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Organophosphate compounds, polybrominated diphenyl ethers and novel brominated flame retardants in European indoor house dust: Use, evidence for replacements and assessment of human exposure

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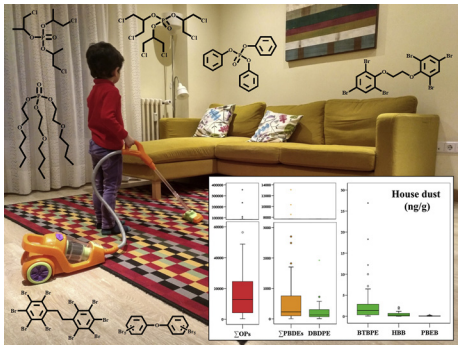
GRAPHICAL ABSTRACT



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ABSTRACT

52 pollutants including organophosphate flame retardants and plasticizers (OPs), polybrominated diphenyl ethers (PBDEs) and novel brominated flame retardants (NBFRs) were evaluated in household dust from Belgium, Italy and Spain. Pollutant pattern was dominated by ΣOPs (12.8 μg/g; median) followed in decreasing order by ΣPBDEs (229 ng/g), decabromodiphenyl ethane (DBDPE, 130 ng/g), 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE, 1.35 ng/g), hexabromobenzene (HBB, 0.28 ng/g) and finally pentabromoethylbenzene (PBEB, 0.03 ng/g). Country differences and substitution of regulated chemicals by unregulated ones were explored. Results clearly reflected a decrease in c-penta and c-octaBDE commercial mixtures, which are mainly substituted by OPs, BTBPE and PBEB. On the other hand, c-decaBDE concentrations increased in Spanish case. However, positive correlations with its proposed substitute (DBDPE) and recent restricted policies make it possible to assume that this trend will change in the coming years. On the basis of the relationship between pollutants, house characteristics and inhabitant habits, potential sources were studied. Finally, data obtained were used to determine estimated daily intakes (EDI) via house dust ingestion and dermal absorption for toddlers and adults at central and upper percentiles. Calculated EDI levels even at worst case scenario were below available reference dose (RfD) values in all cases.

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1. Introduction

Changes in terms of social habits have favored the entry of thousands of anthropogenic organic compounds into homes, whose implications in human health in some cases have not been conveniently evaluated. Exposure to these pollutants is increasing as the time spent at home does, and therefore, a proper characterization is mandatory to obtain a reliable picture of the presence of chemicals, verify substitution of regulated ones and assess indoor human exposure. Among all of these pollutants that can be found in homes, flame retardants (FRs) stand out. FRs are human-made chemicals added to a wide variety of consumers and industrial products like textiles, electric and electronic equipment, construction products and paints, among others, for the purpose of retarding flammability and reducing the human and material damages of fire (Alaee et al., 2003). However, evidence that they also cause harm to the people health and ecosystems have triggered the implementation of regulations (*e.g.* inclusion of commercial formulations of polybrominated diphenyl ethers (PBDEs) c-penta, c-octa, and c-decaBDE mixtures, in annex A of Stockholm Convention) (United Nations Environmental Programme (UNEP), 2017; United Nations Environment Programme (UNEP), 2010) at a global scale. Nonetheless, the industry is still forced to meet market demand and safety standards, so restrictions on the use and/or production of a substance could lead to an increase in the use of its alternative. Among these proposed substitutes, organophosphate flame retardants (OPFRs) or novel brominated flame retardants (NBFRs) like decabromodiphenyl ether (DBDPE) raise concern about their potential toxicity.

Applied materials may slough off from the surface via physical processes such as abrasion or weathering from products and accumulate in the dust (Webster et al., 2009). Afterwards, OPFRs, PBDEs and NBFRs in dust could enter into human body via inhalation, ingestion and dermal contact (Chen et al., 2019; Cao et al., 2019; Rantakokko et al., 2019). These last two exposure patterns are especially important for children and toddlers that spend a lot of time on floors and carpets and whose dust ingestion rates increase following hand-to-mouth behavior (United States Environmental Protection Agency (U.S. EPA), 2017). Some FRs have been identified to be associated to developmental delays and therefore the exposure of children during certain windows of vulnerability (critical periods of structural and functional development) may lead to a greater risk in the adulthood (Agency for Toxic Substances and Disease Registry (ATSDR), 2012; Wei et al., 2015). Accordingly, indoor dust monitoring is especially necessary to establish the exposure risk on this sensitive population group.

Surveys detecting BFRs and OPFRs in house dust started to be published in the early 2000s and most of them pointed out the indoor environment as a recognized vector of exposure to these pollutants. Twenty years later it is necessary to evaluate the current presence of these pollutants in order to corroborate compliance to international policies. Besides, identified emerging pollutants with influence in human health should be studied and included in human exposure assessments. In a previous study, we reported the presence of perfluorinated substances in house dust samples from three European countries (Belgium, Italy and Spain) (De la Torre et al., 2019). Here, the study of legacy and NBFRs together with organophosphate flame retardants and plasticizers (OPs) is presented. Geographical differences and temporal trends were compared with previous studies, considering also the influence of surroundings, home characteristics and occupant habits as potential OP and BFR sources. Finally, quantified concentrations were used to calculate human exposure through dust ingestion and dermal absorption for adults and toddlers at central and worst case scenarios.

2. Material and methods

2.1. Target compounds

Samples were analyzed for 7 OPs (tri-n-butyl phosphate (TNBP, CAS No. 126-73-8), tris(2-chloroethyl) phosphate (TCEP, CAS No. 115-96-8), tris(2-chloroisopropyl) phosphate (TCIPP, CAS No. 13674-84-5), tris (1,3-dichloro-2-propyl) phosphate (TDCIPP, CAS No. 13674-87-8), triphenyl phosphate (TPHP, CAS No. 115-86-6) and 2-ethylhexyl diphenyl phosphate (EHDP, CAS No. 1241-94-7), tris(2-butoxyethyl) phosphate (TBOEP, CAS No. 78-51-3)) and 45 BFRs (41 PBDEs, 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE, CAS No. 37853-59-1), hexabromobenzene (HBB, CAS No. 87-82-1), pentabromoethylbenzene (PBEB, CAS No. 85-22-3) and DBDPE (CAS No. 84852-53-9)).

2.2. Sample collection

Sixty-five household dust samples were obtained from homes widely distributed in Belgium (n = 22), Italy (n = 22) and Spain (n = 21), as described previously (De la Torre et al., 2019). Sampling was assumed by the home occupants that were asked to vacuum the entire home with their domestic vacuum cleaners. Each dust sample corresponded to a vacuum cleaner bag and was the result of cleaning a single home between September 2016 and January 2017. In addition, all participants involved in the investigation were asked to fill in a complete questionnaire regarding building characteristics, occupant habits and/or outdoor surrounding characteristics (see De la Torre et al., 2019 for details) (De la Torre et al., 2019). After sampling was completed, vacuum cleaner bags were covered with aluminum film and stored in a polyethylene sealable bag for preserving from humidity, light and other external factors which might change its composition. Upon arrival at the laboratory, bulk dust samples were sieved through a stainless steel sieve (500 μm), homogenized and stored at −20 °C until analysis.

2.3. Analytical method

The analytical method can be found in supplementary material (SM). The analytical method, including extraction and extract clean up, has been published elsewhere (Brommer et al., 2012). In brief, dust samples were allowed to equilibrate at room temperature for 24 h before being weight, spiked with ^{13}C-labelled surrogate standards (Table S-1) and extracted three times with 2 mL Hexane (Hex): Acetone (Ac) 3:1 v/v, vortexed 1 min, ultra-sonicated 5 min and centrifuged at 2000 *g* for 2 min. Supernatants were combined and evaporated to incipient dryness under a flow of nitrogen and redissolved with 1 mL Hex. Fractionation was carried out on a 0.5 g Florisil columns eluted with 8 mL Hexane (Fraction 1) and 10 mL of ethyl acetate (Fraction 2). Fraction 1, containing BFRs, was concentrated ≈0.5 mL and subjected to an additional clean up on a 0.5 g acid silica column modified with 44% H_2SO_4 and eluted with 10 mL of Hex: dichloromethane (DCM) 3:1 v/v. Prior to instrumental analysis, samples were concentrated to dryness under a flow of nitrogen and redissolved in nonane spiked with internal standards (Table S1). Brominated flame retardant (41 PBDEs, DBDPE, BTBPE, HBB and PBEB) and OP instrumental analysis were performed by high (Micromass Ultima NT HRMS) and low resolution (Agilent 5973 MSD) mass spectrometry, respectively. Details of the gas chromatographic and mass spectrometric method conditions are found in Table S2.

2.4. Quality control

The average recovery of surrogates ranged from 69 to 97 % and from 62 to 107% for BFRs and OPs, respectively. The limits of quantification (LOQs) of the method were calculated as the concentration corresponding to a signal-noise ratio ≥10 and are shown in Table S3. Two participants from each country (n = 6) were asked to prepare a

field blank sample, vacuuming diatomaceous earth. Field and procedural blanks were treated as samples through the entire process. Concentrations of all analytes in procedural blanks were below LOQs. However mean country-specific field blank levels, < 5% of sample concentrations in all cases, were subtracted from samples. House dust standard reference material (SRM 2585; National Institute of Standards and Technology (NIST)) was analyzed (n = 3) and compared to certified concentrations and data reported in the literature to check method accuracy and precision (Table S3).

2.5. Statistical analysis

Statistical analyses were performed with SPSS 14.0 for Windows software. Analyte concentrations were not normally distributed (Shapiro-Wilk and Anderson-Darling test), hence Spearman rank correlation coefficient was derived to investigate bivariate relationship and H Kruskal-Wallis tests were used to evaluate differences between groups. In order to include all samples, those with concentrations below LOQ were replaced by the LOQ divided by the square root of two. For exploring bivariate correlations (Spearman test) values below LOQ were removed. A significant level of $p < 0.05$ (two-tailed) was accepted, but to improve discussion when it reached $p < 0.01$ it was also mentioned in the text.

3. Results and discussion

31 targeted analytes presented quantification frequencies (Q_f) above 60% in household dust from Belgium, Italy and Spain. Main descriptive statistics for OPs, PBDEs and NBFRs in house dust for each country, as well as the total sample, are shown in Figs. 1 and 2 and Table S4. Profiles of OPs and PBDEs were also calculated (Fig. 3). Total median values obtained in the three countries (n = 65) were used to establish a first chemical pattern, where ΣOPs (sum of seven OPs; 12.8 μg/g, 100%; median, Q_f Table S4), were the predominant pollutants followed in decreasing order by ΣPBDEs (sum of 20 PBDEs; 229 ng/g, 100%), DBDPE (130 ng/g, 100%), BTBPE (1.35 ng/g, 78%), HBB (0.28 ng/g, 77%) and PBEB (0.03 ng/g, 77%).

3.1. Organophosphate compounds

Phosphate esters are commercial additives used since the 1940s not only as flame retardants but also as plasticizers, lacquer, paint, glue, floor finish wax, anti-foam agent, hydraulic fluids, and in industrial processes (Agency for Toxic Substances and Disease Registry (ATSDR), 2012; Wei et al., 2015; Marklund et al., 2003) (Table S5). Therefore it is not strange that OP levels in the house dust from Belgium, Italy and Spain were two orders of magnitude higher than PBDEs. OPs were quantified in all samples with concentrations ranging from 0.429 to 355 μg/g for the ΣOPs (sum of TNBP, TCEP, TCIPP, TDCIPP, TPHP, TBOEP and EHDP). No differences ($p > 0.05$) were found between countries for ΣOPs (Fig. 2). Considering all data, OP pattern is dominated by TBOEP (30%; Fig. 3) and TCIPP (27%) followed then by TPHP (14%) and TDCIPP (12%), EHDP (10%), TCEP (5%) and finally TNBP (4%). However, while this OP pattern was corroborated for Spanish and Italian samples, the contribution of TCIPP in Belgian dust increased up to 39%.

It is not unexpected that TCIPP dominated chloroalkyl phosphate esters contribution. TCIPP presented the highest registered volume (10 000–100 000 tonnes per year (t/y) in 2018) under the Regulation (EC) No. 1907/2006 on Registration, Evaluation and Authorization of Chemicals (REACH)) (European Chemicals Agency (ECHA), 2018) among all OPs considered in the present study. TCIPP is used as flame retardant in all types of flexible polyurethane foams such as baby mattresses, baby slings, and residential upholstered furniture. In TDCIPP case, the registered volume decreases to 1000–10 000 t/y because it's higher cost, and is mainly used for automotive applications (European Chemicals Agency (ECHA), 2018). Finally, TCEP is a substance of very high concern (SVHC) and included in the candidate list for authorization and currently not used anymore as flame retardant for flexible polyurethane foams in the EU, but may be present as an impurity in other commercial flame retardants or in imported articles with an assumed total use in EU of around 1000 t/y (European Chemicals Agency (ECHA), 2010). The use of TCEP was substituted by TCIPP, but also TCIPP, TDCIPP and TPHP were recognized c-pentaBDE replacements (Stapleton et al., 2009; Phillips et al., 2017). Therefore it seems plausible to think that current restrictions regarding c-decaBDE both at

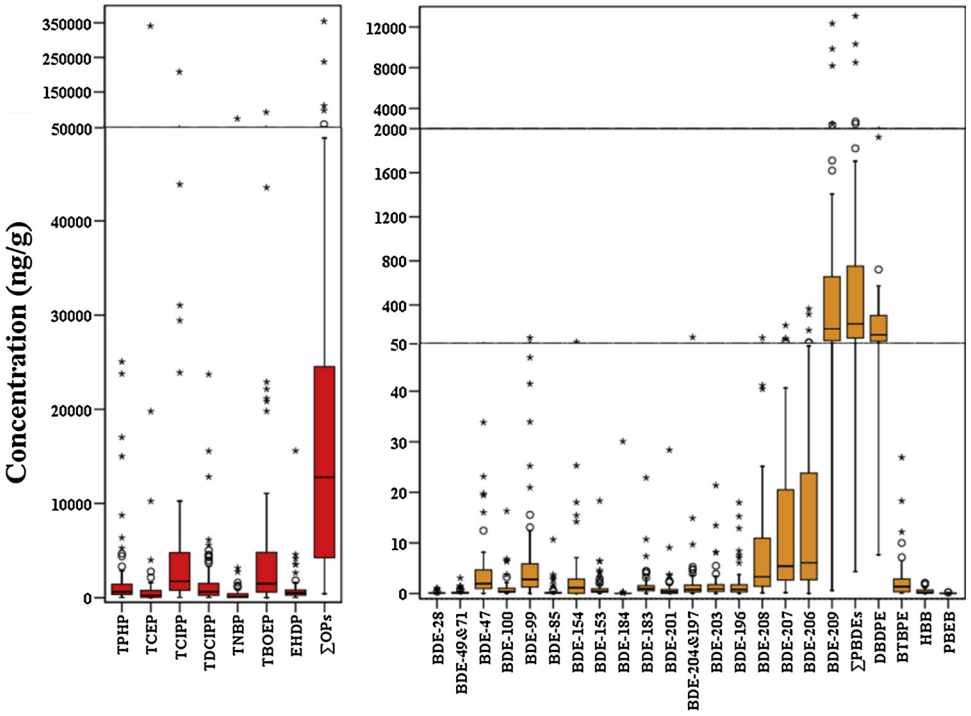

Fig. 1. Box plots of dust OP, PBDE and NBFR concentrations (ng/g) in European homes. The boxes represent the inter-quartile range (IQR) and the center line within the box the median. The circles and asterisk represent outliers (data above 75th percentile (P75) + 1.5 × IQR) and extreme (data above P75 + 3 × IQR) values, respectively.

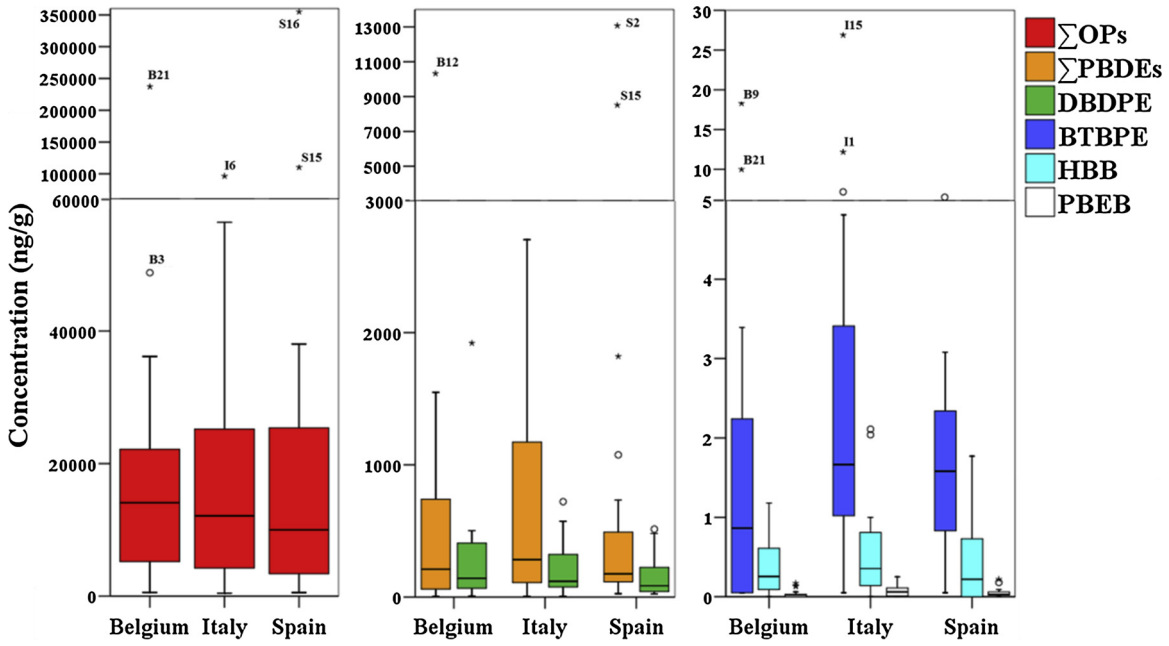

Fig. 2. Box plots of ΣOPs (sum of seven OPs), ΣPBDEs (sum of 20 PBDEs), DBDPE, BTBPE, HBB and PBEB house dust concentrations (ng/g) from Belgium (BE), Italy (IT) and Spain (SP). The boxes represent the inter-quartile range (IQR) and the center line within the box the median. The circles and asterisk represent outliers (data above 75th percentile (P75) + 1.5 × IQR) and extreme (data above P75 + 3 × IQR) values, respectively.

European (The European Commission (EC), 2017) and worldwide (United Nations Environmental Programme (UNEP), 2017) scale, could trigger an increase in OPFR market demands. Data were examined for correlations between house dust concentrations on the premise that significant positive associations are indicative of the existence of a common source. Strong positive correlations found between chloroalkyl (TCEP, TCIPP and TDCIPP) and aryl (TPHP) phosphate esters ($r_s > 0.332$, $p < 0.01$; Table S6) could evidence both plasticizer and

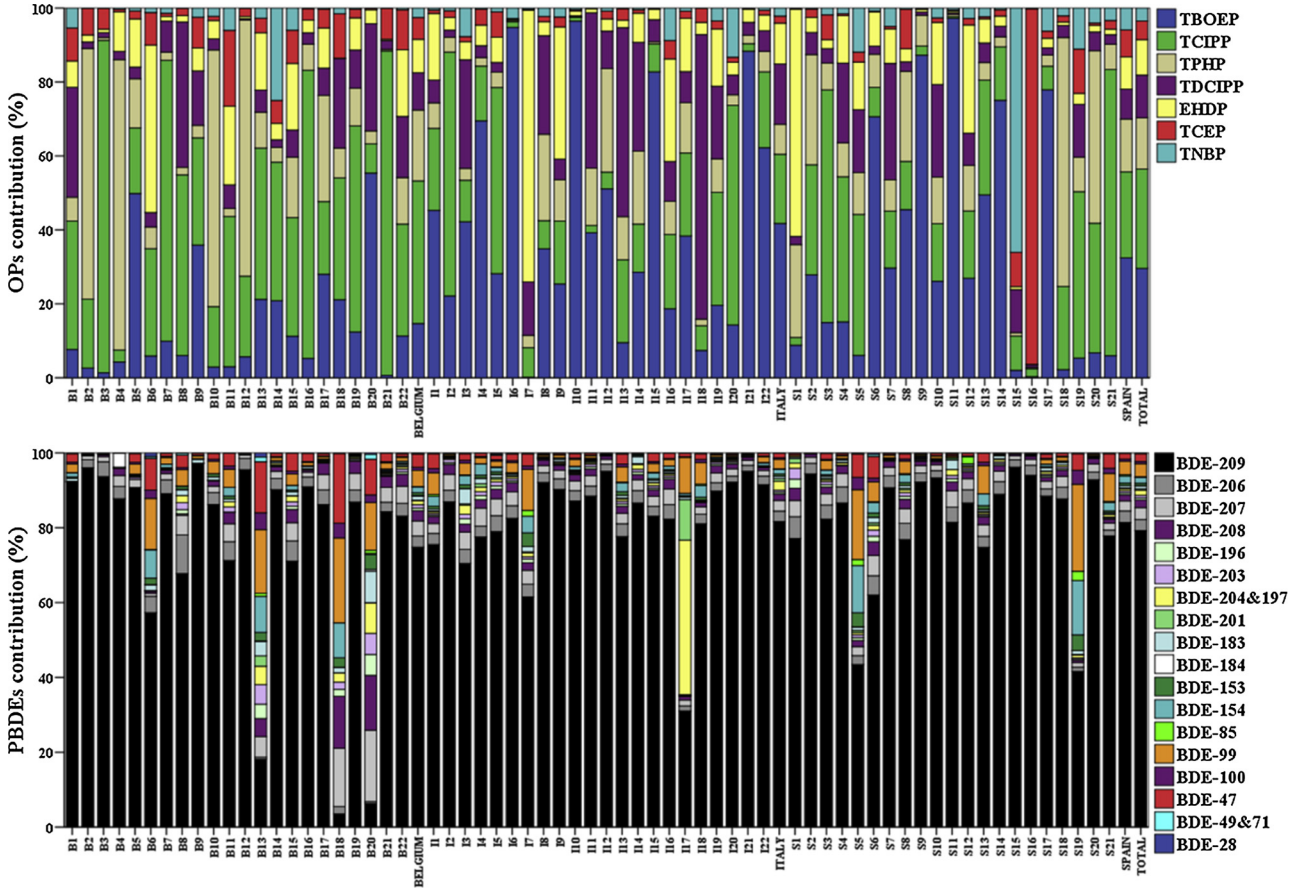

Fig. 3. Profiles of OPs and PBDEs obtained in house dust from Belgium, Italy and Spain.

flame retardant use since these OPs only share this two applications (Table S5). Interestingly, levels of TPHP in the dust were positive correlated with c-decaBDE ($r_s > 0.439$, $p < 0.01$), c-octaBDE ($r_s > 0.267$, $p < 0.05$) or even c-pentaBDE ($r_s = 0.333$, $p < 0.01$) main congeners, but did not with any NBFR evaluated. This result could reflect a historical use for this OPFR. On the other hand, positive associations found between TCIPP and TDCIPP with PBEB ($r_s > 0.309$, $p < 0.05$), and DBDPE with TDCIPP ($r_s = 0.278$, $p < 0.05$) would imply a recent use for these chloroalkyl OPFRs. Information gathered using questionnaires was used to evaluate possible relationships with building characteristics, occupant habits and/or outdoor surroundings of potential emission sources, however only TCEP and TCIPP showed a moderate increase with the percentage of the floor covered by textiles ($r_s > 0.276$, $p < 0.05$).

Regarding alkyl OPs, application areas seem to play a very important role. TBOEP, TNBP and EHDP presented similar ECHA registered volumes (1000–10000 t/y). Nevertheless, flame retardant use has been only recognized for TBOEP (Table S5). This fact could be responsible for the lack of correlations between TNBP levels in the dust and any other OP, PBDE or NBFR evaluated in the present study ($p > 0.05$). However, on contrary to what at first could be expected EHDP house dust concentrations shown positive association with c-pentaBDE ($r_s > 0.368$, $p < 0.01$) and c-octaBDE ($r_s > 0.311$, $p < 0.05$) major PBDE congeners but also with NBFR (PBEB and BTBPE; $r_s > 0.440$, $p < 0.01$) suggesting: i) EHDP flame retardant use, ii) their presence in the same consumer products and/or iii) similar migration rates and behavior once leaving consumer products. It is also noteworthy that among OPs evaluated only EHDP presented higher levels in homes located in industrial neighborhoods. According to ECHA records, EHDP is commercialized under Disflamoll DPO® and Santicizer 141® trade names and used at industrial sites in coating products, adhesives, sealants and polymers (European Chemicals Agency (ECHA), 2019a). Nevertheless, no public registered data on the types of manufacture using this substance are available. According to last update (25-Feb-2019) of ECHA EHDP information, only three EHDP suppliers operate in Europe: ICL-IP Bitterfeld GmbH (Germany), Lanxess Deutschland GmbH (Germany) and Polyadd Limited (UK). Interestingly, ECHA received the registrant dossiers in 2018 and 2019, which emphasizes the future projection of this chemical on the European market.

In general, levels of OPs in house dust collected worldwide are in the range of ng/g to μg/g (Chen et al., 2019; Cao et al., 2019; Rantakokko et al., 2019; Brommer et al., 2012; Stapleton et al., 2009; Cequier et al., 2014; Kademoglou et al., 2017; Coelho et al., 2016; Yadav et al., 2019). However, pollutant contents can vary widely from country to country which may be attributed to diversified lifestyles in different cultures, building and decorating characteristics, residents' habits or consumer products, but also to the economic status of a region. Therefore, temporal tendencies and pollutant substitution degree were evaluated considering all previously published studies reporting data from Belgium, Italy and Spain (Table S7). This approach has considered the type of dust (collected from the floor or elevated surfaces) and the sampling method (using commercial vacuum cleaners or the following standardized protocols that specify the areas of the house and the equipment used to vacuum), as well as, the year in which samples were obtained. Concentrations of OPs obtained in the present study for Belgium samples were comparable with those reported in floor dust collected following a standardized protocol in 2006 (n = 2), 2008 (n = 33) and 2010 (n = 6) in the same country (Van den Eede et al., 2011; Van Den Eede et al., 2012). Likewise, OP levels quantified in Spanish samples fell within the range previously reported for floor dust collected from conventional vacuum cleaner bags (Van Den Eede et al., 2012; García et al., 2007a, b; Cristale et al., 2016; Quintana et al., 2017) or filters mounted in a nozzle adapted to a vacuum cleaner (Björnsdotter et al., 2018). As far as the authors know, the presence of OPs in Italian house dust has not been evaluated so far being concentrations presented here the first data available.

3.2. Legacy and novel brominated flame retardants

As happened for OPs, PBDEs were quantified above LOQ in all samples with data ranging from 4.32 to 13,073 ng/g (min-max for ΣPBDEs; Table S4). A characteristic PBDE congener pattern was obtained in the three countries, with BDE-209 as the predominant congener, comprising 75, 82, 81% (median for Belgium, Italy and Spain) followed by BDE-99 (4, 3, 4%), BDE-207 (4, 3, 3%), BDE-206 (3, 3, 3%), and BDE-47 (4, 1, 2%). Strong positive correlation ($r_s > 0.924$, $p < 0.01$; Table S6) was found between BDE-209, -206, -207 and -208 evidencing a c-decaBDE origin (La Guardia et al., 2006). Similarly, positive relationships were found between c-pentaBDE ($r_s > 0.679$, $p < 0.01$) and c-octaBDE ($r_s > 0.653$, $p < 0.01$) congeners, reflecting the presence of materials that still contain these banned formulations in European home indoor environment. Positive relationships between BDE-209 and other PBDE, including main c-penta and c-octaPBDE congeners, were also found but interestingly correlation decreased with congener bromination degree octa- ($r_s > 0.644$), hepta- ($r_s > 0.396$), hexa- ($r_s > 0.344$), penta- ($r_s > 0.321$) and tetraPBDE ($r_s > 0.406$). This result could reflect the photodegradation of c-decaBDE (Stapleton and Dodder, 2008) but also the presence of tri- to heptaBDEs in decabrominated formulations (Wang et al., 2018). Among all data, ΣPBDE values in two houses from Spain (8.5 and 13.1 μg/g; S15 and S2) and one from Belgium (10.3 μg/g; B12) stand out. As shown in Fig. 2, these values were mainly due to extreme decaBDE concentrations, where BDE-209 congener contribution (96, 94 and 95% for S15, S2 and B12; Fig. 3) closely resembles the one described for two (94% of BDE-209 in Saytex102E and Bromkal 82-0DE) (La Guardia et al., 2006) of the four (FR-1210 and Great Lakes DE-83R) c-decaBDE commercial mixtures that were marketed in Europe (European Chemicals Agency (ECHA), 2019b). Therefore maximum ΣPBDE concentrations could be attributable to a fresh c-decaBDE input. Nonetheless, information from questionnaires did not reveal an unequivocal source for these values, being only the high percentage of the floor covered by textiles in these houses (20, 25 and 50%) compared to median value (5%), something that can be stated as a possible hypothesis. Considering data from the three countries, only concentrations for some PBDEs (BDE-204&197, -203, -196, -207 and -206) showed moderate correlations with the number of children living in the home (Table S6). Interestingly, flats presented higher ΣPBDEs levels compared to detached houses. At first, this result seems to be related to house size (m^2), however no correlation was found between pollutant content and this variable. Generally, detached houses occupy more volume (m^3) than flats, and also their greater access to natural ventilation could favor the renewal of air and dust.

In 2004 we conducted a previous study with house dust samples collected from Belgium, Italy and Spain with the same sampling approach (Fabrellas et al., 2005). Data obtained is included in Table S7. Homes evaluated unfortunately were not the same. However similar sample size (n = 78 in 2004 and n = 65 in 2017) and targeted PBDEs (21 and 33 PBDE congeners evaluated in 2004 and 2017, respectively) allow the establishment of temporal trends. Considering data obtained from the three countries, concentrations of BDE−28, −47, −100, −99, −154, −153 and −183 clearly decreased ($p < 0.01$) from 2004 to 2017. At the opposite end, levels of BDE-209 have increased in the last 13 years. Interesting differences were obtained when data from each country were evaluated separately. House dust samples collected in Belgium and Spain reflected significant decrease for c-pentaBDE (BDE−28, −47, −100, −99, −154, −153) and c-octaBDE (BDE-183) main congeners, which could be easily associated to the European ban of these mixtures since 2004, but this was only observed for BDE−28 and −47 in Italian case. On the other hand, samples from Spain revealed a clear increase of BDE-209 concentrations while no statistical differences were found in dust collected from Belgium and Italy. In 2017 c-decaBDE was included in Annex XVII of European Union

Regulation (EC) No 1907/2006 (entry 67; Reg EU 2017/227) (The European Commission (EC), 2017) by virtue of which shall not be manufactured or placed on the market after 2 March 2019. Therefore the market is expected to move now to alternative flame retardants, which are doomed to substitute decabrominated formulations. As happened for c-penta and c-octaBDE, the recent inclusion of c-decaBDE in Annex A of Stockholm Convention (United Nations Environmental Programme (UNEP), 2017) allows predicting a similar trend on a global scale.

DBDPE is an additive flame retardant available on the market since the mid-1980s for the same applications or product as c-decaBDE (washing, cleaning, polishing, lubrication, greasing and/or waxing products, toners and inks, fillers, sealants and adhesives, putties or even modeling clay, cosmetic and personal care products) (European Chemicals Agency (ECHA), 2019c). DBDPE was proposed in 2007 as a substitute for c-decaBDE mixtures in Europe (European Chemicals Agency (ECHA), 2019c). Therefore, concentrations quantified in household dust samples, ranging from 7.67 to 1921 ng/g, which are positively correlated to BDE-209 ($r_s = 0.341$, $p < 0.01$), not only evidenced that BDE-209 substitution is taken place, but also may reflect similar application areas, and/or behavior once sloughed off from consumer products. The ratio of BDE-209 to DBDPE might give an indication of the level of replacement of c-decaBDE by DBDPE (Cequier et al., 2014). Ali et al (Ali et al., 2011) and Van Den Eede et al (Van Den Eede et al., 2012) reported 2.1 and 2.5 ratios for Belgian house dust samples collected in 2008 and 2006–2010, respectively. Interestingly, these values were higher compared to the median ratio obtained in the present study for samples collected a decade later (1.05) in the same country. This result could reflect a decrease in the use of c-decaBDE in favor of DBDPE and resembles values obtained by Kademoglou et al (< 1 for samples collected in 2013–2018) (Kademoglou et al., 2017) in Norway where c-decaBDE use was banned in 2008. Samples from Italy and Spain presented higher BDE-209/DBDPE values (2.0 and 2.5, respectively) compared to Belgium ones. Unfortunately, lack of data regarding DBDPE levels in dust from Italy and the large dispersion of BDE-209/DBDPE ratios previously reported in Spain by Van Den Eede et al (0.02; n = 1) (Van Den Eede et al., 2012) and Cristale et al (11.5; n = 5) (Cristale et al., 2016) prevent temporary evaluation. Nevertheless, these values are in the range of those described in other European countries like Sweden (1.7 and 2.1) (Sahlström et al., 2015; Norrgran Engdahl et al., 2017), Germany (1.3 and 6.5) (Brommer et al., 2012; Fromme et al., 2014) or Portugal (5) (Coelho et al., 2016). Both DBDPE and c-decaBDE are currently High Production Volume (HPV) chemicals in Europe. Nonetheless, currently manufacture and/or imports in the European Economic Area for the former (10 000–100 000 t/y for DBDPE) (European Chemicals Agency (ECHA), 2019c) are higher compared to the latter (1 000–10 000 in case of c-decaBDE) (European Chemicals Agency (ECHA), 2019b) so that it could be expected BDE-209/DBDPE ratios below 1 in the future. In this sense, the recent inclusion of c-decaBDE mixture in the Stockholm Convention will surely increase the worldwide use of the proposed substitute.

High quantification frequencies ($Q_f > 75\%$) were also obtained for BTBPE, HBB and PBEB. No differences between countries were found (Fig. 2), with levels ranging from < 0.07 to 26.9, < 0.003 - 2.11 and < 0.003 – 0.25 ng/g, for BTBPE, HBB and PBEB, respectively (Table S4). Novel BFRs evaluated in the present study are at pre-registered ECHA registration status and therefore no reliable information regarding production volume or uses at present is available. BTBPE is an additive flame retardant marketed since the mid-1970s, with an estimated worldwide production of 16 710 t in 2001 (Ren et al., 2017). Since 2004, BTBPE was used as a replacement of c-octaBDE in polystyrene, thermoplastics and resins (Directive 2003/11/EC) (The European Parliament and the Council of the European Union (EU), 2003) but on contrary to what could be expected it was classified as a low production volume (LPV) chemical in 2012, which implies that the import or production volume was more than 10 t but less than 1000 t/y (International Council for the Exploration of the Sea (ICES), 2017). BTBPE concentrations quantified in the dust for the three countries showed a positive correlation with major octaBDE congeners (BDE-183; $r_s = 0.750$, $p < 0.01$; Table S6). However, considering that BDE-183 and BTBPE concentrations in the dust did not reflect statistically significant differences, and c-octaBDE congeners also correlated with some OPs (TPHP, TCEP, TCIPP, TDCIPP or EHDP) or even DBDPE ($r_s > 0.347$, $p < 0.01$), utilization of these chemicals as c-octaBDE replacement cannot be ruled out.

As shown in Fig. 1, bromobenzenes (HBB and PBEB) offered the lowest concentrations among all NBFRs, indicating a low current usage in Europe. Nevertheless, median HBB dust concentrations (0.28 ng/g) were one order of magnitude higher than PBEB (0.028). To the best of the author's knowledge, HBB is not currently produced in the EU, but it is included in the list of substances of possible concern –section A- of the Convention for the Protection of the Marine Environment of the North-East Atlantic (OSPAR Convention). According to OSPAR, PBEB was classified as a low production volume (LPV) chemical in 2002 but is not currently produced or used by any OSPAR signatory states (International Council for the Exploration of the Sea (ICES), 2017). PBEB is an additive flame retardant used in polyurethane foam, textiles, adhesives, circuit boards and cable coatings (Haglund et al., 2016). While there is only evidence of HBB use as an additive to paper, plastic and electronic devices in Japan (International Council for the Exploration of the Sea (ICES), 2017; Covaci et al., 2011). Therefore, a positive correlation found between levels of both bromobenzenes ($r_s = 0.502$, $p < 0.01$) in the dust evidenced similar application areas in Europe. Nonetheless, it was noteworthy that while HBB levels were not associated to c-penta, c-octa, nor c-decaBDE congeners, PBEB concentrations in the dust did for the first one ($r_s > 0.415$, $p < 0.01$). This result could suggest that in the same way that BTBPE substituted c-octaBDE and DBDPE did for c-decaBDE, PBEB has been used as a penta-BDE replacement. Curiously, while neither of two bromobenzenes was associated with BDE-209, they did moderately with DBDPE ($r_s = 0.309$ and 312, $p < 0.05$). Again, positive associations between substitutes of different banned mixtures highlight the joint use of several chemicals in a wide variety of applications.

3.3. Human exposure assessment

As mentioned before, exposure from indoor dust can occur through several pathways: inhalation, ingestion, and dermal absorption. Nevertheless, calculation of estimated daily intake (EDI) via inhalation was discarded since the present study reported levels of OPs and BFRs in settle dust (exposure via ingestion) that differs from suspended dust (exposure via inhalation). Therefore, measured concentrations in the house dust were used to estimate exposure for dust intake only via oral ingestion and dermal absorption. Two scenarios were considered, a central scenario (combining median concentrations (50th percentile; P50) in house dust and central tendencies of dust ingested) and a worst case scenario (95th percentile concentrations (P95) and upper percentiles for intake rates). As mentioned before, ΣOPs and ΣBFRs concentrations not differed between countries, therefore P50 and P95 values were calculated with total samples. Calculations were conducted for two different age classes, toddlers (from 12 to ≤ 35 months of age) and adults (18 ≤ 64 years of age) based on definitions by the European Food Safety Authority (European Food Safety Authority (EFSA), 2011). Estimated daily intakes via house dust ingestion ($EDI_{ingestion}$; ng/kg bw /day) and dermal absorption (EDI_{dermal}; ng/kg bw /day) were calculated as shown in Eqs. (1) and (2), and described elsewhere (Chen et al., 2019; Cao et al., 2019; Rantakokko et al., 2019; Cequier et al., 2014).

$$EDI_{ingestion} = (C_{dust} \times IR_{dust} \times AF_{gastro} \times HEF)/BW \quad (1)$$

$$EDI_{dermal} = (C_{dust} \times DAS \times ESA \times AF_{dermal} \times HEF)/BW \quad (2)$$

Where C_{dust} is the pollutant concentration (P50 and P95 concentrations;

ng/g). IR_{dust} are recently updated dust ingestion rates of indoor settle dust (50 and 20 mg/day for the central tendency and 100-60 mg/day for the upper percentile for toddlers and adults) (United States Environmental Protection Agency (U.S. EPA), 2017). AF_{gastro} is the gastrointestinal absorption fractions (100% for both OPs and BFRs) (Van den Eede et al., 2011; Jones-Otazo et al., 2005; Roosens et al., 2009). *HEF* is the indoor home exposure fraction (86% for toddlers and 64% for adults) (Pawar et al., 2017). *BW* is the body weight (13.8 kg for toddlers and 80 kg for adults) (U.S. Environmental Protection Agency (U.S. EPA), 2011). DAS is the dust adhered to skin rate (0.04 mg/cm^2 for toddlers and 0.01 mg/cm^2 for adults) (Pawar et al., 2017). ESA is the exposed skin area (2564 cm^2 for toddlers and 4615 cm^2 for adults) (Chen et al., 2019;). AF_{dermal} is the dermal absorption fraction (17% for TPHP, EHDP, TNBP and TBOEP, 28% for TCEP, 25% for TCIPP, 13% for TDCIPP; 4.23% for BDE-28, 2.85% for tetraBDEs, PBEB and HBB, 1.96% for pentaBDEs, 0.89% for hexaBDE, heptaBDEs and BTBPE, 0.05% for octaBDEs, nonaBDEs, BDE-209 and DBDPE) (Rantakokko et al., 2019; Cequier et al., 2014; Abdallah et al., 2015; Abdallah et al., 2016). Complete results together with reference dose (RfD) values, tolerable daily intakes (TDI) and minimal risk levels (MRLs), if available, are included in Table S8. In all cases dust ingestion was the main exposure way. However, relative contribution of exposure pathways differed between pollutants. For ΣOPs dermal absorption exposure route, contributed 29% (central scenario) and 31% for toddlers and adults, respectively. Nevertheless, in ΣBFRs case (sum PBDE and NBFRs) it was almost negligible (< 1%). These results are due to the higher dermal bioaccessibility of OPs compared to BFRs (Pawar et al., 2017; Abdallah et al., 2015, 2016) and are in agreement with previous studies both for OPs and BFRs (Chen et al., 2019; Rantakokko et al., 2019). Total EDI values for the sum of OPs ranged from 1.23 to 23.1 ng/kg bw/d (adults - toddlers) at the median, and from 43.7 to 593 ng/kg bw/d (adults - toddlers) at worst case scenarios. OP estimated body burdens at worst case scenario were more than 1000 times below most protective threshold (RfD) (Van den Eede et al., 2011) values in adult cases, but intakes for toddlers were only 70 times below most protective RfD, merely a factor of 9 in TBOEP case. Total daily intakes for ΣPBDEs ranged from 0.04 to 1.30 ng/kg bw/day (median and worst case scenarios) for adults, and from 0.66 to 16.9 ng/kg bw/day for toddlers. These values, even at worst case scenarios were well below RfDs for all PBDEs. Therefore, OPs and BFRs uptake via ingestion and dermal absorption of household dust pose a low risk for the general population.

4. Conclusions

House dust samples from three European countries (Belgium, Italy and Spain) were analyzed for PBDEs and NBFRs together with OPs. Pollutant pattern was dominated by ΣOPs (12.8 μg/g median; TCIPP and TBOEP > TDCIPP, TPHP, EHDP > TCEP > TNBP) followed in decreasing order by ΣPBDEs (229 ng/g; BDE − 209 > > BDE − 206, − 207, − 99 and − 47), DBDPE (130 ng/g), BTBPE (1.35 ng/g), HBB (0.28 ng/g) and finally PBEB (0.03 ng/g). ΣOPs and ΣBFRs concentrations not differed between countries. OP level reported in the present study for Belgium and Spain fell within the range of house dust collected since 2006 in these countries. On the other hand, results clearly reflected a significant decrease for c-pentaBDE (BDE − 28, − 47, − 100, − 99, − 154, − 153) and c-octaBDE (BDE-183) main congeners, which are mainly substituted by OPs, BTBPE and PBEB in Belgian and Spanish samples, but this was only observed for BDE-28 and -47 in Italian case. On the other hand, c-decaBDE concentrations not only did not decrease but even increased in Spanish dust.

Influence of building characteristics and/or occupant habits in household dust pollutants content were evaluated. EHDP presented higher concentrations in homes located in industrial neighborhoods. Flats aroused higher ΣPBDEs levels compared to detached houses. TCEP and TCIPP showed a moderate increase with the percentage of the floor covered by textiles Finally, OP, PBDE and BFR measured concentrations in the house dust were used to estimate human exposure for dust intake via oral ingestion and dermal absorption. In all cases, dust ingestion was the main exposure route, and total EDI levels even at the worst case scenario were below available RfD values indicating a low health risk for toddlers and adults.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jhazmat.2019.121009.

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