20.4	3		
SUM	**4.1**	**26**	**6.80**	**10**	**14.3**
RfD (USEPA, 2017)	7000	10000	20000	NA	NA
RfD (Van den Eede et al., 2011)	2200	8000	1500	7000	NA
RfD (Ali et al., 2012)	22000	80000	15000	70000	NA
RfD (Saito et al., 2007)	NA	3600 [a]	NA	NA	NA
RfD (Zhao et al., 2019)	NA	NA	NA	NA	600 [b]
HQ (USEPA, 2017)	0.00059	0.0026	0.00034	-	-
HQ (Van den Eede et al., 2011)	0.0019	0.0032	0.0045	0.0015	0.024 [b]
HQ (Ali et al., 2012)	0.00019	0.00032	0.00045	0.00015	-
HQ (Saito et al., 2007)	-	0.007 [a]	-	-	-
High-end exposure					
Adults (High)	TCEP	TCIPP	TDCIPP	TPHP	EHDPP
Dust - (Brommer and Harrad, 2015)	1.3	13	3.1	5.6	5.1
Drinking water - (this study)	0.39	0.40	0.015	0.13	0.085
Food – (Gbadamosi et al., 2022)	9.1	16	15	38	41
Dermal - (Abdallah et al., 2016)	10	23	4.3		
SUM	**21**	**52**	**22**	**44**	**46**
HQ (USEPA, 2017)	0.0030	0.0052	0.0011	-	-
HQ (Van den Eede et al., 2011)	0.0094	0.0065	0.015	0.0063	0.077 [b]
HQ (Ali et al., 2012)	0.00094	0.00065	0.0015	0.00063	-
HQ (Saito et al., 2007)	-	0.014 [a]	-	-	-

[a] Saito et al., 2007; [b] Zhao et al., 2019; NA = Not available

Appendix for chapter five

Appendix 5.1: Names, abbreviations, formulas, and physicochemical properties of the target OPEs in the present study

OPEs classification	Name	Abbreviation (Chemical formula)	CAS#	MW	P (mmHg at 25°C)	S (mg/L at 25°C)	BP (°C)	Log K_{OW}	Log K_{OC}	Log K_{OA}	BAF
Chlorinated-OPEs	Tris(2-chloroethyl) phosphate	TCEP ($C_6H_{12}Cl_3O_4P$)	115-96-8	285.49	0.0613	**7000**	351	1.63	2.47	7.42	0.425
	Tris(2-chloroisopropyl) Phosphate	TCIPP ($C_9H_{18}Cl_3O_4P$)	13674-84-5	327.57	$5.64x10^{-5}$	**1200**	>270	2.89	3.10	8.20	3.27
	Tris(1,3-dichloro-2-propyl) Phosphate	TDCIPP ($C_9H_{15}Cl_6O_4P$)	13674-87-8	430.89	$2.98x10^{-7}$	7	237	3.65	3.96	10.6	21.4
Aryl-OPEs	Triphenyl phosphate	TPHP ($C_{18}H_{15}O_4P$)	115-86-6	326.28	$1.12x10^{-5}$	1.9	370	4.59	3.71	8.45	113.3
	2-Ethylhexyl diphenyl Phosphate	EHDPP ($C_{20}H_{27}O_4P$)	1241-94-7	362.40	$5x10^{-5}$	1.9	421	6.30	4.20	8.92	855.2
	Tri-m-tolyl phosphate	TMTP ($C_{21}H_{21}O_4P$)	56-04-2	368.4	$7.8x10^{-7}$	-	260	6.34	$4.1x10^{4}$	-	-
Alkyl-OPEs	Tris(2-butoxyethyl) phosphate	TBOEP ($C_{18}H_{39}O_7P$)	78-51-3	398.48	$1.23x10^{-6}$	**$1.20x10^{3}$**	414	3.65	5.66	13.0	25.56
	Tri-n-butyl phosphate	TNBP ($C_{12}H_{27}O_4P$)	126-73-8	266.31	$3.49x10^{-3}$	7.35	289	4.00	3.27	9.21	39.81

Where: S = solubility (mg/L) in water at 25°C; P = vapor pressure (mmHg) at 25°C; log K_{ow} = n-octanol: water partition coefficient; KOC=Organic carbon-water partition coefficient; KOA=Octanol-Air partition coefficient; BAF: bioaccumulation factor and, MW = molecular weight. The data are compiled from databases (Chemspider, 2021) and Pantelaki and Voutsa (2019).

Appendix 5.2: Characteristics of the sampled microenvironments (Residential homes, offices, medical centres and car/buses)

Residential homes (n = 20)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
No. of electrics and electronics	6	7	5	8	5	6	5	4	3	6	5	7	4	3	3	4	5	4	6	4
No. of furniture and mattresses	8	9	7	9	6	8	5	6	8	4	9	7	8	8	7	6	5	4	6	6
Carpeted	Y	Y	Y	N	N	Y	N	Y	Y	Y	N	N	N	Y	Y	N	Y	Y	Y	N
Rugged/ceramic tiles	N	N	N	Y	Y	N	Y	N	N	N	Y	Y	Y	N	N	Y	N	N	N	Y
Painted	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	Y	Y	N	Y	N	Y	Y	Y
Wall-paper	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	N	N	Y	N
Ventilated (Air conditioners)	N	N	N	Y	N	N	Y	Y	N	Y	Y	Y	N	N	N	Y	N	N	N	Y
Year of construction	1990	1987	1992	2003	1994	2000	2006	2016	1991	1989	1997	2004	2012	2015	2013	2007	2017	2005	2011	1998
Offices (n = 20)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
No. of electrics and electronics	2	3	4	3	2	1	4	4	5	3	2	3	4	3	3	3	2	5	4	4
No. of furniture and mattresses	5	4	4	5	5	5	4	4	5	3	5	4	5	5	4	3	4	5	3	4
Carpeted	Y	N	N	Y	N	Y	N	N	N	Y	N	Y	N	N	Y	N	Y	Y	N	Y
Rugged/ceramic tiles	N	N	N	N	Y	N	Y	Y	Y	Y	Y	N	Y	Y	N	N	N	N	Y	N

Painted	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wall-paper	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Ventilated (Air conditioners)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	Y	Y
Year of construction	2009	2012	2008	1982	1991	1986	2013	2011	1987	1999	2014	1996	2008	2009	1989	1990	1992	1987	2005	2016
Medical centres (n = 14)	1	2	3	4	5	6	7	8	9	10	11	12	13	14						
No. of electrics and electronics	5	6	6	7	5	4	6	5	5	6	4	5	5	4						
No. of furniture and mattresses	3	4	3	5	4	4	5	3	6	4	5	4	5	5						
Carpeted	Y	Y	N	N	N	Y	Y	N	N	N	N	N	N	Y						
Rugged/ceramic tiles	N	N	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	N						
Painted	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y						
Wall-paper	N	N	N	N	N	N	N	N	N	N	N	N	N	N						
Ventilated (Air conditioners)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N						
Year of construction	2012	2009	2019	2013	2018	2015	1993	1990	1986	2017	2013	2018	2011	2013						
Car/buses (n = 10)	1	2	3	4	5	6	7	8	9	10										
No. of electronics	1	2	2	1	1	1	2	1	-	1										
Manufacturer, year	Ford, 1999	Toyota, 2006	Honda, 2003	Hyundai, 2003	Toyota, 2012	Peugeot, 2010	KIA, 2006	Toyota, 2012	Honda, 2000	Honda, 2009										
Ventilated (Air conditioners)	Y	Y	N	Y	Y	Y	Y	Y	N	Y										

Seat cover	Fabric	Leather	Leather	Leather	Leather	Leather	Fabric	Leather	Fabric	Fabric										

Appendix 5.3: Test for normality

Tests of Normality						
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
TCEP	.342	64	<.001	.409	64	<.001
TCIPP	.206	64	<.001	.860	64	<.001
TDCIPP	.256	64	<.001	.549	64	<.001
TPHP	.343	64	<.001	.435	64	<.001
EHDPP	.213	64	<.001	.687	64	<.001
TBOEP	.179	64	<.001	.867	64	<.001
TnBP	.158	64	<.001	.880	64	<.001
TMTP	.358	64	<.001	.516	64	<.001
a. Lilliefors Significance Correction						

Appendix 5.4: Comparison of OPEs Concentrations of OPEs (ng/g) in Indoor dust Microenvironments in this study with those from different countries

Location	Microenvironment	Statistical Parameter	TnBP	TCEP	TCIPP	TBEP	TPHP	TDCIPP	EHDPP	TEP	TMP	TnPP	TEHP	Reference
Nigeria (n=20)	**Office**	**Mean**	**8.6**	**40**	**34**	**66**	**29**	**20**	**32**	**-**	**-**	**-**	**-**	**This study**
Beijing, China (n=23)	Office 1	Median	33	5610	10700	7880	1100	1100	1440	nd	Nd	nd	1740	Cao et al., 2014
Beijing, China (n=17)	Office 2	Median	47	1980	5540	3030	4050	1520	873	nd	Nd	Nd	nd	Cao et al., 2014
Beijing, China (n=16)	Office 3	Median	54	2160	6090	3480	1580	2770	746	nd	Nd	Nd	nd	Cao et al., 2014
Beijing (n=23)	Office	Median	Nd	12879	16133	4189	1928	1007	-	-	-	-	89	Wu et al., 2016
China (n=17)	Office	Median	0.1	15.2	9.2	1.6	0.6	0.4	-	-	-	-	-	Liu et al., 2017
Beijing, China (n=48)	Office (winter)	Average	100	4600	5700	1800	620	550	250	650	-	-	210	Cao et al., 2019
Beijing, China (n=48)	Office (summer)	Average	19	4000	3200	2000	700	440	200	360	-	-	260	Cao et al., 2019
Egypt, Assiut (n=20)	Office	Median	23	31	80	143	73	49	48	nd	Nd	Nd	-	Abdallah and Covaci, 2014
Germany (n=10)	Offices	Average	220	120	3000	7000	2500	150	Nd	nd	Nd	370		Brommer et al., 2012
West Midlands, UK (n=61)	Office	Average	100	5000	44000	-	8200	2100	10000	-	330	-	-	Brommer and Harrad, 2015

Guangzhou City, China (n=8)	Office-AC Dust	Average	ND	519	1560	152	972	499	111	ND	-	-	153	Zheng et al., 2017
Guangzhou City, China (n=8)	Office-Printer Dust	Average	ND	661	1460	1230	5780	574	60.8	ND	-	-	87.7	Zheng et al., 2017
Guangzhou City, China (n=9)	Office-PC table dust	Average	170	414	1010	ND	1220	267	113	ND	-	-	78.7	Zheng et al., 2017
Guangzhou City, China (n=9)	Office-window dust	Average	39.1	564	1970	ND	423	61.8	13.7	26.0	-	-	83.3	Zheng et al., 2017
Guangzhou City, China (n=9)	Office-Floor dust	Average	ND	188	954	1340	460	166	208	155	-	-	135	Zheng et al., 2017
Islamabad and Faisalabad (n=30)	University office	Median	-	-	11	115	170	20	88	nd	Nd	Nd	50	Ali et al., 2014
Sweden (n=2)	Hospital offices	Average	180	1000	5300	120000	2200	560	-	-	-	-	160	Marklund et al., 2003
Nigeria (n = 20)	**Residential homes**	**Average**	**0.02**	**20**	**81**	**88**	**30**	**26**	**25**	-	-	-	-	**This study**
Canada (n=23)	Homes	Median	0.06	0.181	1.47	n.a	2.35	0.917	0.754	n.a	n.a	n.a	-	Vykoukalova et al., 2017
Czech Republic (n=20)	Homes	Median	0.05	0.155	1.86	n.a	0.81	0.183	0.836	n.a	n.a	n.a	-	Vykoukalova et al., 2017
Beijing (n=21)	Homes	Median	122	4992	2048	2259	376	479	-	-	-	-	37	Wu et al., 2016
Beijing, China (n=26)	Residential home (winter)	Average	41	1000	1700	340	1200	150	390	310	-	-	660	Cao et al., 2019
Beijing, China (n=26)	Residential home (summer)	Average	12	670	2400	180	460	130	450	420	-	-	590	Cao et al., 2019

Germany (n=6)	Homes	Average	130	200	740	730	380	<80	Nd	nd	Nd	94	Nd	Brommer et al., 2012
Philippines Malate (n=17)	Homes	Average	0.01	0.032	-	-	0.11	-	-	-	-	-	-	Kim et al., 2013
Philippines Payatas (n=17)	Homes	Average	0.02	0.0064	-	-	0.07	-	0.045	-	-	-	-	Kim et al., 2013
USA (n=20)	Homes	Median	0.11	1.44	2.79	n.a	3.04	3.68	0.889	n.a	Nd	n.a	-	Vykoukalova et al., 2017
Egypt, Assiut (n=20)	House	Median	17	22	28	18	67	72	42	nd	Nd	Nd	Nd	Abdallah and Covaci, 2014
Kuwait (n=15)	House	Median	58	710	1460	855	430	360	190	nd	Nd	Nd	65	Ali et al., 2013
Saudi Arabia (n=15)	House	Median	35	410	1650	205	230	500	220	nd	Nd	Nd	70	Ali et al., 2016
Guangzhou City and Qingyuan (n=11)	Urban House	Median	80	3780	750	320	150	130	360	-	-	-	140	He et al., 2015
Pakistan, Faisalabad (n=15)	Urban House	Median	10	15	10	16.5	175	2.5	67	nd	Nd	Nd	20	Ali et al., 2013
Guangzhou City and Qingyuan (n=25)	Rural House	Median	140	1930	1220	200	1090	150	310	-	-	-	190	He et al., 2015
West Midlands, UK (n=32)	Living room	Average	40	2200	29000	-	10000	2000	2600	-	2000	-	-	Brommer and Harrad, 2015
Nigeria (n = 10)	**Cars/buses**	**Average**	**26**	**8.2**	**71**	**99**	**19**	**18**	**37**	**-**	**-**	**-**	**-**	**This study**

Egypt, Assiut (n=20)	Cars	Median	59	127	291	190	135	61	54	nd	Nd	nd	-	Abdallah and Covaci, 2014
Germany (n=12	Cars	Average	110	950	3100	2100	3000	130000	Nd	nd	Nd	24000	Nd	Brommer et al., 2012
Kuwait (n=15)	Cars	Median	730	1765	30725	4465	1760	7630	520	nd	Nd	Nd	135	Ali et al., 2013
Pakistan, Faisalabad (n=15)	Cars	Median	18	75	100	16	245	29	37	nd	Nd	Nd	13	Ali et al., 2013
Saudi Arabia (n=15)	Cars	Median	60	1200	1650	50	470	2700	180	nd	Nd	Nd	150	Ali et al., 2016
Thessaloniki, Greece (n=25)	Car Dust	Median	-	114	2607	896	295	2509	167	-	30	-	10	Christia et al., 2018
West Midlands, UK (n=61)	Cars	Average	140	1950	83000	-	15000	110000	2900	-	1000	-	-	Brommer and Harrad, 2015
Egypt, Assiut (n=20)	Public places	Median	73	234	232	68	629	416	44	nd	Nd	Nd	-	Abdallah and Covaci, 2014
Islamabad and Faisalabad (n=30)	Electronic shops	Median	n.a	n.a	75	<15	195	<10	45	nd	Nd	Nd	35	Ali et al., 2014
Nigeria (n = 14)	**Medical centres**	**Average**	**14**	**35**	**13**	**53**	**5.4**	**6.2**	**23**	**-**	**-**	**-**	**-**	**This study**
Sweden (n=3)	Hospital wards	Average	70	3800	2300	210000	2000	2100	-	-	-	-	180	Marklund et al., 2003

Appendix 5.5: Statistical summary of the EDI for the Indoor dust ingestion and dermal absorption (ng/kg bw/day) of OPEs for adults and toddlers in this study

OPE		Dust ingestion (ng/kg body weight/day)						Dermal absorption (ng/kg body weight/day)					
		Toddlers			Adults			Toddlers			Adults		
	RfD (ng/kg bw/day)	Mean	Median	95th Percentile	Mean	Median	95th Percentile	Mean	Median	95th Percentile	Mean	Median	95th Percentile
Car/buses (n=10)													
TCEP	7000 [a]	0.01	0.009	0.10	0.001	0.001	0.004	0.007	0.005	0.014	0.001	$4x10^{-4}$	0.001
TCIPP	10,000 [a]	0.10	0.11	0.56	0.007	0.007	0.025	0.054	0.055	0.072	0.004	0.004	0.006
TDCIPP	20,000 [a]	0.03	0.02	0.28	0.002	0.001	0.012	0.007	0.005	0.019	0.001	$4x10^{-4}$	0.001
TPHP	7000 [b]	0.03	0.02	0.19	0.002	0.002	0.008	0.009	0.008	0.016	0.001	0.001	0.001
EHDPP	600 [c]	0.05	0.05	0.28	0.004	0.004	0.012	0.019	0.019	0.025	0.001	0.001	0.002
TBOEP	1500 [b]	0.14	0.12	1.03	0.010	0.008	0.045	0.050	0.041	0.090	0.004	0.003	0.007
TnBP	10,000 [a]	0.04	0.04	0.23	0.003	0.002	0.010	0.013	0.012	0.020	0.001	0.001	0.002
TMTP	-	0.03	$2x10^{-5}$	0.41	0.002	0.000	0.018	0.009	$1x10^{-5}$	0.036	0.001	$5x10^{-7}$	0.003
$\sum_8$OPEs	-	**0.43**	**0.37**	**3.08**	**0.030**	**0.026**	**0.135**	**0.169**	**0.146**	**0.291**	**0.013**	**0.011**	**0.023**
Offices (n=20)													
TCEP	7000 [a]	0.142	0.020	3.085	0.0022	0.0003	0.0301	0.08	0.01	0.44	0.0014	0.0002	0.0078
TCIPP	10,000 [a]	0.122	0.067	1.384	0.0019	0.0010	0.0135	0.06	0.03	0.18	0.0011	0.0006	0.0031
TDCIPP	20,000 [a]	0.071	0.045	0.609	0.0011	0.0007	0.0059	0.02	0.01	0.04	0.0003	0.0002	0.0007

TPHP	7000 [b]	0.104	0.066	1.106	0.0016	0.0010	0.0108	0.04	0.02	0.10	0.0006	0.0004	0.0017
EHDPP	600 [c]	0.116	0.078	1.461	0.0018	0.0012	0.0143	0.04	0.03	0.13	0.0007	0.0005	0.0022
TBOEP	1500 [b]	0.237	0.192	1.586	0.0037	0.0030	0.0155	0.08	0.07	0.14	0.0014	0.0012	0.0024
TnBP	10,000 [a]	0.031	0.029	0.234	0.0005	0.0005	0.0023	0.01	0.01	0.02	0.0002	0.0002	0.0004
TMTP	-	0.003	$2x10^{-5}$	0.063	$4x10^{-5}$	$3x10^{-7}$	$6x10^{-4}$	$9x10^{-4}$	$1x10^{-5}$	0.01	$2x10^{-5}$	$1x10^{-7}$	$1x10^{-4}$
$\sum_8$OPEs		**0.824**	**0.50**	**9.529**	**0.0129**	**0.0078**	**0.0930**	**0.33**	**0.19**	**1.05**	**0.0059**	**0.0033**	**0.0184**
Residential homes (n=20)													
TCEP	7000 [a]	0.06	0.04	0.55	0.003	0.002	0.018	0.03	0.02	0.08	0.002	0.001	0.005
TCIPP	10,000 [a]	0.25	0.26	1.73	0.013	0.014	0.056	0.13	0.13	0.22	0.007	0.008	0.013
TDCIPP	20,000 [a]	0.08	0.06	0.66	0.004	0.003	0.021	0.02	0.01	0.04	0.001	0.001	0.003
TPHP	7000 [b]	0.09	0.06	0.62	0.005	0.003	0.020	0.03	0.02	0.05	0.002	0.001	0.003
EHDPP	600 [c]	0.08	0.06	0.76	0.004	0.003	0.025	0.03	0.02	0.07	0.002	0.001	0.004
TBOEP	1500 [b]	0.27	0.24	2.17	0.014	0.012	0.070	0.09	0.08	0.19	0.005	0.005	0.011
TnBP	10,000 [a]	$1x10^{-4}$	$1x10^{-4}$	$2x10^{-4}$	$3x10^{-6}$	$3x10^{-6}$	$8x10^{-6}$	$2x10^{-5}$	$2x10^{-5}$	$2x10^{-5}$	$1x10^{-6}$	$1x10^{-6}$	$1x10^{-6}$
TMTP	-	0.02	0.00	0.48	0.001	$2x10^{-6}$	0.016	0.01	$1x10^{-5}$	0.04	$5x10^{-4}$	$1x10^{-6}$	0.002
$\sum_8$OPEs	-	**0.85**	**0.71**	**6.97**	**0.044**	**0.037**	**0.226**	**0.35**	**0.30**	**0.70**	**0.020**	**0.017**	**0.041**
Medical centres (n=14)													
TCEP	7000 [a]	0.0006	0.0006	0.0038	$4.4x10^{-5}$	$4.3x10^{-5}$	0.0002	0.0004	0.0003	0.0005	$3x10^{-5}$	$3x10^{-5}$	$4x10^{-5}$
TCIPP	10,000 [a]	0.0024	0.0024	0.0124	0.0002	0.0002	0.0005	0.0012	0.0012	0.0016	$1x10^{-4}$	$1x10^{-4}$	$1x10^{-4}$

TDCIPP	20,000 [a]	0.0011	0.0009	0.0102	$7.9x10^{-5}$	$6.0x10^{-5}$	0.0004	0.0003	0.0002	0.0007	$2x10^{-5}$	$2x10^{-5}$	$5x10^{-5}$
TPHP	7000 [b]	0.0010	0.0008	0.0067	$6.9x10^{-5}$	$5.9x10^{-5}$	0.0003	0.0003	0.0003	0.0006	$3x10^{-5}$	$2x10^{-5}$	$5x10^{-5}$
EHDPP	600 [c]	0.0042	0.0018	0.0593	0.0003	0.0001	0.0026	0.0015	0.0006	0.0052	$1x10^{-4}$	$5x10^{-5}$	$4x10^{-4}$
TBOEP	1500 [b]	0.0096	0.0089	0.0529	0.0007	0.0006	0.0023	0.0034	0.0031	0.0046	$3x10^{-4}$	$2x10^{-4}$	$4x10^{-4}$
TnBP	10,000 [a]	0.0025	0.0023	0.0134	0.0002	0.0002	0.0006	0.0009	0.0008	0.0012	$7x10^{-5}$	$6x10^{-5}$	$9x10^{-5}$
TMTP	-	0.0017	0.0023	0.0157	0.0001	0.0002	0.0007	0.0006	0.0008	0.0014	$5x10^{-5}$	$6x10^{-5}$	$1x10^{-4}$
$\sum_8$OPEs	-	**0.0232**	**0.0200**	**0.1744**	**0.0016**	**0.0014**	**0.0076**	**0.0085**	**0.0074**	**0.0157**	$\mathbf{7x10^{-4}}$	$\mathbf{6x10^{-4}}$	$\mathbf{1x10^{-3}}$
∑EDIs in all Microenvironments	-	**2.13**	**1.59**	**19.8**	**0.09**	**0.07**	**0.46**	**0.86**	**0.63**	**2.05**	**0.04**	**0.03**	**0.08**

Appendix for chapter six

Appendix 6.1: Limits of quantification (LOQs) for the different food groups analysed (ng/g ww).

OPEs	TCEP	TCIPP	TDCIPP	TPHP	EHDPP	TnBP	TBOEP	TMTP
Dried and smoked fish (n=26)	0.14	0.25	0.13	0.46	0.29	1.06	0.49	0.34
Roasted meat and cow hide (n=23)	0.15	0.27	0.14	0.49	0.31	1.14	0.52	0.36
Milk (liquid and powder) (n=6)	0.16	0.29	0.14	0.52	0.33	1.20	0.55	0.39
Cereals (n=10)	0.15	0.27	0.13	0.49	0.31	1.15	0.53	0.34
Wheat flour (Semo) (n=3)	0.16	0.27	0.14	0.50	0.32	1.16	0.53	0.34
Cassava flour (Fufu) (n=3)	0.19	0.34	0.17	0.62	0.39	1.44	0.66	0.43
Yam powder (Poundo yam) (n=3)	0.15	0.28	0.14	0.50	0.32	1.17	0.54	0.35
Plantain snacks (n=3)	0.19	0.33	0.17	0.61	0.38	1.40	0.64	0.42
Cassava flakes (Garri) (n=5)	0.15	0.26	0.13	0.48	0.30	1.10	0.51	0.33
Melon (Egusi) (n=3)	0.16	0.28	0.14	0.52	0.33	1.20	0.55	0.36

Appendix 6.2: Concentrations of OPEs in foodstuffs purchased from African stores in the UK and local markets in Nigeria

Dried and smoked fish collected from Nigeria (n = 9)	TCEP	TCIPP	TDCIPP	EHDPP	TPHP	TnBP	TBOEP	TMTP	∑OPEs
Mean	0.52	0.37	0.31	<LOQ	1.21	<LOQ	1.89	<LOQ	5.11
Median	0.48	0.31	0.06	<LOQ	1.55	<LOQ	0.24	<LOQ	3.46
Standard deviation	0.28	0.23	0.40	-	0.79	-	2.54	-	4.25
Minimum	0.14	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
Maximum	1.04	0.88	1.04	<LOQ	2.20	<LOQ	6.36	<LOQ	12.4
97.5th Percentile	0.98	0.82	1.02	<LOQ	2.16	<LOQ	6.14	<LOQ	11.9
DF (100%)	100	78	33	0	67	0	33	0	
Dried and smoked fish collected from African stores in UK (n = 17)									
Mean	0.45	0.58	0.25	2.34	3.26	0.53	2.75	<LOQ	10.3
Median	0.38	0.43	0.06	1.16	2.94	0.53	0.24	<LOQ	5.91
Standard deviation	0.27	0.32	0.36	2.80	2.19	-	3.41	-	9.36
Minimum	0.12	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
Maximum	1.01	1.35	1.13	7.70	7.64	0.53	8.53	<LOQ	28.1
97.5th Percentile	0.93	1.23	1.01	7.61	7.17	0.53	8.50	<LOQ	27.1
DF (100%)	100	100	18	71	94	0	53	0	
Roasted meat collected from Nigeria (n = 7)									
Mean	0.23	0.20	0.89	1.40	0.24	0.53	3.12	<LOQ	6.78
Median	0.24	0.22	0.27	0.14	0.23	0.53	0.24	<LOQ	2.03
Standard deviation	0.09	0.05	0.96	1.73	0.04	-	4.25	-	7.12
Minimum	0.13	0.12	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
Maximum	0.36	0.27	1.97	3.55	0.31	0.53	9.69	<LOQ	16.8
97.5th Percentile	0.35	0.26	1.97	3.50	0.30	0.53	9.24	<LOQ	16.3
DF (100%)	100	100	80	40	40	0	40	0	
Roasted meat collected from African stores in UK (n = 16)									
Mean	0.56	0.43	0.45	2.73	1.11	0.51	8.54	<LOQ	14.5

Median	0.50	0.37	0.32	2.89	0.27	0.55	6.48	<LOQ	11.5
Standard deviation	0.37	0.25	0.44	2.40	1.29	0.07	9.12	0.00	13.9
Minimum	0.12	0.11	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
Maximum	1.25	1.00	1.35	8.71	4.07	0.58	29.4	<LOQ	46.5
97.5th Percentile	1.20	0.88	1.28	7.61	3.74	0.53	26.30	<LOQ	41.7
DF (100%)	100	100	63	75	56	6	63	0	
Cereal collected from Nigeria (n=5)									
Mean	0.16	0.40	0.85	0.70	0.63	0.53	0.87	0.16	4.30
Median	0.13	0.37	0.36	0.14	0.73	0.53	0.24	0.16	2.65
Standard deviation	0.06	0.15	1.11	0.97	0.36	0.00	1.09	0.00	3.75
Minimum	0.11	0.28	0.06	0.14	0.23	0.53	0.24	0.16	1.75
Maximum	0.23	0.56	2.12	1.83	0.94	0.53	2.13	0.16	8.49
97.5th Percentile	0.23	0.55	2.03	1.74	0.93	0.53	2.03	0.16	8.20
DF (100%)	100	100	80	40	80	0	20	0	
Cereal collected from African stores in UK (n=5)									
Mean	0.23	0.21	0.46	5.13	6.15	0.16	<LOQ	<LOQ	12.7
Median	0.27	0.21	0.48	5.27	6.24	0.18	<LOQ	<LOQ	13.0
Standard deviation	0.08	0.01	0.10	0.87	0.93	0.03	-	-	2.03
Minimum	0.13	0.20	0.35	4.19	5.18	<0.15	<LOQ	<LOQ	-
Maximum	0.28	0.23	0.56	5.93	7.03	0.20	<LOQ	<LOQ	14.5
97.5th Percentile	0.28	0.22	0.55	5.89	7.00	0.12	<LOQ	<LOQ	
DF (100%)	100	100`	100`	100	100	100	0	0	

Where LOQ =limit of quantification

Appendix 6.3: Comparing estimated dietary intake (EDIs, ng/kg bw/day) with previous studies from different countries, oral reference dose (RfD, ng/kg bw/day)

Reference, Location	Statistical Parameter	Population group	TCEP	TCIPP	TDCIPP	TPHP	TnBP	EHDPP	TMPP	TBOEP	TMTP	TEHP	TEP	TMP	TiBP	∑OPEs
RfDs (USEPA, 2017; Li et al., 2018)			7000	10000	20000	-	10000	-	20000	-	-	100000	-	10000	-	NA
This study	Mean	Children	12.6	13.5	33.8	92.3	29.7	58.2	-	183	7.77	-	-	-	-	431
	High-end		19.9	23.2	52,6	176	37.2	159	-	295	7.77	-	-	-	-	771
This study	Mean	Adults	12.5	14.6	36.9	90.6	30.8	52.2	-	159	7.65	-	-	-	-	404
	High-end		21.3	25.1	56.9	176	39.0	162	-	311	7.65	-	-	-	-	798
Bi and Su (2023)	Mean	Adults	21.9	8.71	-	27.1	15.6	1.35	-	17.0	-	2.78	8.10	-	-	
	P95		131	12.9	-	105	46.7	5.00	-	54.3	-	9.46	27.2	-	-	
Wang et al., 2022	Median	Adults	13.6	14.3	0.553	5.13	2.66	-	-	0.772	-	-	0.858	-	-	65.4
	P95		100	41.5	4.93	157	15.6	-	-	6.00	-	-	182	-	-	474
Zhou et al., 2022	Mean	Infants	6.9	2.4	8.2	0.4	0.8	6.2	-	0.4	-	-	16.1	-	-	50.2
	P95		19.2	8.5	23.3	0.5	0.8	29.9	-	0.8	-	-	66.5	-	-	179.4
Sala et al., 2022	Mean	Adults	1.18	0.45	4.94	1.43	0.29	-	-	1.1	-	-	-	-	-	12.3

Reference, Location	Statistical Parameter	Population group	TCEP	TCIPP	TDCIPP	TPHP	TnBP	EHDPP	TMPP	TBOEP	TMTP	TEHP	TEP	TMP	TiBP	∑OPEs
	95th Percentile		2.98	0.72	12.6	3.10	0.35	-	-	1.93	-	-	-	-	-	37.1
Gbadamosi et al., 2022 (UK)	Mean	Toddler	12.5	19.4	20.5	117	4.97	116	-	102	27.6	-	-	-	-	420
		Children	6.70	11.0	10.4	27.0	2.33	29.8	-	56.0	12.0	-	-	-	-	155
		Adults	2.34	4.16	3.73	10.3	1.05	14.2	-	22.0	4.59	-	-	-	-	62.3
		Elderly	3.07	5.20	4.84	12.5	1.31	14.2	-	27.5	5.60	-	-	-	-	74.3
Gbadamosi et al., 2022 (UK)	High-end exposure	Toddler	41.6	71.5	74.2	284	19.5	296	-	641	119	-	-	-	-	1547
		Children	25.0	42.8	42.5	108	12.3	107	-	446	52.3	-	-	-	-	836
		Adults	9.07	16.1	15.0	38.4	4.39	41.3	-	134	19.3	-	-	-	-	278
		Elderly	12.7	22.1	20.4	52.5	6.01	55.3	-	181	26.9	-	-	-	-	377
Malarvannan et al. (2015), Flanders (Belgium)	Mean	General population	0.010	0.10	0.012	0.034	-	0.028	-	0.017		-	-	-		-
		High intake	0.25	2.5	0.29	0.84	-	0.70	-	0.43		-	-	-		
	Mean	Male	162	72	37	68	-	-		39		160	-	-	-	539
		Female	182	82	42	77				44		174				601

Reference, Location	Statistical Parameter	Population group	TCEP	TCIPP	TDCIPP	TPHP	TnBP	EHDPP	TMPP	TBOEP	TMTP	TEHP	TEP	TMP	TiBP	∑OPEs
Zhang et al. (2016), Tianjin (China)	95th Percentile	Male	236	105	103	114	-	-	-	60		282	-	-	-	818
		Female	247	112	112	126	-	-	-	67		290	-	-	-	880
Ding et al. (2018), Eastern China	Mean	Adult	8.7	6.4	0	2.3	3.0	-	0.43	5.8		26.5	1.5	0.4	-	55.0
		Children	0.7	11.4	0	4.0	5.0		1.6	10.9		49.1	2.2	0.7		97.7
Poma et al. (2017), Uppsala (Sweden)	Mean		6.0	8.5	11.9	9.7	-	48.6	-	-		-	-	-	-	-
Xu et al. (2017), Norway	95th Percentile		28	41	0	34	-	280	-	0		-	-	-	-	-
Poma et al. (2018), Belgium	Mean	Men	2.9	19.5	9.9	47.4	5.7	15.7	-	-		5.0	-	-	-	106.1
		Women	2.6	16.5	8.4	42.0	5.2	14.0				4.5				93.2
		All adult	2.8	18.5	9.6	46.6	5.5	14.9				4.9				102.8
He at al. (2018), Southeast Queensland (Australia)	Mean		4.1	25	<1.1	<0.15	6.7	<5.0	<0.16	1.8		<0.088	-	-	-	-

Reference, Location	Statistical Parameter	Population group	TCEP	TCIPP	TDCIPP	TPHP	TnBP	EHDPP	TMPP	TBOEP	TMTP	TEHP	TEP	TMP	TiBP	∑OPEs
Wang and Kannan, 2018, Albany, New York, USA	Median	Infants (<1 yr)	0.92	3.93	0.68	1.41	4.07	0.28	0.11	7.33		1.52	0.92	-	1.64	37.9
		Toddlers (1-<6 yrs)	3.61	12.4	2.91	3.65	12.0	0.94	0.29	46.8		7.23	2.95	-	4.79	135
		Children (6-<11 yrs)	1.48	5.93	0.82	1.72	5.56	0.36	0.14	16.7		1.86	1.12	-	2.12	56.6
		Teenagers (11-<21 yrs)	0.90	3.18	0.41	0.86	2.78	0.18	0.07	11.8		0.93	0.56	-	1.03	32.2
		Adults (> 21 yrs)	0.71	2.43	0.29	0.61	2.04	0.13	0.05	9.50		0.66	0.40	-	0.74	25.1
Wang and Kannan, 2018, Albany, New York, USA	95^{th} percentile	Infants (<1 yr)	5.99	31.3	17.7	6.75	23.6	11.7	7.14	113		18.7	14.1	-	6.49	453
		Toddlers (1-<6 yrs)	16.5	95.0	60.0	14.8	64.0	24.1	25.8	397		46.0	39.7	-	17.4	1340
		Children (6-<11 yrs)	10.3	42.5	23.5	9.35	32.4	15.9	9.13	205		22.8	17.3	-	7.70	662
		Teenagers (11-<21 yrs)	6.32	21.2	11.1	5.04	16.5	8.66	3.91	122		12.7	8.45	-	3.76	347

Reference, Location	Statistical Parameter	Population group	TCEP	TCIPP	TDCIPP	TPHP	TnBP	EHDPP	TMPP	TBOEP	TMTP	TEHP	TEP	TMP	TiBP	∑OPEs
		Adults (> 21 yrs)	5.57	15.4	7.92	4.03	12.7	6.90	2.44	102		9.50	5.93	-	2.70	266
Zhao et al. (2019), Nanjing (China)	Mean	Adults	14.3	1.7	-	2.6	2.0	8.4	0.2	0.7		1.6	12.7	-	-	44.3
	95^{th} percentile	Adults	32.1	3.1	-	5.0	3.3	18.9	0.4	1.1		3.0	23.5	-	-	78.5